011142

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Memorandum

Subject: The HED Chapter of the Reregistration Eligibility Decision Document (RED) for Metalaxyl, Case# 0081

From: Flora Chow, Section Head Flora Chow
Reregistration Section 12 July 94
Chemical Coordination Branch
Health Effects Division (7509C)

To: Esther Saito, Acting Chief
Reregistration Branch
Special Review and Reregistration Division (7508W)

Through: Debra Edwards, Chief Debra Edwards
Chemical Coordination Branch 7/18/94
Health Effects Division (7509C)

Richard Schmitt, Acting Director Richard Schmitt
Health Effects Division (7509C)

Attached to this memo are the Product Chemistry Assessment and the Human Health Assessment for the Metalaxyl Reregistration Eligibility Decision Document (RED). The science chapters that formed the bases for the HED assessments also are provided. References for the MRIDs cited in the assessments may be found at the end of the appropriate science chapters.

Metalaxyl is a systemic fungicide used on a variety of agricultural commodities (food and feed crops) as well as on ornamentals and turf plants and trees. Other allowable use sites are commercial/industrial lawns and household domestic outdoor uses. There appears to be no indoor residential uses for metalaxyl.

A tolerance reassessment was performed by CBRS, the details of which may be found in pp 63-72 of the CBRS science chapter. Maximum residue limits (MRLs) for metalaxyl residues in plant commodities have been established by Codex. The Codex MRLs and the applicable U.S. tolerances may be found in pp 73-74 of the CBRS science chapter.

1 of 41

011142

HED does not have any health concern for acute dietary exposure. For chronic dietary exposure, the HED Reference Dose Committee established a Reference Dose (RfD) of 0.08 mg/kg/day, based on an increased alkaline phosphatase activity and an increase in relative liver weights found in a 6-month dog feeding study.

The DRES analysis indicates a dietary burden of 16% of the RfD for the general population based on TMRC exposures. Based on ARC exposures, the dietary burden is estimated at 8% of the RfD. All other population subgroups also are at exposures below the RfD. Although the ARC estimate is a more accurate estimate of dietary risk, it itself is likely to be an overestimate because tolerance level residues or high end residues for meat, milk and eggs were assumed on all commodities.

There is a potential for eye effects from acute exposure to metalaxyl; the acute Toxicity Category for eye irritation is II. Testing of end-use products and appropriate labeling will address acute toxicity concerns. Beyond the acute effect, HED does not have any other health concerns for workers or homeowners exposed to metalaxyl, primarily because of an animal study indicating a lack of toxicity at dermal doses of up to 1000 mg/kg/day (dermal exposure is the expected route of human exposure).

The following product chemistry and residue chemistry data are required to support the reregistration eligibility of all current uses of metalaxyl. They may be considered confirmatory because health risk from dietary exposure to metalaxyl appears minimal.

- Product chemistry -- Some physical/chemical characteristics of the MP remain outstanding. Additionally, a certification by the registrant that the suppliers of starting materials and the manufacturing process for the metalaxyl technical product have not changed since the last comprehensive product chemistry review is required (alternatively, a complete updated product chemistry data package may be submitted instead).

- GLN 171-4 (b): Animal Metabolism -- Data showing percent conversion of HMMA metabolites to DMA are outstanding (enforcement method recovery data for HMMA metabolites).

- GLN 171-4 (e): Storage Stability -- Storage stability data are outstanding for a representative oilseed and a grain crop, and for all processed plant commodities from an oilseed, a grain, and a fruit or fruiting vegetable. In addition, storage stability data are outstanding for livestock commodities. Storage stability data are needed for metalaxyl and representative metabolites, including CGA-94689.

- GLN 171-4 (k): Magnitude of the Residue in Plants -- To support multiple foliar applications of the 50% WP formulation (EPA Reg. No. 100-735) to strawberries, fruiting vegetables, and asparagus, the registrant must either (1) submit available

2

011142

bridging data for representative commodities which show that residues are similar for late season, foliar applications of WP and EC formulations of metalaxyl at rates similar to those registered for these crops, or (2) perform 3 side by side field trials each for asparagus, strawberries, and tomatoes (9 total trials) in geographically representative growing areas using the 50% WP formulation and a representative EC formulation.

- GLN 171-4 (l): Magnitude of the Residue in Processed Food/Feed -- Because cotton gin byproducts and tomato paste are considered processed food/feed commodities, residue data on these matrices are required.

Recommendations:

1. The correct chemical nomenclature for the metalaxyl metabolite included in the tolerance expression is N-(2-hydroxymethyl-6-methyl*phenyl*)-N-(methoxyacetyl) alanine methyl ester. The metalaxyl tolerance expressions in 40 CFR 180.408 (a) and (c), 105.4000 (a), 186.4000 (a) should be corrected by deleting "N-(2-hydroxymethyl-6-methyl)-N-(methoxyacetyl) alanine methyl ester" and inserting the correct chemical name.

2. Specific recommendations on tolerances are discussed in the CBRS science chapter.

3. Specific personal protective equipment and restricted entry interval recommendations are discussed in the Human Health Assessment.

Attachments

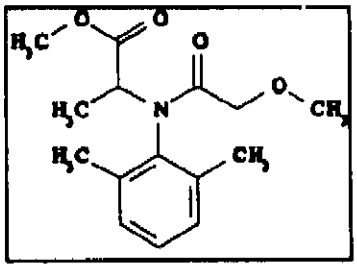
cc: S. Hummel
R. Gardner
L. Morris
J. Wintersteen

01142

PRODUCT CHEMISTRY ASSESSMENT

Description of Chemical

Metalaxyl [N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-alanine methyl ester] is a systemic fungicide registered for use on a variety of crops/sites (primarily citrus, cotton, cucurbits, onions, ornamentals, potatoes, soybeans (seed treatment), tobacco, tomatoes, and turf).



Empirical Formula:	$C_{15}H_{21}NO_4$
Molecular Weight:	279.3
CAS Registry No.:	57837-19-1
Shaughnessy No.:	113501

Identification of Active Ingredient

Technical metalaxyl is a white to beige crystalline solid with a melting point of 71-72 °C and a vapor pressure of 2.2×10^{-6} mmHg at 20 °C. The solubility of metalaxyl in water at 20 °C is 7.1 g/L. Metalaxyl is also readily soluble in most organic solvents (e.g., 65% soluble in methanol and 55% soluble in benzene).

Manufacturing-use Products

There is one metalaxyl manufacturing-use product (MP), the 90% technical (T; EPA Reg. No. 100-601), which is registered to Ciba-Geigy Chemical Company (REFS, 03/22/94).

Data Requirements

The current status of the product chemistry data requirements for the Ciba-Geigy metalaxyl technical is presented in the "Product Chemistry Data Summary" (see Appendix). Technical

011142

metalaxyl contains low levels of nitrosamines; the amount is not expected to be of dietary concern because nitrosamines were detected at less than 1 ppm.

All of the product chemistry data requirements pertaining to the TGAI are satisfied for the Ciba-Geigy 90% T (EPA Reg. No. 100-601); however, some physical/chemical characteristics of the MP remain outstanding. Additionally, a certification by the registrant that the suppliers of starting materials and the manufacturing process for the metalaxyl technical product have not changed since the last comprehensive product chemistry review is required (alternatively, a complete updated product chemistry data package may be submitted instead).

011142

HUMAN HEALTH ASSESSMENT

1. TOXICOLOGY ASSESSMENT

The metalaxyl toxicology database is adequate and will support reregistration eligibility for food and non-food uses.

a. Acute Toxicity

Acute Toxicity

Test	Result	Category
Acute Oral LD_{50} (rat)[1]	669 mg/kg	III
Acute Oral LD_{50} (mouse)[2]	788 mg/kg	III
Acute Oral LD_{50} (hamster)[3]	7120 mg/kg	IV
Acute Dermal LD_{50} (rabbit)[4]	>6000 mg/kg	III
Acute Inhalation LC_{50}	Requirement waived[5]	N/A
Eye Irritation (rabbit)[6]	Moderate Irritant	II
Dermal Irritation (rabbit)[7]	Mild Irritant	IV
Skin Sensitization (guinea pig)[8]	Negative	N/A

[1] MRID 00063990
[2] MRID 00063991
[3] MRID 00154308
[4] MRID 00063993
[5] Because metalaxyl cannot be prepared and tested in a respirable form, the requirement for an acute inhalation study was waived by HED on May 10, 1991.
[6] MRID 00084108
[7] MRID 00084107
[8] MRID 00084109
N/A = not applicable

011142

b. Subchronic Toxicity

A 90-day study was conducted with male and female Sprague-Dawley rats fed diets containing 0, 50, 250, or 1250 ppm of metalaxyl. The diet concentrations were equivalent to chemical intakes of 3.4, 17, and 83 mg/kg/day, respectively. At the high dose, food consumption by males was slightly reduced and minimal liver cell hypertrophy was increased in females. Based on these findings, the LOEL was 83 mg/kg/day and the NOEL was 17 mg/kg/day. (MRID 00084110)

A 21-day dermal study was conducted with male and female New Zealand white rabbits. Metalaxyl was applied to intact or abraded skin at dose levels of 10, 100, or 1000 mg/kg/day for 6 hours/day, 5 days/week. Endpoints evaluated included body weight, food consumption, hematology, clinical chemistry, organ weights, and histopathology. No treatment-related dermal or systemic effects were observed at any dose level. Therefore, the NOEL for dermal and systemic toxicity was the highest dose tested, 1000 mg/kg/day. (MRID 00072394)

c. Chronic Toxicity

A 6-month study was conducted with beagle dogs fed diets containing 0, 50, 250, or 1000 ppm of metalaxyl. The diet concentrations were equivalent to chemical intakes of 0, 1.6, 7.8, and 30.6 mg/kg/day for males, and 0, 1.7, 7.4 and 32.4 mg/kg/day for females, respectively. Exposure to the high dose was associated with an elevation in serum alkaline phosphatase and an increase in liver weight (absolute and relative to brain weight). No clinical signs or findings in hematology, urinalysis, or histopathology were related to treatment. The LOEL was 25 mg/kg/day and the NOEL was 6.3 mg/kg/day. (MRID 00071598)

In a chronic toxicity/carcinogenicity study, male and female Sprague-Dawley rats were fed diets containing 0, 50, 250, or 1250 ppm of metalaxyl for 2 years. These levels were equivalent to 2.5, 13, and 63 mg/kg/day, respectively. The high dose produced an increase in liver weight (relative to body weight) and an increased incidence of periacinar vacuolation of hepatocytes. Based on the liver changes, the systemic LOEL was 63 mg/kg/day and the NOEL was 13 mg/kg/day. (MRID 00098481, 00132009, 00150185)

d. Carcinogenicity

A 2-year chronic toxicity/carcinogenicity study was conducted with male and female Sprague-Dawley rats. Metalaxyl was administered in the diet at concentrations of 0, 50, 250, or 1250 ppm, which were equivalent to intakes of 2.5, 13, and 63 mg/kg/day, respectively. (MRID 00098481, 00132009, 00150185)

A 2-year carcinogenicity study was conducted with male and female Swiss mice. Metalaxyl was administered in the diet at concentrations of 0, 50, 250, or 1250 ppm, which were

011142

equivalent to intakes of 7.5, 38, and 190 mg/kg/day, respectively. (MRID 00103354, 00150094)

In 1985 the EPA reviewed four major issues concerning the rat and mouse carcinogenicity studies: (1) parafollicular cell adenomas in the thyroid of female rats, (2) adrenal medullary tumors (pheochromocytomas) in male rats, (3) liver tumors in male mice, and (4) use of a maximum tolerated dose. (50 FR 49690)

Concerns about the incidence of thyroid tumors in female rats was mitigated by the following evidence: (1) no progression of adenomas (benign) to carcinomas (malignant), (2) no increase in hyperplastic changes, (3) no dose-response relationship, and (4) two re-evaluations of microscopic slides showing no treatment-related effect. Similar microscopic reassessments of the adrenal gland of male rats and the liver of male mice indicated no compound-related effect on tumor incidence in these organs.

