7/8/94

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

7-8-94

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Transmittal of EFED List A Summary Report for Metalaxyl (Chemical # 113501) Case # 0081

FROM: Betsy Grim
Science Analysis and Coordination Staff
Environmental Fate and Effects Division

THRU: Evert K. Byington, Chief
Science Analysis & Coordination Staff,
Environmental Fate and Effects Division

TO: Esther Saito, Acting Chief
Reregistration Branch,
Special Review & Reregistration Division

Attached please find the following documents for the completed EFED summary report of Metalaxyl.

1. EFGWB Science Chapter
2. EEB Science Chapter
3. SACS Reregistration Summary Report

Metalaxyl exceeds a level of concern for ground-water quality. In addition, data gaps were identified for this reregistration case. If you have any questions concerning this case, please contact Betsy Grim, 305-7634.

CC:\ (with SACS Reregistration Summary Report attached)

Anne Barton
Hank Jacoby
Elizabeth Leovey
List A File
Lou True
Tony Maciorowski
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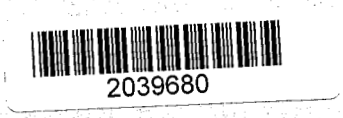

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SUBJECT: EFED List A Summary Report for Metalaxyl

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FROM: Betsy Grim
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TO: Esther Saito, Acting, Chief
Reregistration Branch,
Special Review & Reregistration Division

Background

Use Profile

Metalaxyl is a systemic fungicide used to control air- and soil-borne diseases on a wide range of crops, as well as foliar diseases caused by the downy mildews. Foliar sprays comprised of metalaxyl and conventional protectant fungicides are recommended for the control of airborne diseases on hops, potatoes, tobacco, and vines. Metalaxyl alone is used as a soil application for the control of soil-borne pathogens causing root and lower stem rots on crops such as avocados and citrus, and for primary systemic infections of downy mildew on hops and in tobacco seedbeds. Metalaxyl is used as a seed treatment for the control of systemic downy mildews and damping off of various crops such as corn, peas, sorghum, and sunflowers. Single active ingredient formulations include emulsibiable concentrate, granular, flowable, and wettable powder. Multiple active ingredient formulations include thiabendazole, captan, PCNB, and chloroneb.

Levels of Concern Exceedances

Metalaxyl exceeds the Level of Concern for ground water quality.

Both laboratory and field studies indicate that metalaxyl is persistent and mobile and may leach in many soils. For this reason, the December 1981 Registration Standard required the completion of ground-water monitoring studies for metalaxyl. In 1987, EPA recommended that retrospective studies be conducted for metalaxyl because of its long history of use and the potential for metalaxyl and its major degradate (CGA-62826) to reach groundwater. On March 9, 1993, EFGWB indicated to SRRD that sufficient information was available to regulate metalaxyl and that additional ground-water studies were not necessary at that time. The retrospective ground-water monitoring studies were placed on reserve in 1993.

Although metalaxyl does not pose a threat to nontarget species, it does exceed the Level of Concern (LOC) end-points for ground-water quality based on EFED ground-water criteria for mobility and persistence.

Risk Reduction Measures

1. EFED recommends that the metalaxyl label be amended to include a ground-water advisory. This advisory should state:

   "This chemical is known to leach through soil into ground water under certain conditions as a result of agricultural use. Use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in ground-water contamination."

2. EFED recommends that metalaxyl be considered a candidate for Restricted Use. Metalaxyl exceeds all seven of the proposed persistence and mobility triggers for Restricted Use, indicating that is has high potential to move to ground water. Monitoring data demonstrate that metalaxyl and its primary degradate (CGA-62826) have the potential to leach to groundwater. Metalaxyl has been detected in ground water in five states at levels typically ranging up to 3 parts per billion (ppb). Concentrations have been reported as high as 236 ppb, but are not likely to be the result of normal field use.

3. EFED recommends that SRRD request the registrant to propose a level in ground water that, if reached, would result in voluntary action to prohibit or cancel the use of metalaxyl in the affected area.

Value of the Additional Information

Environmental Fate. At this time, three data requirements in the environmental fate guidelines are not fulfilled for metalaxyl: aerobic aquatic metabolism (162-4), field dissipation for terrestrial uses (164-1), and aquatic field dissipation (164-2). Although these three guidelines are not fulfilled, EFED has sufficient information available from the acceptable and supplemental studies to make a sound qualitative assessment for the fate of metalaxyl in the environment.

o 162-4 Aerobic aquatic metabolism (MRID # 42259802)

This study did not satisfy the data requirements because the registrant did not provide any data related to the concentration of metalaxyl in the sediment or water individually. The only data in the report was data related to the concentration of metalaxyl in the sediment/water combined.

o 164-1 Soil Dissipation (MRID #s 41765001, 41765002, 41809301)

None of the submitted field dissipation studies completely satisfy the data requirements for Field Dissipation For Terrestrial Uses. However, EFGWB believes that little further information will be gained from the submission of additional field dissipation studies. Sufficient data has been presented that demonstrates metalaxyl and its primary degradate CGA-62826, are capable of leaching to the 36-to-48 inch soil depth (which is further confirmed by groundwater and drinking water studies where metalaxyl and its degradate CGA-62826 were detected). Although studies were scientifically sound, adequate freezer storage stability data were not provided. In addition, in one study, 41890301, the patterns of leaching of metalaxyl and CGA-62826 were confounded by an apparent problem with contamination during sampling, and adequate freezer storage stability data were not provided.

o 164-2 Aquatic Field Dissipation (MRID #s 42259803, 42259804)

These studies were not acceptable because soil samples containing metalaxyl and its major degradate, CGA-62826, were stored frozen for up to 436 days before analysis; however, storage stability experiments with soil was performed for only up to 180 days. Therefore, the registrant should provide data that show metalaxyl and CGA-62826 are stable when stored frozen for up to 436 days to upgrade the study to acceptable.