Although the highest dose tested (1250 ppm) was not a maximum tolerated dose (MTD) in either study, the EPA concluded that the rat and mouse studies were sufficient to demonstrate that metalaxyl did not have carcinogenic potential in laboratory animals and further testing was unwarranted. The conclusion was supported by the following evidence: (1) the doses in both studies were high enough to produce treatment-related changes in liver weight and/or histology (i.e., increased liver weight and hepatocellular vacuolation in rats; fatty infiltration in the liver of mice), (2) no structural relationship to known carcinogens, (3) no genotoxic activity, and (4) no effect on neoplasm incidence in mice or rats of either sex at any dose level tested.

In December 31, 1985, the Health Effects Division Carcinogenicity Peer Review Committee classified metalaxyl as a Group E carcinogen (evidence of non-carcinogenicity for humans) based on the available data.

e. Developmental Toxicity

A developmental toxicity study was conducted with pregnant Charles River COBS CD rats administered doses of 0, 50, 250, or 400 mg/kg/day by gavage on days 6 through 15 of gestation. Dams were sacrificed on day 20 of gestation. Doses of 250 mg/kg/day and higher were maternally toxic producing ataxia and convulsions. The 400 mg/kg/day dosage resulted in mortality of one-third of the dams. Doses of 250 mg/kg/day and higher produced fetotoxicity manifest as an increased incidence of unossified sternebrae. The LOEL was 250 mg/kg/day and the NOEL was 50 mg/kg/day for both maternal and developmental toxicity. (MRID 00144423, 00148867)

A developmental toxicity study was conducted with Dutch belted rabbits given doses of 0, 30, 150, or 300 mg/kg/day of metalaxyl on days 7 through 19 of gestation. Does were sacrificed on day 28 of gestation. The high dose does showed a slight loss in body weight. In a range-finding study, 500 mg/kg/day decreased maternal body weight and 1000

011142

mg/kg/day produced mortality. No treatment-related developmental toxicity was observed at any dose level. The LOEL for maternal toxicity was 300 mg/kg/day and the NOEL was 150 mg/kg/day. The highest dose tested, 300 mg/kg/day, was the NOEL for developmental toxicity. (MRID 00144371, 00144372, 00148866, 00154938)

f. Reproduction

A 3-generation reproduction study was conducted with SPF Crl:COBS CD (SD) rats. Metalaxyl was administered in the diet at concentrations of 0, 50, 250, or 1250 ppm. These levels were equivalent to 2.5, 13, and 63 mg/kg/day, respectively. There were no treatment-related effects on parental body weight, food consumption, mating, fertility, gestation length, or macroscopic observations. Pre- and post-implantation loss, litter size and weight, and incidence of fetal malformations/variations were also unaffected by treatment. The NOEL for reproductive toxicity was the highest dose tested, 63 mg/kg/day (1250 ppm). (MRID 00071600)

g. Mutagenicity

Metalaxyl was negative in bacterial and mammalian gene mutation, in vivo cytogenetics, and several other genotoxicity assays.

Three studies evaluated metalaxyl in the Salmonella typhimurium reverse mutation assay (Ames assay) using tester strains TA 98, TA 100, TA 1535, and TA 1537. Metalaxyl did not increase the frequency of reverse mutations with or without metabolic activation (S9) at concentrations ranging from 25-2025 μg/plate, 20-5000 μg/plate, and 10-5000 μg/plate in the three experiments. (MRID 00084113, 00154301, 00154302)

A gene mutation assay in mammalian cells was conducted using the L5178Y (TK +/-) mouse lymphoma cell line. Concentrations of metalaxyl ranged from 0.125 to 1 mg/ml without S9 and 0.0625 to 0.5 mg/ml with S9. Metalaxyl did not increase forward mutations at the thymidine kinase (TK) locus. (MRID 00103362, 00154309)

Metalaxyl did not increase the frequency of reverse mutations in yeast cells (Saccharomyces cereviseae) at concentrations of 400 to 10,000 μg/ml with or without metabolic activation. Concentrations of 8000 μg/ml and greater were cytotoxic. Assays for recombination and gene conversion were unreliable. (MRID 00103359)

In an in vivo cytogenetics study, male and female Chinese hamsters were administered two consecutive daily oral doses of 0, 595, 1190, or 2380 mg/kg of metalaxyl. The highest dose was one-third the oral LD_{50} in hamsters (7120 mg/kg). Bone marrow cells were scored 24 hours later for nuclear changes which included single Jolly bodies, fragments of nuclei in erythrocytes, micronuclei in erythroblasts, micronuclei in leukopoietic cells, and polyploid cells. Metalaxyl had no effect on the incidence of nuclear anomalies. (MRID 00103361, 00154307)

011142

A dominant lethal test was conducted with male NMRI mice given a single oral dose of 0, 65, or 195 mg/kg of metalaxyl. The highest dose was one-fourth the reported LD_{50} in mice (788 mg/kg). Each male was cohabited with two untreated females each week for 8 consecutive weeks. Metalaxyl had no effect on mating, pregnancy, number of implants, or embryo viability. A positive control was not used in the study. (MRID 00084114, 00154310)

Metalaxyl was tested twice in the unscheduled DNA synthesis (UDS) assay using primary cultured rat hepatocytes. Concentrations tested ranged from 16-2000 μg/ml in both experiments. Another UDS assay was conducted using human fibroblasts. Metalaxyl concentrations ranged from 4 to 500 μg/ml. Concentrations up to cytotoxic levels were tested in each assay. Metalaxyl did not increase unscheduled DNA synthesis above control levels in any of the three assays. (MRID 00103363, 00154306, 00160037, 00154663)

h. Metabolism

Four studies with rats evaluated the absorption, distribution, excretion, and/or metabolism of orally administered metalaxyl. A dermal absorption study with rats was also conducted.

In a single dose study, male and female rats were administered 0.5 or 25 mg/kg of metalaxyl by gavage. Over 60% of the low or high dose was excreted within 24 hours in urine or feces. Negligible amounts were eliminated in expired air. Low tissue residues six days after treatment indicated no appreciable bioaccumulation. Female rats eliminated the majority of the dose (55-65%) in urine, and males eliminated most (60-70%) in feces. Although metabolites were not identified, the chromatographic pattern was similar for both sexes and doses. (MRID 00071613)

A metabolism study was conducted with female rats administered a single oral dose of 28 mg/kg. Within 48 hours 96% of the dose had been excreted in urine or feces. Consistent with the previous study, females excreted over 60% of the dose in urine and about 30% in feces. Approximately 20% of the metabolites in urine were identified. Hydrolysis of the ether and ester bonds was shown to be a significant metabolic pathway. Glucuronidase treatment of urine fractions indicated metabolites were either unconjugated or glucuronide conjugates. Fecal metabolites were not identified. (MRID 000716614)

A similar study (females rats given 28 mg/kg as single oral dose) corroborated that ester and ether bond hydrolysis is a primary metabolic pathway. Secondary pathways included oxidation of methyl groups of the phenyl moiety and oxidation of the phenyl moiety itself. Some metabolites in urine were present as glucuronic acid conjugates. A large portion of the metabolites were unidentified. (MRID 00099084)

A recent comprehensive study evaluated metalaxyl pharmacokinetics with male and female Sprague-Dawley rats following a single intravenous dose (1 mg/kg), single oral low dose (1 mg/kg), single oral high dose (200 mg/kg), or repeated oral low doses (1 mg/kg/day for 14

10

011142

days). The absorption, distribution, and elimination patterns were consistent with previous findings. No major dose or sex differences were observed except that urine was the predominant elimination route for females whereas feces was the major route for males. Metalaxyl was readily absorbed (similar i.v. and oral elimination profiles), extensively metabolized (< 1% parent compound in excreta), and rapidly eliminated (70-80% in 24 hours). Ten metabolites were identified. The majority of urinary metabolites were conjugated (glucuronide or sulfate) whereas fecal metabolites were mostly unconjugated. The major metabolite in urine and feces was N-(2,6-dimethylphenyl)-N-(hydroxyacetyl) alanine. Three major and one minor metabolic pathways were proposed. One pathway involved hydrolysis of the ether, followed by oxidation of the resulting alcohol, ester hydrolysis, or N-dealkylation of the ester chain. A second pathway involved oxidation of an aromatic methyl to the benzylic acid or ester hydrolysis. The third major pathway was ester hydrolysis, sometimes followed by benzylic acid formation. The minor pathway involved hydroxylation at the meta position of the phenyl ring. Two major metabolites in urine were not identified. Additional data on major unidentified metabolites must be provided to upgrade this study to acceptable. (MRID 41664501)

A dermal absorption study was conducted with male and female rats treated with 1 or 10 mg/kg. Thirty percent of the dose was absorbed from the skin within 8 hours. The absorption half-times were 12 and 20 hours for males at the low dose and high dose, respectively, and 13 hours for females at both dose levels. Within 72 hours 70-80% of the applied dose had been excreted. The elimination half-times were 36 and 49 hours for males and 42 and 44 hours for females at the low and high doses, respectively. Females eliminated the majority of the dose in urine whereas males eliminated most in feces. (MRID 00161402)

i. Neurotoxicity

Neurotoxicity studies are not required.

j. Other Toxicological Considerations

Smoke Inhalation Study. Because metalaxyl is used on tobacco, a 90-day smoke inhalation study was conducted. Male and female Fischer 344 rats were exposed to smoke from cigarettes containing 0, 130, 3900, or 13,000 ppm of metalaxyl for 4 hours/day, 5 days/week. The maximum air concentration of metalaxyl was 5 μg/l. The concentrations in test cigarettes were 100 to 10,000 times average residue levels and 30 to 100 times greater than the expected maximum residue levels. Although the study was limited in its ability to simulate human exposure, the results were adequate to demonstrate toxicological effects from exposures are unlikely beyond that from exposures associated with heavy smoking. The profile of residues in inhalable smoke indicated 30% was metalaxyl, 4% was 2,6-dimethylaniline, and 65% was unidentified material. (MRID 00103364, 00109471)

011142

k. Reference Dose (RfD)

The RfD was established as 0.08 mg/kg/day based on a NOEL of 7.8 mg/kg/day and an uncertainty factor of 100. The NOEL was obtained from a 6-month dog study. The RfD was first approved by the HED (5/23/86) and Agency (7/8/86) Reference Dose Committees and has been updated without change (4/3/94).

In 1982 the FAO/WHO Joint Meeting on Pesticide Residues allocated an Acceptable Daily Intake (ADI) of 0.03 mg/kg/day for metalaxyl.

011142

2. EXPOSURE ASSESSMENT

a. Dietary Exposure

Metalaxyl [N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester] is a fungicide registered for use as a seed treatment, soil application, and/or foliar application on a variety of food and feed crops, including: alfalfa, almonds, apples, artichokes (Jerusalem), asparagus, avocados, beets (table/garden), blueberries, broccoli, cabbage, carrots, cassava, cauliflower, cereal grains, chicory, Chinese broccoli (gai lon), Chinese cabbage (tight heading varieties), citrus fruits, corn, cotton, cranberries, cucurbit vegetables, dill, eggplants, forage grasses, forage legumes, ginger, ginseng, grapes, hops, horseradish, legume vegetables, lettuce, okra, onions (bulb and green), papaya, parsnips, peanuts, peppers, pineapples, potatoes, radishes, raspberries, rice, rutabaga, salify, soybeans, spinach, stone fruits, strawberries, sugar beets, sweet potato, tomato, turnips, walnuts, and yams.

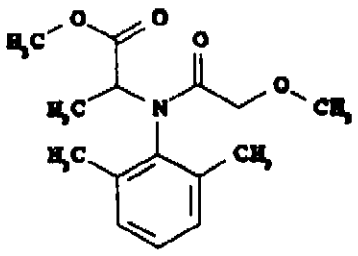
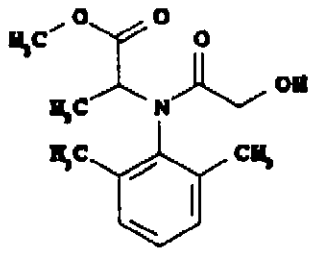
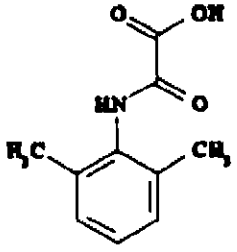
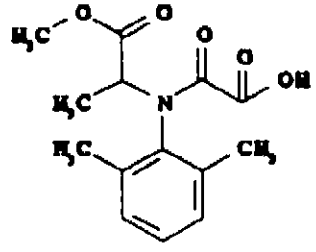
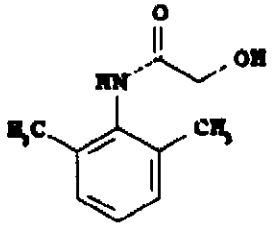
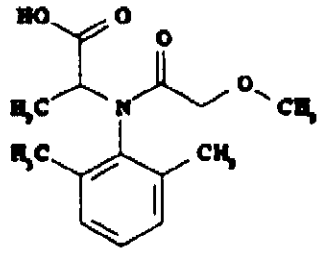
Tolerances for residues of metalaxyl in/on raw and processed plant commodities and animal commodities are currently expressed in terms of the combined residues of metalaxyl [N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester] and its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-methyl)-N-(methoxyacetyl) alanine methyl ester or N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl) alanine methyl ester [*Source: 40 CFR 180.408(a), (b), and (c), 40 CFR 185.4000, and 40 CFR 186.4000*]. The correct chemical nomenclature for the metalaxyl metabolite included in the tolerance expression is N-(2-hydroxymethyl-6-methyl*phenyl*)-N-(methoxyacetyl) alanine methyl ester. The metalaxyl tolerance expressions in 40 CFR 180.408 (a) and (c), 105.4000 (a), 186.4000 (a) should be corrected by deleting "N-(2-hydroxymethyl-6-methyl)-N-(methoxyacetyl) alanine methyl ester" and inserting the correct chemical name.

Metabolites which may not be covered by the current tolerance expression have been identified in livestock metabolism studies. Up to 34% of the residue in ruminants and poultry are compounds containing the 2-hydroxymethyl-6-methyl aniline moiety other than N-(2-hydroxymethyl-6-methylphenyl)-N-methoxyacetyl alanine methyl ester, which is currently regulated. 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. However, additional data are required to demonstrate the recovery of HMMA-containing metabolites as 2,6-dimethylaniline 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. These data are outstanding, but considered confirmatory, since sufficient information is available to do a reasonable upper bound dietary exposure assessment. Residues of concern not recovered by enforcement methodology, and therefore not included in the tolerance expression, are nevertheless included in the anticipated residues for risk assessment purposes. The chemical structures of the metabolites of concern are presented in Figure A.

011142

Figure A *(continued)*.

Figure A. The chemical structure of metalaxyl and its metabolites of concern.

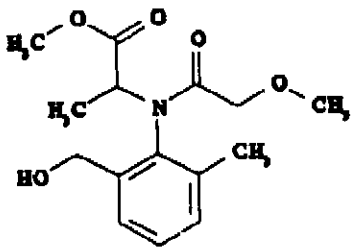
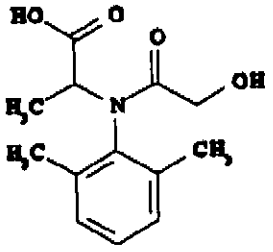
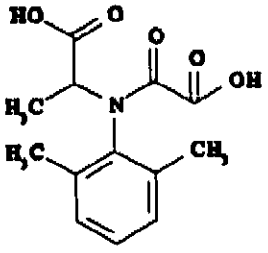
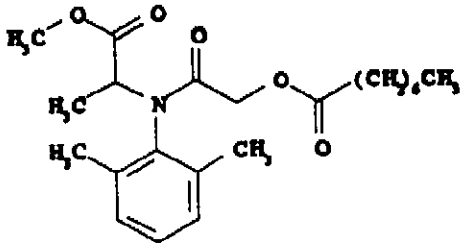
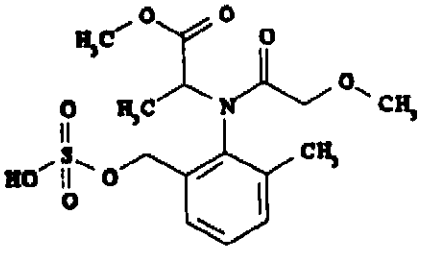
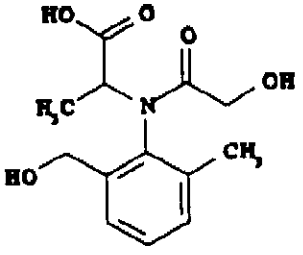
Structure Metabolite: Chemical name	Structure Metabolite: Chemical name
 **metalaxyl**: N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester	 N-(2,6-dimethylphenyl)-N-(hydroxyacetyl)alanine methyl ester
 N-(oxalyl)-2,6-dimethylaniline	 N-(oxalyl)-N-(2,6-dimethylphenyl)alanine methyl ester
 N-(2,6-dimethylphenyl)-2-hydroxyacetamide	 N-(2,6-dimethylphenyl)-N-(methyloxyacetyl)alanine

(continued)

14

011142

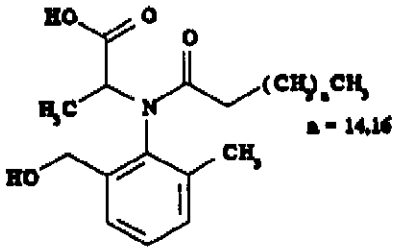
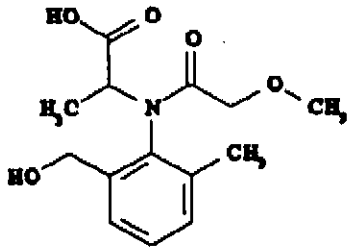
Figure A *(continued)*.

Structure Metabolite: Chemical name	Structure Metabolite: Chemical name
 N-[2-hydroxymethyl)-6-methylphenyl]-N-(methoxy acetyl)alanine methyl ester	 N-(2,6-dimethylphenyl)-N-(hydroxyacetyl)alanine
 N-(oxalyl)-N-(2,6-dimethylphenyl)alanine	 N-decanoic acid ester of N-(2,6-dimethylphenyl)-N-(hydroxyacetyl)alanine methyl ester
 Sulfuric acid ester of N-[2-hydroxymethyl)-6-methyl-phenyl]-N-(methoxyacetyl)alanine methyl ester	 N-[2-(hydroxymethyl)-6-methylphenyl]-N-(hydroxyacetyl)alanine

15

011142

Figure A *(continued)*.

Structure **Metabolite:** Chemical name	Structure **Metabolite:** Chemical name
 N-Fatty acid amide conjugates of N-[2-hydroxymethyl)-6-methylphenyl]alanine	 N-[2-(hydroxymethyl)-6-methylphenyl-N-(methoxyacetyl)alanine

16

011142

GLN 171-3: Directions for Use. There are 18 end-use products (Eps) of metalaxyl, presently registered to Ciba-Geigy Corporation, that may be used on food/feed crops (REFS 03/22/94). These Eps are presented below.

Registrant EPA Reg. No.	Acceptance Date	Formulation Class	Product Name
Ciba-Geigy Corporation			
100-664	1/25/94	1% G	Ridomil PC® 11G Granular Fungicide
100-713	1/25/94	1% G	Ridomil PC® Granular Fungicide
100-676	1/15/90 [a]	2% G	Subdue® Granular Fungicide
100-628 [b]	12/2/93	5% G	Ridomil® 5G Fungicide
100-646	1/15/90 [a]	5% G	Subdue® 5G Fungicide
100-749	3/4/94	7% WP	Ridomil® MZ Fungicide
100-658	1/31/94	9% WP	Ridomil®/Bravo® 81W Fungicide
100-629 [c]	11/19/92	10% WP	Ridomil® MZ58 Fungicide
100-720	1/31/94	10% WP	Ridomil®/Copper 70W Fungicide
100-639	10/19/92	25% WP	Apron® 25W Fungicide
100-717	1/14/94	25% WP	Subdue® II Fungicide
Not available [d]	--	35% WP	Apron® 70 SD Fungicide
Not available [e]	--	35% WP	Apron® 35 SD Fungicide
100-672	1/15/90 [a]	45% WP	Apron® T69 Fungicide
Not available [f]	--	45% WP	Apron® T69 SD Fungicide
100-735	5/3/94	50% WP	Ridomil® 50W Fungicide
100-738	2/26/93	50% WP	Apron® 50W Fungicide
100-607 [g]	12/7/93	2 lb/gal EC	Ridomil® 2E Fungicide
100-619	12/7/93	2 lb/gal EC	Subdue® 2E Fungicide
100-626	9/18/89	2 lb/gal EC	Apron® 2E Fungicide
100-684	6/8/89	3 lb/gal FlC	Apron® Flowable Fungicide

[a] Copy of label was obtained from a Product Label DCI dated 1/15/90.
[b] Includes SLN Nos. AR90000502 and OK90000500.
[c] Includes SLN Nos. ME92000200, ND92000200, and WA92004200.
[d] Includes SLN Nos. CA85007300, ID83003300, and WA83003500.
[e] Includes SLN No. WA90003300.
[f] Includes SLN Nos. CA87000700, ID86001900, and WA86002800.
[g] Includes SLN Nos. AR90000501, AZ85000800, AZ86001500, CA82002400, CA85006800, CA86001800, CA90004700, CO88000100, FL86000200, FL89002300, ID89000500, LA92000400, OK90000500, OR89000800, TX91001100, WA87000200, and WA89001500.

011142

The 50% wettable powder (WP) formulation (EPA Reg. No. 100-735) was registered recently. The label permits the first post emergence use of a EP formulation on a number of crops. Multiple foliar and other post-emergence applications are permitted throughout the growing season. These uses are not supported by residue data. A tabular summary of the residue chemistry science assessments for reregistration of metalaxyl is presented in Table B (see Appendix). The conclusions listed in Table B regarding the reregistration eligibility of metalaxyl food/feed uses are based on the use patterns registered by the basic producer, Ciba-Geigy Corporation.

GLN 171-4 (a): Plant Metabolism. The qualitative nature of the residue in plants is adequately understood. Studies with potatoes, lettuce, grapes, and tobacco indicate that metalaxyl is taken up, translocated, and extensively metabolized by plants. Metabolism involves oxidation of a 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. The residues to be regulated in plant commodities are those in the current tolerance expression, which include 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.

GLN 171-4 (b): Animal Metabolism. The qualitative nature of the residue in animals is adequately understood. Metabolism in ruminants is via hydrolysis to the ester alcohol and acid alcohol, which may then be de-alkylated. In ruminants, metalaxyl may also be oxidized to benzylic alcohol or phenolic compounds. Some breakdown products may be conjugated with glucuronic acid. A major residue in milk is a mixture of the N-octanoic- and N-decanoic acid ester of metabolite CGA-67869 [(N-(2,6-dimethylphenyl)-N-(hydroxyacetyl)-aniline methyl ester]. 2,6-DMA-based residues accounted for up to ~50% of the residues in ruminant tissues. HMMA containing compounds comprised 34% of the residue in kidney and 12-14% in muscle and fat. The parent compound is rapidly excreted.

In poultry, metalaxyl is hydrolyzed to either the benzyl alcohol or the ester alcohol. The benzylic alcohol is converted to a sulfate and the ester alcohol is conjugated with fatty acid or converted to the acid alcohol, which is subsequently hydrolyzed to the benzylic alcohol. The predominant residues in poultry are the disubstituted free acid forms of the hydroxy metabolite CGA-94689 isomers (~47% in thigh muscle and 24% in egg), the sulfuric acid conjugate of the hydroxy metabolite (30% in thigh muscle), fatty acid conjugates of the disubstituted free acids of CGA-94689 (27% in fat), and CGA-107955, N-(2,6-dimethylphenyl)-N-hydroxyacetyl)alanine (40% in fat).

The HED Metabolism Committee (9/10/93) has determined that the residues to be regulated are metalaxyl, metabolites that can be converted to 2,6-dimethylaniline (2,6-DMA), and those containing the 2-hydroxymethyl-6-methylaniline (HMMA) moiety. Some metabolites containing the HMMA moiety may be convertible to 2,6-DMA and thus measured by the

011142

current enforcement methodology. Data showing percent conversion of HMMA metabolites to DMA are outstanding (enforcement method recovery data for HMMA metabolites). The wording of the tolerance expression for livestock commodities will be determined after these data are submitted. Current residue levels estimated for livestock commodities represent an upper bound for HMMA containing metabolites.

GLN 171-4 (c) and (d): Residue Analytical Methods - Plants and Animals. Adequate enforcement methods are available for the determination of residues of metalaxyl and regulated metabolites in plants. Methods I and II in PAM, Vol. II, correspond to Methods AG-348 and AG-349. Method AG-395, an improved modification of AG-348, has undergone successful Agency validation with plant matrices.

Metabolites which may not be covered by the current tolerance expression have been identified in livestock commodities. Additional validation data are needed to demonstrate that 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 Method II in PAM, Vol. II, and AG-395, both of which have undergone successful Agency validation, and adequately recovers metalaxyl, per se. Method AG-576 may be adequate for enforcement of tolerances in animal commodities, if it is proven to adequately recover all residues of concern. If significantly less than 100% of the total toxic residue is recovered using Method AG-572, then residue levels used in future risk assessments may need to be adjusted to account for this.

Metalaxyl, per se, is completely recovered (>80%) using FDA Multiresidue Protocol D (PAM, Vol. I, Section 232.4), and is not recovered by Protocol E (PAM, Vol. I, Sections 211.1/231.1 and 212.1/232.1) [*Source: PESTDATA, PAM, Vol. I, Appendix, 8/93*]. Multiresidue data for representative metalaxyl metabolites have been forwarded to FDA.

GLN 171-4 (e): Storage Stability. Adequate storage stability data are available to support residue studies on raw agricultural commodities stored less than 24 months at temperatures of -20 °C or less, with the exception of oilseed and grain crops. An interim storage stability study on cranberries, potatoes, peppers, and spinach indicates that weathered residues determined as 2,6-DMA are stable in samples stored at -20 °C for 18 to 24 months. A final report reflecting 38 months storage of these matrices is expected to be confirmatory. Storage stability data for metalaxyl and representative metabolites in a representative oilseed (e.g., soybean or nut) and grain (e.g., wheat) are required.

No storage stability data are available to support processing studies. Storage stability data for metalaxyl and representative metabolites are required from all processed commodities of an oilseed, a grain, and a fruit or fruiting vegetable.

Storage stability data for metalaxyl and representative metabolites in livestock commodities representing one year of frozen storage are required. Considering the demonstrated storage stability on several crops, the outstanding storage stability data are considered confirmatory.

011142

GLN 171-4 (k): Magnitude of the Residue in Plants. All data requirements for magnitude of the residue in plants have been evaluated and deemed adequate, except for the 50% WP formulation. For other formulations, field trials were performed representing the various conditions under which the pesticide can be applied. Geographical representation is adequate and a sufficient number of trials reflecting representative formulation classes were conducted.

To support multiple foliar applications of the 50% WP formulation (EPA Reg. No. 100-735) to strawberries, fruiting vegetables, and asparagus, the registrant must either (1) submit available bridging data for representative commodities which show that residues are similar for late season, foliar applications of WP and EC formulations of metalaxyl at rates similar to those registered for these crops, or (2) perform 3 side by side field trials each for asparagus, strawberries, and tomatoes (9 total trials) in geographically representative growing areas using the 50% WP formulation and a representative EC formulation. If residues resulting from application of the 50% WP are substantially higher than those using the EC formulation, then additional field trial data may be required. These data are considered confirmatory.

Tolerances have not been established for forage, fodder, and straw for the cereal grains group (excluding wheat, barley, and oats).

GLN 171-4 (l): Magnitude of the Residue in Processed Food/Feed. Processing studies have been conducted on the following RACs: apples, citrus, cereal grains, cottonseeds, grapes, hops, legume vegetables, peanuts, pineapples, potatoes, prunes, sunflowers, soybeans, sugar beets, and tomatoes. All data requirements for magnitude of the residue data in processed food/feed commodities have been deemed adequate to determine the extent to which residues of metalaxyl concentrate upon processing of the raw agricultural commodity.

Residues concentrate in the following food commodities: citrus oil; potato granules/flakes, and chips; prunes; raisins; sugar beet molasses, and tomato puree.

Residues concentrate in the following processed feed items: apple pomace (wet); citrus, molasses and pulp; grape pomace (wet and dried), grape raisin waste; legume vegetable cannery waste; peanut meal; pineapple, process residue, potato peels (dried); soybean hulls and meal; sugar beet molasses, sunflower meal; and tomato pomace (dried).

Food/feed additive tolerances for potato granule/flakes, potato chips, and tomato pomace must be proposed.

Because cotton gin byproducts and tomato paste are considered processed food/feed commodities, residue data on these matrices are required. The data are considered confirmatory.

GLN 171-4 (j): Magnitude of the Residue in Meat, Milk, Poultry, and Eggs. Tolerances for the combined residues of metalaxyl and its metabolites convertible to 2,6-dimethyl aniline

011142

and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl) alanine methyl ester have been established for meat, fat, kidney, liver, and meat byproducts of cattle, goats, horses, sheep and poultry and for milk and eggs. The evaluation of the submitted ruminant feeding studies is deferred until the adequacy of the analytical method used is determined.

The results from the submitted poultry feeding study indicate that residues of metalaxyl will not exceed the established tolerances in poultry tissues and eggs. However, judgement of the adequacy of the available data is reserved until the analytical method used is determined to be adequate and adequate storage stability data are provided.

There are no established or proposed direct animal uses for metalaxyl. The existing ruminant and poultry feeding studies are adequate for risk assessment.

GLN 165-1: Confined Rotational Crops. The registrant has submitted three confined rotational crop studies (MRID Nos. 42196501 through 42196503), which are under review.

GLN 165-2: Field Rotational Crops. Tolerances have been established for the indirect or inadvertent residues of metalaxyl in rotational crops resulting from the application of metalaxyl to the primary crops. A field rotational crop study (MRID No. 41870308) has been submitted and is under review.

b. Occupational and Residential Exposure

Metalaxyl [N-(2,6-Dimethylphenyl)-N-(methoxyacetyl)alanine, methyl ester] is a systemic fungicide used to control certain diseases, in over one hundred sites. End-use product formulations include granulars (containing 1% to 5% a.i.), wettable powders (containing 7% to 50% a.i.), dusts (containing 6.25% to 12.5% a.i.), pelleted/tableted (0.3% a.i.), emulsifiable concentrates (containing 11.5% to 25.1% a.i.), flowable concentrates (containing 28.35% to 33.3% a.i.), and liquid-ready to use (containing 2.8% to 3.5% a.i.). The granular, wettable powder and emulsifiable concentrate formulations are also formulated as multiple active ingredients end-use products.

Metalaxyl is used on a variety of agricultural commodities as well as on ornamentals and turf plants and trees. Ornamental uses include: ornamental and/or shade trees, ornamental herbaceous plants, ornamental lawns and turf, and ornamental woody shrubs and vines. Other allowable use sites are commercial/industrial lawns and household domestic outdoor uses. Terrestrial interioscape use includes Disney World Epcot display crops. Metalaxyl is also applied to golf course turf.

Applications can be made using aerial, ground, chemigation, slurry or mist-type seed treaters, or sprayers. Based on the existing use information, there appear to be no indoor residential uses for metalaxyl.

011142

Applications may be foliar or soil incorporated, surface spraying (broadcast or band), drenching, sprinkler or drip irrigation, soil mix or seed treatment. Maximum application rates range from 0.135 to 8.0 lbs a.i./acre for agricultural crops and from 0.25 to 1.12 oz a.i./100 lb seed for agricultural seed treated. For ornamental turf and ornamental trees and plants, application rates range from 0.33 to 1.35 lbs a.i./acre and from 0.90 to 7.20 lbs a.i./acre, respectively. Depending on use, end-use products may be applied in multiple applications. For several crops, pre-harvest intervals have been established which range from 0 (i.e., soybeans) up to 45 days (i.e., raspberries).

Mixer/Loader/Applicator (Handler) Exposure. Mixer/loader/applicator (i.e., handler) exposure study requirements are addressed by Subdivision U of the Pesticide Assessment Guidelines. Mixer/loader/applicator (M/L/A) exposure data (Guideline Series 230) were not required by the *Registration Standard for Products Containing Metalaxyl.*

Based on the use patterns described above, several exposure scenarios are plausible as defined by the types of application equipment and procedures that might be employed by metalaxyl handlers. For examples, open mixing of liquids for foliar application to onions using center pivot irrigation, or loading of granular formulation for soil broadcast treatment to non-bearing nut trees using groundboom equipment.

Exposure data requirements are triggered based on the potential for exposure and the toxicological significance of the active ingredient. Metalaxyl meets the exposure criteria, but not the toxicity criteria. Therefore, exposure data for occupational and residential activity patterns (M/L/A) associated with the use of metalaxyl are not required for reregistration eligibility. Similarly, an exposure assessment is not required.

Post-Application Exposure. Post-application exposure study requirements (i.e., reentry) are addressed by Subdivision K of the Pesticide Assessment Guidelines. Post-application dermal and inhalation exposure monitoring along with concurrent soil and foliar residue dissipation data (Guideline Series 130) were not required in the *Registration Standard for Products Containing Metalaxyl.* The registrant was given the option to provide human exposure (dermal and inhalation) monitoring data .

The potential for post-application exposure to workers entering treated sites exists and may be significant (e.g., human exposure to ornamental lawns or turf after pesticide treatment). However, metalaxyl does not meet the toxicity criteria for requiring post-application exposure data. Therefore, neither exposure data nor an exposure analysis are required for reregistration eligibility.

011142

3. RISK CHARACTERIZATION

a. Dietary Risk

Toxicological Endpoint. Based on a review of the toxicology database, the Toxicology Endpoint Selection Committee concluded that there are no endpoints of concern for acute dietary exposure. For chronic dietary exposure, the HED Reference Dose Committee established a Reference Dose (RfD) of 0.08 mg/kg/day, based on a No Observed Effect Level (NOEL) of 7.8 mg/kg/day and an uncertainty factor of 100. The NOEL was derived from a 6-month dog feeding study which demonstrated increased alkaline phosphatase activity and an increase in relative liver weights at 31 mg/kg/day.

Residue Information. Food uses evaluated in the DRES chronic exposure analysis were the published uses of metalaxyl listed in 40 CFR §180.408 and 185.4000. Residues that are regulated include metalaxyl, and metabolites that can be converted to 2,6-DMA and those containing the HMMA moiety. Residue levels estimated for livestock commodities represent upper bound estimates including the HMMA containing metabolites. Anticipated residue data were not available for any of the commodities. A summary of the residue information used in this analysis is attached as Table 1 of the DRES memo.

Results from the tolerance reassessment indicate that some of the tolerance levels should be changed. Specifically, a tolerance of 1 ppm is recommended for cabbage and cauliflower, which currently have tolerances of 2 ppm. In the DRES analysis the higher value was used for these commodities. For leafy vegetables (excluding *Brassica* and spinach), an increase in the tolerance from 0.1 ppm to 5 ppm is recommended. The tolerance increase has not been published in the Federal Register yet, but has been included here as a pending tolerance of 4.9 ppm; the published tolerance of 0.1 ppm added to this pending tolerance results in the 5 ppm tolerance recommended for reregistration.

Percent of crop treated information was available; the information "Percent of Various U.S. Crops Treated Annually with Metalaxyl 1989-1992" was provided by the Biological and Economic Analysis Division (E. Maurer memo, 2/7/94).

Chronic Exposure Analysis and Dietary Risk. The DRES chronic analysis used tolerance level residues to calculate the Theoretical Maximum Residue Contribution (TMRC) for the overall U.S. population and 22 population subgroups. These exposure estimates were then compared to the RfD to arrive at the potential chronic dietary risk. The TMRC from published and proposed uses recommended through reregistration are listed below.

Subgroup	Exposure (mg/kg/day)	%Reference Dose
U.S. population	0.012493	16%
Children (ages 1-6)	0.024593	31%

011142

The percent of crop treated information were used to calculate the Anticipated Residue Contribution (ARC) for those same population groups. The ARC is considered the more accurate estimate of dietary exposure. The ARC for the overall U.S. population from published *and* proposed uses recommended through reregistration are listed below.

Subgroup	Exposure(mg/kg/day)	%Reference Dose
U.S. population	0.006588	8%
Children (ages 1-6)	0.012275	15%

The ARC for the U.S. population from the published uses of metalaxyl being recommended through reregistration is 6.1×10^{-3} mg/kg/day, which represents 8% of the RfD. The proposed tolerances on leafy vegetables (excluding *Brassica* and spinach) result in an ARC of 4.7×10^{-4} mg/kg/day, representing 0.6% of the RfD for metalaxyl.

The ARC from published uses for the most highly exposed DRES subgroup, children (ages 1 through 6), is 1.2×10^{-2} mg/kg/day, which represents 15% of the RfD. The ARC from the proposed uses contributes 6.1×10^{-4} mg/kg/day, or 0.8% of the RfD. Added together, the resultant ARC is 1.2×10^{-2} mg/kg/day, representing 15% of the RfD for metalaxyl (some rounding errors may occur during summations by the DRES analysis system).

Summaries of the TMRCs, ARCs, and their representations as percentages of the RfD are provided in Tables 2 and 3 of the DRES memo. The U.S. population and all the DRES subgroups have TMRCs and ARCs for chronic dietary risk below the RfD when published and proposed tolerances are considered. It appears that chronic dietary risk is minimal for this chemical for published and proposed tolerances. Although the ARC estimate is a more accurate estimate of dietary risk, it itself is likely to be an overestimate because tolerance level residues or high end residues for meat, milk and eggs were assumed on all commodities.

b. Occupational and Residential Risk

Toxicology Endpoints. There is a potential for eye effects from acute exposure to metalaxyl; the acute Toxicity Category for eye irritation is II. Metalaxyl is in acute Toxicity Category III for oral toxicity and dermal toxicity. It is in Toxicity Category IV for dermal irritation and does not appear to be a skin sensitizer. Based on a review of the toxicology database, the Toxicology Endpoint Selection Committee concluded that there are no endpoints of concern for short term occupational or residential exposure (1 to 7 days). There are also no endpoints of concern for intermediate term occupational or residential exposure (1 week to several months). The bases for the conclusions are as follows: (1) the maternal effects in the rat developmental toxicity study were ataxia and convulsions at 250 mg/kg/day and higher and mortality at 400 mg/kg/day (NOEL = 50 mg/kg/day), (2) the developmental toxicity observed at maternally toxic dose levels in the rat were delays in ossification of

011142

sternebrae, (3) the maternal effects in the rabbit developmental toxicity study were body weight decreases at 300 mg/kg/day and above, as well as mortality at 1000 mg/kg/day (NOEL = 150 mg/kg/day), and (4) the absence of toxicity at dermal doses of up to 1000 mg/kg/day in the 21-day rabbit study.

Occupational and Residential Risk. Significant potential for exposure exists for both handlers of metalaxyl and for those exposed after application of metalaxyl during reentry operations (e.g., at planting treatment of lettuce). Potential post-application exposure concerns relate to workers and to users in residential settings. However, exposure studies (and exposure analysis) are not required to assess the risk to humans exposed to metalaxyl during or after pesticide application because there are no toxicology endpoints of concern, except for potential eye irritation (Toxicity Category II). Potential eye effects are addressed by appropriate labeling and personal protective equipment requirements.

Restricted Entry Interval. HED recommends a 12-hour restricted entry interval (REI) for end-use products containing metalaxyl as an active ingredient. This recommendation is based on the acute dermal toxicity of the active ingredient (Category III) and is established in accordance with in-scope WPS uses. For uses outside the scope of WPS (i.e., residential uses), HED recommends the "sprays have dried" or "dusts have settled" statement. For uses not within the scope of the WPS, additional entry restrictions should not be added; however, any entry restrictions on the current product labeling for those uses must be retained.

Additionally, when metalaxyl is used in conjunction with other active ingredients, the REI should be based on the most toxic active ingredient (i.e., new metalaxyl WPS label for water soluble bag has a 48-hour REI because of another active ingredient).

Personal Protective Equipment (PPE) Requirements. PPE selection for handlers will be based on the end-use product. The following statements to be included on metalaxyl labels are located on the attached Pesticide Worksheets -- Parts One and Two: **Reduced PPE When Engineering Controls Used; User Safety Statements; Application Restrictions; Entry Restrictions; Early-Entry PPE**; and **Notification Statements** (see Appendix).

Except for residential uses, the Agency is requiring PPE for applicators and other handlers as well as early entry workers consistent with the PPE level required for pesticides classified as Toxicity Category III for acute dermal toxicity. Protective eyewear is required for pesticide products classified as Toxicity Category II for ocular irritation. (40 CFR Part 156, the Worker Protection Standard). For further information see PR Notices 93-7 and 93-11.

25

011142

DATA REQUIREMENTS AND RECOMMENDATIONS

The following product chemistry and residue chemistry data are required to support the reregistration eligibility of all current uses of metalaxyl. They may be considered confirmatory because health risk from dietary exposure to metalaxyl appears minimal.

Product chemistry. Some physical/chemical characteristics of the MP remain outstanding (see "Product Chemistry Data Summary," Appendix). Additionally, a certification by the registrant that the suppliers of starting materials and the manufacturing process for the metalaxyl technical product have not changed since the last comprehensive product chemistry review is required (alternatively, a complete updated product chemistry data package may be submitted instead).

GLN 171-4 (b): Animal Metabolism. Data showing percent conversion of HMMA metabolites to DMA are outstanding (enforcement method recovery data for HMMA metabolites).

GLN 171-4 (e): Storage Stability. Storage stability data are outstanding for a representative oilseed and a grain crop, and for all processed plant commodities from an oilseed, a grain, and a fruit or fruiting vegetable. In addition, storage stability data are outstanding for livestock commodities. Storage stability data are needed for metalaxyl and representative metabolites, including CGA-94689.

GLN 171-4 (k): Magnitude of the Residue in Plants. To support multiple foliar applications of the 50% WP formulation (EPA Reg. No. 100-735) to strawberries, fruiting vegetables, and asparagus, the registrant must either (1) submit available bridging data for representative commodities which show that residues are similar for late season, foliar applications of WP and EC formulations of metalaxyl at rates similar to those registered for these crops, or (2) perform 3 side by side field trials each for asparagus, strawberries, and tomatoes (9 total trials) in geographically representative growing areas using the 50% WP formulation and a representative EC formulation.

GLN 171-4 (l): Magnitude of the Residue in Processed Food/Feed. Because cotton gin byproducts and tomato paste are considered processed food/feed commodities, residue data on these matrices are required.

Recommendations:

1. The correct chemical nomenclature for the metalaxyl metabolite included in the tolerance expression is N-(2-hydroxymethyl-6-methyl*phenyl*)-N-(methoxyacetyl) alanine methyl ester. The metalaxyl tolerance expressions in 40 CFR 180.408 (a) and (c), 105.4000 (a), 186.4000 (a) should be corrected by deleting "N-(2-hydroxymethyl-6-

011142

methyl)-N-(methoxyacetyl) alanine methyl ester" and inserting the correct chemical name.

2. Specific recommendations on tolerances are discussed in the CBRS science chapter.

3. Specific personal protective equipment and restricted entry interval recommendations are provided in the "Active Ingredient Worksheets, Parts One and Two."

27

011142

APPENDIX

28

011142

PRODUCT CHEMISTRY DATA SUMMARY
METALAXYL, 90% T (EPA Reg. No. 100-601)

Guideline Number	Requirement	Are Data Requirements Fulfilled? [a]	MRID Number [b]
61-1	Product Identity and Disclosure of Ingredients	Y	**00104498** 41055201 *41912901* 42409201 [c] 42762801 [d] 42762802 [d] CSF dated 5/2/93 [d]
61-2	Starting Materials and Manufacturing Process	Y	41055201 *41912901*
61-3	Discussion of Formation of Impurities	Y	41055201 41055202 *41912901*
62-1	Preliminary Analysis	Y	41055202 42319901 [c] 42762801 [d] 42762802 [d]
62-2	Certification of Ingredient Limits	Y	41055201 41055202 *41912901* 42409202 [c]
62-3	Analytical Methods to Verify the Certified Limits	Y	41055202 *41912901*
63-2	Color	Y	**00104483**
63-3	Physical State	Y	**00104483**
63-4	Odor	Y	**00104483**
63-5	Melting Point	Y	**00104483**
63-6	Boiling Point	N/A [e]	
63-7	Density, Bulk Density or Specific Gravity	Y	**00104483**
63-8	Solubility	Y	**00104483**
63-9	Vapor Pressure	Y	**00104483**
63-10	Dissociation Constant	Y	**00104483**
63-11	Octanol/Water Partition Coefficient	Y	**40435001**
63-12	pH	Y	**40435001**
63-13	Stability	Y	**00104483**
63-14	Oxidizing or Reducing Action	N	
63-15	Flammability	N/A [e]	
63-16	Explodability	N	
63-17	Storage Stability	N	
63-18	Viscosity	N/A [e]	
63-19	Miscibility	N/A [e]	
63-20	Corrosion Characteristics	N	

[a] Y = Yes; N = No; N/A = Not Applicable.

[b] **Bolded** references were reevaluated/reviewed in the Metalaxyl Guidance Document dated 9/88; underlined references were reviewed in the Metalaxyl Reregistration Standard Update dated 3/13/91; *italicized* references were reviewed under CB No. 8166, D165989, dated 4/16/92, by J. Abbotts; remaining references reviewed as noted.

[c] CB Nos. 10303 and 9962, D181027 and D178783, dated 9/29/92, by K. Dockter

[d] CB No. 11937, D191625, dated 6/30/93, by K. Dockter.

[e] Data are not required because the TGAI/MP is a solid at room temperature.

011142

Table B. Residue Chemistry Science Assessments for Reregistration of Metalaxyl.

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
171-3: Directions for Use	N/A	No[2]	
171-4 (a): Plant Metabolism	N/A	No	*00071601 00071602* 00071603 00071604 *00071605* 00071606 00071607 00071608 00071609 00071610 00114379 00128102
171-4 (b): Animal Metabolism	N/A	Yes[3]	*00071611 00071612* **41664503 41664504 41664505 41664506** 42115801[4] 42115802[4] 42115803[4] 42115804[4] 42115805[4] 42115806[4]
171-4 (c/d): Residue Analytical Methods	N/A	No	00071622 00071623 00071676 *00104378* 00104656 00148440 00157480 **40503101 41055203 41689701 41689702** 42115809[4] 42115810[4] 42115807[4] 42115808[4]
171-4 (e): Storage Stability	N/A	Yes[5]	00148440 40106601[6] 41449001[7] 42021101[8] 42115809[4] 42350101[9] 42919401[3] 41912902[10]
171-4 (k): Magnitude of the Residue in Plants			
Root and Tuber Vegetables Group	0.5 [§180.408(a)]	No[11]	40838301[12] 40838302[12] 40838303[12]
- Beets	0.1 [§180.408(a)]	No[13]	00128102
- Ginseng	3.0 [§180.408(a)]	No	41688900[14] 41688901[14]
- Potatoes	0.5 [§180.408(a)]	No[11]	*00104654* 00071616 00098428[15]
- Sugar beets	0.1 [§180.408(a)]	No[13]	00128102
	0.5 (roots) [§180.408(a)][11]	No	40569301[16]
Leaves of Root and Tuber Vegetables Group	15.0 [§180.408(a)]	No	40838301[12] 40838302[12] 40838303[12]
- Beet, tops	0.1 [§180.408(a)]	No[13]	00128102
- Sugar beet, tops	10.0 [§180.408(a)]	No[13]	40569301[16]

(continued)

011142

Table B *(continued).*

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
Bulb Vegetables Group			
- Onions, dry bulb	3.0 [§180.408(a)]	No	00071615 00098428 00130694 00148103
- Onions, green	10.0 [§180.408(a)]	No	00071615 00098428 00130694
Leafy Vegetables (Except Brassica Vegetables) Group	0.1 [§180.408(a)]	No[17]	41587801[18] 42021101[17]
- Lettuce, head	5.0 [§180.408(a)]	No[17]	00071615 00097511 00114377 00103695 40775801[19]
- Spinach	10.0 [§180.408(a)]	No	00071672 00114378 00130695 40790201[20] 41636201[21]
Brassica (Cole) Leafy Vegetables Group			
- Brassica (cole) leafy vegetable group [except broccoli, cabbage, and cauliflower]	0.1 [§180.408(a)]	No[22]	
- Broccoli	2.0 [§180.408(a)]	No	00071615 00130773
- Cabbage	2.0 [§180.408(a)]	No[22]	00071615 00130773
- Cauliflower	2.0 [§180.408(a)]	No[22]	00071615 00130773
Legume Vegetables Group			
- Legume vegetables group	0.2 [§180.408(a)]	No[23]	00129003 **40569303**
- Soybean, grain	1.0 [§180.408(a)]	No	00071672 00104390 00148440
Foliage of Legume Vegetables Group	8.0 [§180.408(a)]	No	00129003 00071672 00104390 00148440 **40569303**
Fruiting Vegetables (Except Cucurbits) Group	1.0 [§180.408(a)]	Yes[24]	00148103 00148440 00157480
Cucurbit Vegetables Group	1.0 [§180.408(a)]	No	00071615 00098428 00130693 00148103
Citrus Fruits Group	1.0 [§180.408(a)]	No	00117969 00133020 00148440
Pome Fruits Group			
- Apples	0.2 [§180.408(a)]	No	00126315 00141519
Stone Fruits Group	1.0 [§180.408(a)]	No	00164650[25]
Small Fruits and Berries Group			
- Blueberries	2.0 [§180.408(a)]	No	00164649[25]

(continued)

011142

Table B *(continued)*.

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
- Cranberries	4.0 [§180.408(a)]	No	41996401[26]
- Grapes	2.0 [§180.408(a)]	No	00138818[27] 00155845[27] 41150101[28]
- Raspberries	0.5 [§180.408(a)]	No	00127769
- Strawberries	10.0 [§180.408(a)]	Yes[29]	00155237[30] 40880401[31]
Tree Nuts Group			
- Almonds	0.5 (nutmeats) 10.0 (hulls) [§180.408(a)]	No	00164651[25]
- Walnuts	0.5 [§180.408(a)]	No	00164651[25]
Cereal Grains Group			
- Grain, crops	0.1 [§180.408(a)]	No[32]	00071672 00104387 00128102 41689701 41689702 41870301[33]
Forage, Fodder and Straw of Cereal Grains Group (except wheat, barley, and oats)	None	No[32]	00128102 41689701 41689702 41870301[33] 41870305[33] 41912903[34]
Grass Forage, Fodder, and Hay Group			
- Grasses, forage	0.1 [§180.408(a)]	No[35]	
Non-grass Animal Feeds Group	none	No[36]	
- Alfalfa	6.0 (forage) 20.0 (hay) [§180.408(a)]	No No	40832901[37]
Miscellaneous Commodities			
- Asparagus	7.0 [§180.408(a)]	Yes[38]	00154446[38]
- Avocados	4.0 [§180.408(a)]	No	00074488
- Cottonseed	0.1 [§180.408(a)]	Yes[39]	00109402 41870305[33]
- Hops, green	2.0 [§180.408(a)]	No[40]	00079433 40746901[41] 40909401[42]
- Papaya	0.1 [§180.408(c)]	No	40490501[43]
- Peanut	0.2 (nutmeats) 20.0 (vines) 20.0 (hay) 2.0 (hulls) [§180.408(a)]	No No[44] No No	00128738 41870306[45] 42498701[46]

(continued)

011142

Table B *(continued).*

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
- Pineapples	0.1 (fruit) 0.1 (fodder) 0.1 (forage) [§180.408(a)]	No No[47] No[47]	00109472
- Sunflowers	0.1 (seeds) 0.1 (forage) [§180.408(a)]	No No	00128102 4191290210
- Tobacco	N/A	No	00100467 00100476 00100477 00100478 00104485 00140371 00148440 42196503
171-4(l): Magnitude of the Residue in Processed Food/Feed			
- Apples	2.0 (pomace, dry) 0.4 (pomace, wet) [§186.4000 (a)]	No[46] No	00126315
- Citrus	7.0 (oil) [§185.4000 (a)] 7.0 (molasses) 7.0 (pulp) [§186.4000 (a)]	No No No	00117969
- Cereal grains group (except wheat, barley, and oats)	None	No	41870301[33] 41870302[33] 41870303[33] 42498701[49] 42259805[50]
- Cottonseed	None (cotton gin bypdts)	Yes[39]	
- Grapes	6.0 (raisins) [§185.4000 (a)] 10.0 (raisin waste) 10.0 (pomace, dry) 10.0 (pomace, wet) [§186.4000 (a)]	No	00138818[27] 00155845[27] 41150101[28]
- Hops	20.0 (dried) [§185.4000 (d)] 2.0 (dry) 20.0 (spent) [§186.4000 (d)]	No[40] No[40] No[40]	00079433 40746901 40909401
- Peanut	1.0 (meal) 2.0 (soapstock) [§186.4000 (a)]	No No[51]	00128738
- Pineapples	None	No[52]	42233501[52]

(continued)

011142

Table B *(continued)*.

GLN: Data Requirements	Current Tolerances, ppm [40 CFR]	Must Additional Data Be Submitted?	References [1]
- Potatoes	4.0 (processed, including potato chips) [§185.4000 (a)] 4.0 (waste, dried, processed) [§186.4000 (a)]	No[53]	41870307[54]
- Prunes (dried)	4.0 [§185.4000 (a)]	No	00164650[25]
- Soybean	2.0 (hulls) 2.0 (meal) 2.0 (soapstock) [§186.4000 (a)]	No No No[55]	00071672
- Sugar beet	1.0 (molasses) [§186.4000 (a)]	No[56]	401066016 40569301[57]
- Sunflower	None	No[58]	41870304[59] 42498701[60]
- Tomatoes	20.0 (pomace, dry and wet) [§186.4000 (a)] 3.0 (processed) [§185.4000 (a)]	Yes[61]	00148440 00157480
171-4 (j): Magnitude of the Residue in Meat, Milk, Poultry, and Eggs			
- Fat, kidney, and liver of cattle, goats, hogs, horses, poultry, and sheep	0.4 [§180.408 (a)]	Reserved	00100753 42115809[4] 00071673 00071674
- Meat and meat byproducts (except kidney and liver) of cattle, goats, hogs, horses, poultry, and sheep	0.05 [§180.408 (a)]	Reserved	00100753 42115809[4] 00071673 00071674
- Eggs	0.05 [§180.408 (a)]	Reserved	00071673 42115809[4]
- Milk	0.02 [§180.408 (a)]	Reserved	00071674
165-1: Rotational Crops (Confined)		Reserved	42196501[62] 42196502[62] 42196503[62]
165-2: Rotational Crops (Field)		Reserved	41870308[63]
- Barley, oat, and wheat	2.0 (forage, fodder, and straw) [§180.408 (b)]		00114376 00071672 00104387
	0.2 (grain) [§180.408 (b)]		00114376 00071672 00104387
	1.0 (milling fractions) [§185.4000 (b) and §186.4000 (b)]		00114376

(continued)

011142

Table B ***(continued)***.

1. **Bolded** references were reviewed in the Update of 3/13/91. Unbolded references were reviewed in the Residue Chemistry Science Chapter (6/22/87) of the Metalaxyl Final Reregistration Standard and Tolerance Reassessment (FRSTR) (Guidance Document date 9/88). *Italicized* references were reviewed in the 12/81 Registration Standard. Otherwise, references were reviewed as noted.

2. A revised label for SLN No. LA920004 must be submitted with the following restriction: When using this product as directed in making a direct soil application at planting to water seeded rice, do not use Apron®-treated rice seed or any other rice seed that has been treated with metalaxyl (CBTS Nos. 11708 and 11709, DP Barcodes D189772 and D189764, 5/5/93, F. Griffith).

   In addition, The registrant must amend the labels for the 1% G formulations (EPA Reg. Nos. 100-664 and 100-713) to impose a 75-day PHI for peanuts and remove the feeding restriction for cotton forage, which CBRS considers to be impractical.

3. CB No. 9102, D172350, S. Hummel, 9/16/93. Additional method validation data are needed, including recoveries of representative metalaxyl metabolites including at least one containing the 2,6-dimethyl aniline moiety, CGA-94689, P1, and P2.

4. CB No. 9102, DP Barcode D172350, 9/15/93, S. Hummel.

5. A storage stability data requirement is outstanding for a representative oilseed (e.g., soybeans or a nut) and a grain crop (e.g., wheat). Storage stability data requirements are also outstanding for all processed plant commodities from an oilseed, a grain, and a fruit or fruiting vegetable. In addition, storage stability data requirements are outstanding for livestock commodities (CBRS No. 12888, DP Barcode D197066, 2/17/94, S. Hummel). Storage stability data are needed for metalaxyl and representative metabolites including CGA-94689.

6. CB No. 1996 and 2013, 3/13/87, F. Griffith.

7. CBRS No. 7193, 1/15/91, R. Perfetti.

8. CBTS No. 8898, DP Barcode D171050, 12/18/91, R. Lascola.

9. CBTS No. 10062, DP Barcode No. D179628, 7/3/92, M. Peters.

10. CBRS No. 8166, DP Barcode D165608, 4/16/92, J. Abbotts.

11. The group tolerance for root and tuber vegetables should be renamed "root and tuber vegetables group (except ginseng)," concomitant with the revocation of the established tolerances for beets, potatoes, and sugar beets.

12. PP#9F3698, CB Nos. 4788 to 4791, 8/3/89, J. Garbus; CB No. 5836, 10/23/89, J. Garbus; CB No. 6176, 2/14/90, J. Garbus; CB No. 8625, 12/12/91, K. Dockter.

13. The 0.1 ppm tolerances on beets, beet tops, and sugar beets are based on residue data generated from field trials on treated seeds. As group tolerances for root and tuber vegetables (except ginseng) and for leaves of root and tuber vegetables will cover these commodities, and as the preplant and foliar uses have superseded the seed treatment uses, these tolerances should be revoked.

(continued)

011142

Table B *(continued)*.

14. PP#1E3926, CB No. 7340, 2/22/91, G. Otakie; CB No. 7787, 4/8/91, G. Otakie; CBTS Nos. 9054 and 9058, 3/6/92, W. Chin.

15. CB No. 60, 2/14/86, W. Anthony.

16. PP#3F3617/FAP#8D5554, CB Nos. 3908 through 3912, 11/28/88, F. Griffith; and CB Nos. 5934, 5935, and 6545, 4/30/90, F. Griffith.

17. CBTS recommends in favor of establishing a crop group tolerance of 5 ppm for leafy vegetables, (except Brassica), excluding spinach. Once the 5 ppm group tolerance has been established, the 5 ppm tolerance for lettuce should be revoked (PP#0F3893; CBTS No. 8898, DP Barcode 171050, 12/18/91, R. Lascola; and CBTS No. 9710, DP Barcode 176810, 5/12/92, R. Lascola).

18. CBTS No. 7171, DP Barcode D156811, 6/21/91, S. Bacchus.

19. CB No. 4808, 2/9/89, L. Propst.

20. CB No. 4809, 2/14/89, L. Propst; and CB No. 7418, 1/24/91, M. Metzger.

21. CBRS No. 7165, DP Barcode D156892, 2/19/91, K. Dockter.

22. The established 0.1 ppm crop group tolerance for Brassica (cole) leafy vegetables group (except broccoli, cabbage, and cauliflower) was established to cover seed treatments. However, as there is no registered seed treatment on any member of this group, this tolerance should be revoked. A petition proposing a crop group tolerance of 5 ppm on brassica leafy vegetables to cover soil and foliar uses is in reject status (PP#2F04072, DP Barcode D174355, 1/15/93, M. Peters). Data submitted with this petition (MRID 42159801) indicate that the established 2 ppm tolerances for cabbage and cauliflower can be reduced to 1 ppm. Data submitted with the petition indicate that a crop group tolerance is inappropriate because residue levels differ by more than a factor of 5.

23. The group tolerance for the legume vegetable group should be changed to "legume vegetables group excluding soybeans."

24. Post emergence use of the 50% WP formulation on fruiting vegetables is not supported. Supporting data must be provided or the use removed from the 50% WP label.

25. PP#7F3470/FAP#7H5520, CB Nos. 1676, 1677, and 1678, 3/6/87, M. Nelson; CB Nos. 2604, 2699, and 2700, 8/26/87, M. Nelson; and CB Nos. 3788 and 3789, 5/13/88, M. Nelson.

26. PP#1E4024, CB No. 8582, DP Barcode D168812, 10/31/91, J. Morales; and CBTS No. 9537, DP Barcode D175506, 7/17/92, J. Morales.

27. PP#4G3031/FAP#4H5424, 5/30/84, L. Cheng; and CB No. 960, 6/3/86, L. Cheng.

28. PP#6F3362/FAP#6H5493, CB Nos. 5557 and 5558, 12/11/89, G. Otakie; and CB Nos. 7646 and 7647, DP Barcodes D160990 and D161029, 9/9/91, G. Otakie.

29. Post emergence use of the 50% WP formulation on strawberries is not supported. Supporting data must be provided or the use removed from the 50% WP label.

(continued)

011142

Table B *(continued)*.

30. PP#6F3337, CB No. 360, 2/21/86, M. Firestone; CB No. 988, 9/9/86, M. Firestone; and CB No. 2301, 9/3/87, M. Kovacs.

31. CB Nos. 4814, 4815, and 4816, 5/10/89, M. Kovacs; and CB No. 5895, 11/2/89, D. Edwards.

32. CBRS recommends that the proposed tolerances of 0.1 ppm in/on cereal grains group (excluding wheat, barley, and oats) and 1 ppm in/on forage, fodder, and straw of cereal grains group (excluding wheat, barley, and oats) be established concomitant with the revocation of the group tolerance for grain crops (PP#1F3993; CBRS No. 10833, DP Barcode D183914, 9/30/93, D. Miller).

33. CBRS No. 8043, DP Barcode D164655, 6/1/92, L. Cheng.

34. CBRS No. 8166, DP Barcode D165608, 4/16/92, J. Abbotts.

35. The tolerance of 0.1 ppm for grasses, forage was established to cover seed treatment. Ciba-Geigy has petitioned for crop group tolerances for grasses, forage at 10 ppm and grasses, hay at 20 ppm to cover proposed soil and foliar uses. This petition is currently in reject status (PP#2F04063; CBTS No. 9338, DP Barcode D173024, 9/22/93, M. Peters).

36. A crop group tolerance for the Non-Grass Animal Feeds Group is not appropriate because of the more than 5 fold difference between residues in alfalfa and clover hays. Individual tolerances must be established. (PP#2F4105, CBTS No. 9625, DP Barcode D175974, M. Rodriguez, 8/17/93).

37. PP#9F3675, CB Nos. 4792, 4793 and 4794, 8/3/89, J. Garbus.

38. PP#6F3330, CB No. 312, 2/7/86, M. Firestone. Postemergence use of the 50% WP formulation is not supported. Supporting data must be provided or the use removed from the 50% WP label.

39. It is unclear from the submitted residue data for cotton if the de-linted or undelinted seed was analyzed. Residue data for the undelinted cottonseed are required. In addition, CBRS now requires residue data for cotton gin byproducts (commonly called gin trash) which includes burrs, leaves, stems, lint, immature seeds, sand, and dirt. As these data requirements are based on the Livestock Feeds Table (Table II) for Subdivision O (Residue Chemistry) of the Pesticide Assessment Guidelines (June 1994), they are considered confirmatory data.

40. In accordance with PR Notice 93-12 (12/23/93), the regulated raw agricultural commodity for hops is now considered to be dried hops. The 20 ppm tolerance for hops, dried listed under 40 CFR §185.4000(d) should be moved to §180.408(a). The tolerance for the commodities hops, green (0.5 ppm under §180.408[a]) and the feed additive tolerance for hops, dry (2 ppm under 40 CFR § 186.4000[a]) should be revoked. In addition, the 20 ppm tolerance for hops, spent listed under 40 CFR § 186.4000(d) should be revoked as metalaxyl residues in spent hops will now be covered by the tolerance on the RAC.

41. FAP# 7H5532, CB Nos. 4078 and 4190, 9/28/88, S. Willett; and CB No. 4630, 11/17/88. S. Willett.

42. PP#9F3712, CB Nos. 4811, 4812 and 4813, 4/11/89, S. Willett; CB No. 5579, 8/18/89, F. Toghrol; and CBTS No. 9011, DP Barcode D169779, 6/19/92, J. Morales.

43. PP#8E3605, CB No. 3360, 5/5/88, F. Griffith.

44. The tolerance for peanut, vines should be revoked, as this commodity is no longer regulated because it is not a major livestock feed item.

011142

Table B *(continued)*.

45. CBRS No. 8043, DP Barcode D164655, 6/1/92, L. Cheng; and CBRS No. 10743, DP Barcode D183659, 11/24/92, L. Cheng.

46. CBRS No. 11238, DP Barcode D187081, 7/22/93, J. Abbotts.

47. The tolerances for pineapple fodder and forage should be revoked as these commodities are not major livestock feed items.

48. The feed additive tolerance for apple, pomace, dry should be revoked, as the regulated feed item is apple pomace, wet.

49. CBRS No. 11238, DP Barcode No. D187081, 7/22/93, J. Abbotts.

50. CBTS No. 11708 and 11709, DP Barcode D189772 and 189764, 5/5/93, F. Griffith.

51. The tolerance for peanut, soapstock should be revoked as this commodity is not a major livestock feed item.

52. A feed additive tolerance of 0.5 ppm for pineapple, process residue is appropriate and should be proposed and established (CBRS No. 9596, DP Barcode D175852, 6/22/92, R. Perfetti; and CBRS No. 11238, DP Barcode D187081, 7/22/93, J. Abbotts).

53. Metalaxyl residues were found to concentrate up to 15.3x, 2.4x, and 1.4x in dried peel, potato flakes, and potato chips, respectively. Residues did not concentrate in the wet peel. Based on a 0.5 ppm tolerance for potatoes, food additive tolerances for the processed commodities potato granules/flakes and chips be proposed at 2 ppm, concomitant with the revocation of the established 4.0 ppm tolerance for potato, processed (including potato chips). In addition, the feed additive tolerance for potato waste, dried, processed should be increased to 10 ppm from 4 ppm, and renamed as processed potato waste (CBRS No. 8043, DP Barcode D164655, 6/1/92, L. Cheng).

54. CBRS No. 8043, DP Barcode D164655, 6/1/92, L. Cheng.

55. The tolerance for soybean, soapstock should be revoked, as this commodity is not a major livestock feed item.

56. Residues in molasses were found to concentrate up to 10x. Based on the 0.5 ppm tolerance for sugar beets, the feed additive tolerance for molasses listed under 40 CFR §186.4000(a) must be increased from 1.0 to 5 ppm (CB Nos. 3908 through 3912, 11/28/88, F. Griffith; and CB Nos. 5934, 5935, and 6545, 4/30/90, F. Griffith). The feed additive tolerance of 5.0 ppm listed under 40 CFR §186.4000(b) (inadvertent tolerance) should be revoked.

57. CB Nos. 3908 through 3912, 11/28/88, F. Griffith; and CB Nos. 5934, 5935, and 6545, 4/30/90, F. Griffith.

58. The available data indicate that residues concentrated by up to 1.5x in sunflower, meal; a 0.2 ppm feed additive tolerance for sunflower, meal is appropriate (CBRS No. 11238, DP Barcode D187081, 7/22/93, J. Abbotts).

59. CBRS No. 8043, DP Barcode D164655, 6/1/92, L. Cheng.

60. CBRS No. 11238, DP Barcode D187081, 7/22/93, J. Abbotts.

61. Data are required to determine if residues concentrate in tomato paste (Table II, June, 1994)

62. Confined Rotational Crop studies have been submitted and are currently under review.

(continued)

011142

Table B ***(continued).***

63. **Partially reviewed in CB No. 12312, DP Barcode No. D193692, 8/16/93, G. Herndon.**

011142

ACTIVE INGREDIENT WORKSHEET – PART ONE

This two-page Worksheet lists possible label statements to require based on the characteristics of the a.i.

[redacted]CTIVE INGREDIENT: ..Metalaxyl..... Uses Covered by Worksheet: X WPS X NonWPS X Both ☐ Home Use

PERSONAL PROTECTIVE EQUIPMENT

(Fill in sections A and B for an active ingredient ONLY if unusual risk concern, such as delayed-effect or sensitization. PPE requirements for each end-use product will be set based on the acute toxicity of that product.)

A APPLICATOR PPE

Applicators and other handlers ▲ must wear:
☐ (except mixers, loaders, and others exposed to the concentrate)
(Choose this insert if Section B is filled in.)

Choose one item (or none) from each grouping:

16 ☐ Chemical-resistant protective suit ..... EXT
16 ☐ Coveralls over long-sleeved shirt and long pants
17 ☐ Coveralls over short-sleeved shirt and short pants
18 ☐ Long-sleeved shirt and long pants

20 ☐ Chemical-resistant gloves, such as _____

21 ☐ Chemical-resistant footwear plus socks
21 ☐ Shoes plus socks

24 ☐ Goggles
24 ☐ Protective Eyewear

23 [redacted]emical-resistant headgear for overhead exposure

19 ☐ Chemical-resistant apron when cleaning equipment, ▲
(Select insert if not checked below in B) ☐ mixing, or loading

26 ☐ Respirator (specify type in section C)

B MIXER AND LOADER PPE

Mixers and loaders ▲ must wear:
☐ (and others exposed to the concentrate)
(Choose this insert if all persons exposed to the concentrate must wear this PPE and not the PPE selected in section A.)

Choose one item (or none) from each grouping:

16 ☐ Chemical-resistant protective suit ..... EXT
16 ☐ Coveralls over long-sleeved shirt and long pants
17 ☐ Coveralls over short-sleeved shirt and short pants
18 ☐ Long-sleeved shirt and long pants

20 ☐ Chemical-resistant gloves, such as _____

11 ☐ Chemical-resistant footwear plus socks
11 ☐ Shoes plus socks

4 ☐ Goggles
4 ☐ Protective Eyewear

3 [redacted]ical-resistant headgear for overhead exposure

9 ☐ Chemical-resistant apron when mixing or loading

6 ☐ Respirator (specify type in section C)

C TYPE OF RESPIRATOR

[Select respirator type(s) for each active ingredient in category I or II for acute inhalation toxicity OR if respirator chosen in A or B. See Appendix B for instructions about selecting respirator type(s).]

☐ In enclosed areas only
26 ☐ ▲ A supplied-air respirator (MSHA/NIOSH approval number prefix TC-19C) OR (b) a self-contained breathing apparatus (SCBA) (MSHA/NIOSH approval number prefix TC-13F).

☐ In enclosed areas only OR ☐ In outdoor areas only
27 ☐ ▲ A respirator with either an organic-vapor-removing ..... EXT cartridge with a prefilter approved for pesticides (MSHA/ NIOSH approval number prefix TC-23C), or a canister approved for pesticides (MSHA/NIOSH approval number prefix TC-14G).
☐ In enclosed areas only OR ☐ In outdoor areas only
29 ☐ ▲ A dust/mist filtering respirator (MSHA/NIOSH approval number prefix TC-21C).

D REDUCE PPE WHEN ENGINEERING CONTROLS USED

(Already allowed in WPS; Select to allow for NonWPS uses)

31 ☐ When handlers use closed systems, enclosed cabs, or aircraft in a manner that meets the requirements listed in the Worker Protection Standard (WPS) for agricultural pesticides [40 CFR 170.240(d)(4-6)], the handler PPE requirements may be reduced or modified as specified in the WPS.

E USER SAFETY STATEMENTS

(See Appendix F in the GUIDE for other user safety requirements to consider for special situations.)

REQUIREMENTS:

40 X Follow manufacturer's instructions for cleaning/ ..... ALL WPS maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

(Consider the statement below if delayed- or allergic-effect concerns AND formulated as a concentrate.)

40 ☐ Discard clothing and other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them.

.....

RECOMMENDATIONS:

39 X Users should wash hands before eating, drinking, ... ALL chewing gum, using tobacco, or using the toilet.

39 X Users should remove clothing immediately if pesticide ..... ALL gets inside. Then wash thoroughly and put on clean clothing.

39 X Users should remove PPE immediately after handling ..... ALL this product. ▲ As soon as possible, wash thoroughly and change into clean clothing.

[redacted]
(Select this insert if gloves are required PPE.)

40

011142

ACTIVE INGREDIENT WORKSHEET – PART TWO

ACTIVE INGREDIENT: Metalaxyl

Uses Covered by Worksheet ☒ WPS ☐ NonWPS ☒ E

F ENGINEERING CONTROLS

(See Appendix E if considering mandatory engineering controls, such as closed systems, enclosed cabs, or aircraft.)

G APPLICATION RESTRICTIONS

(See p. 46 in the Guide for other application restrictions, such as setback restrictions, to consider for special situations.)

45 Do not apply this product in a way that will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application.
✓ WPS uses. This is a WPS requirement.

☐ All NonWPS uses ☐ All NonWPS uses, except _____
Consider for most nonWPS uses, other than wide-area mosquito control, insect repellents, etc.)

H ENTRY RESTRICTIONS

48 WPS ENTRY RESTRICTIONS
(Set one REI for whole product OR different REI's for different uses. If subpart K data are not available, use acute toxicity of active ingredient to set REI. If delayed-effect concern, consider raising REI one level.)

Choose this item if only one REI for entire product:
☒ Do not enter or allow worker entry into treated areas during the restricted entry interval (REI) of ▲
- ☐ _____ days. . . . . NOT WPS, EPA SET
- ☐ 72 hours. . . . . NOT WPS, EPA SET
- ☐ 48 hours. . . . . I-D/S/EYE
- ☐ 24 hours. . . . . II-D/S/EYE
- ☒ 12 hours. . . . . III/IV-D/S/EYE

Choose this item if two REI's for product:
☐ Do not enter or allow worker entry into treated areas during the restricted-entry interval (REI) of ___ ☐ hours ☐ days, except for _____ (crop with different REI). The REI for _____ (crop with different REI) is ____ ☐ hours ☐ days.

Choose this item if more than two REI's for product:
☐ Do not enter or allow worker entry into treated areas during the restricted entry interval (REI).
- ☐___ ☐hours ☐days REI for _____(specify uses)
- ☐___ ☐hours ☐days REI for _____(specify uses)
- ☐___ ☐hours ☐days REI for _____(specify uses)
- ☐___ ☐hours ☐days REI for _____(specify uses)
- ☐___ ☐hours ☐days REI for _____(specify uses)

58 Longer REI for organophosphates in arid areas:

☐ Each 48-hour REI is increased to 72 hours . . . . . I-D/S/EYE-OP
in outdoor areas where average annual rainfall is less than 25 inches a year.

46 NON-WPS ENTRY RESTRICTIONS
(See p. 50 in the Guide for entry restrictions, ventilation criteria, and notification requirements to consider for nonWPS uses.)

I EARLY ENTRY PPE

(Use the acute toxicity of active ingredient, then adjust if delayed-effects, allergic-effects, or other special concerns.)

☒ PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water is: . . . . . WPS

☐ PPE required for early entry to treated areas that involves contact with anything that has been treated is: . . . . . NonWPS

Choose one item (or none) from each grouping:

16 ☐ Chemical-resistant protective suit . . . . . EXT
16 ☐ Coveralls over long-sleeved shirt and long pants . . . . . I-D/S
17 ☐ Coveralls over short-sleeved shirt and short pants . . . . . II-D/S
17 ☒ Coveralls . . . . . III/IV-D/S
18 ☒ Long-sleeved shirt and long pants . . . . . NonWPS Only
(WPS requires at least coveralls for early entry.)

20 ☒ Chemical-resistant gloves, such as ___ . . . . . I/II/III/IV-D/S

21 ☐ Chemical-resistant footwear plus socks . . . . . I/II-D/S
21 ☒ Shoes plus socks . . . . . III/IV-D/S

24 ☐ Goggles . . . . . EY
24 ☒ Protective Eyewear . . . . . I/II-D

23 ☐ Chemical-resistant headgear for overhead exposure I/II-D/S

26 ☐ Respirator (specify type in section C) . . . . . NonWPS Only or EXT
(WPS allows only handlers (not early-entry workers) to enter during an REI if inhalation is a concern. See p. 14 in the Guide.)

J NOTIFICATION

62 WPS Only: (WPS requires oral warning OR treated area posting for all WPS uses – select this statement to require both.)
☐ Notify workers of the application by warning them orally and by posting warning signs at entrances to treated areas. . . . . I-D/S

62 NonWPS: (Do not select the above statement– a custom statement is required.)

KEY TO PESTICIDE WORKSHEETS

▲	= Insert shaded text here, if selected
	= Text must be selected or crossed out
I, II, III, IV	= Toxicity Categories
1, 2, 3, etc	= Page numbers where discussed in GUIDE
ALL	= Consider for all products
D	= Acute Dermal Toxicity (oral=surrogate)
EXT	= Extraordinary PPE (heat/stress concern)
EYE	= Eye Irritation Potential
INH	= Acute Inhalation Toxicity (oral=surrogate)
NonWPS	= Uses outside Worker Protection Standard
NonWPS only	= Select for NonWPS only; not for WPS
OP	= Organophosphate Pesticide
S	= Skin Irritation Potential
WPS	= Uses under Worker Protection Standard

END