If SRRD believes that a more thorough environmental fate assessment is needed, EFGWB recommends that the additional information needed to fulfill the above data requirements be submitted. The additional information required will make the studies more complete and result in a better quantitative assessment. However, the

environmental fate of metalaxyl is presently predictable by the weight of evidence from the various degradation, metabolism, mobility, dissipation, accumulation and ground and surface water studies, which indicate that the primary routes of dissipation are aerobic metabolism, leaching, surface mobility and plant uptake.

Ecological Effects. Avian reproduction studies are required when birds may be exposed repeatedly or continuously through persistence, bioaccumulation, or multiple application, or if mammalian reproduction tests indicate reproductive hazard. Present product labeling of metalaxyl allows several applications of the end-use product per growing season. There are no avian reproduction studies in the current metalaxyl target database. These studies had not been previously required because of the low acute toxicity of metalaxyl. New scientific knowledge indicates that subtle effects, that may not be evident from acute testing, may occur from chronic exposure to some chemicals. Therefore, EFED now requires these studies to determine the chronic risk of metalaxyl to birds.

GDLN NO.	TYPE OF TEST	MRID OR ID. NO.	REPLACEMENT VALUE
71-4(a)	Avian Reproduction Quail		High
71-4(b)	Avian Reproduction Duck		High

A low replacement value is assigned when there is a low probability that a new test will effectively challenge/change significantly previous assumptions, previously-determined levels of risk and/or decrease the overall level of uncertainty of adverse effects when other, core, scientifically sound and similar type of tests to the one under consideration are in the data base.

A medium replacement value is given to a test when the new results have some probability of altering previous assumptions or levels of risk and/or because it is likely to have a higher value in completing a toxicological data base that would otherwise be somehow incomplete for this type of test and, therefore, vulnerable to sound scientific challenge.

A high replacement value is given to a test when without a new test it would be impossible and scientifically incorrect to make assumptions and a determination of the level of risk involved. Furthermore, without a replacement test the level of uncertainty will remain high and the ecotoxicological data base will be incomplete and totally vulnerable to scientific challenge.

Labeling Requirements for Manufacturing- Use Products

The following label statement is required on all manufacturing-use products:

> "Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or public water unless this product is specifically identified and addressed in an NPDES permit. Do not discharge effluent containing this product to sewer systems without previously notifying the sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA".

Labeling Requirements for End-Use Products

> "For terrestrial uses, do not apply to water or to areas where surface water is present, or to intertidal areas below the mean high water mark. Do not apply when weather conditions favor drift from treated areas. Do not contaminate water when disposing of equipment wash water or rinsate."

Labeling for Endangered Species

> Due to the low toxicity of this chemical, endangered species precautionary labeling will not be required.

A. Environmental Assessment

1. Environmental Fate

At this time, three data requirements in the environmental fate guidelines are not fulfilled for metalaxyl: aerobic aquatic metabolism (162-4), field dissipation for terrestrial uses (164-1), and aquatic field dissipation (164-2). Although these three guidelines are not fulfilled, EFED has sufficient information available from the acceptable and supplemental studies to make a sound qualitative assessment for the fate of metalaxyl in the environment.

a. Environmental Fate Assessment

Based on a review of all studies submitted, metalaxyl was found to be moderately stable under normal environmental conditions. At 20 °C the calculated hydrolytic half-life was 200 days at pH 5 and 7, and 115 days at pH 9. Metalaxyl was photolytically stable in water when exposed to natural sunlight, with a half-life of 400 days, and less than 10 percent of the material photolyzed during the 28-day test period. Studies indicated that metalaxyl is stable to photodegradation on soil, because test results demonstrate no difference between the irradiated sample and the control sample. The aerobic soil metabolism half-life is determined to be about 40 days. In aquatic systems, metalaxyl degrades moderately under both aerobic and anaerobic conditions. Finally, studies indicate that less than 0.5 percent of the applied metalaxyl would be lost to volatilization.

Metalaxyl and its degradates readily leach in sandy to sandy clay loam soils low in organic matter. It is considered to be a strong leacher because 57 and 92 percent of the applied was detected as parent in leachates of two unaged 30-cm soil columns. In addition approximately 44 percent and 34 percent of the applied was parent and the degradate CGA-62826 (N-2,6-dimethylphenyl)-N-(methoxyacetyl)-alanine) in the leachate of an aged soil column of a sandy soil, and 57 percent and 92 percent was parent and the degradate in the leachates of an aged soil column of a silty loam soil.

Under field conditions, the fate of metalaxyl in soil is similar to that under laboratory conditions with reported half-lives of 14 to 56 days. In two aquatic field dissipation studies, metalaxyl dissipated from rice paddy water with half-lives of 5 and 20 days, and from soil with half-lives of 11 and 24 days. The major degradation product formed in the field studies was CGA-62826.

EFED concludes that the primary routes of dissipation of metalaxyl in surface soil appear to be aerobic soil metabolism (half-life ≈40 days), leaching (Kds 0.4-

1.4), and plant uptake (residues accumulate in plants up to 12 months after application). In aquatic systems, such as rice culture, EFED can only tentatively identify a route of dissipation because the compound is stable to hydrolysis (half-life ≈200 days at pH 5 and 7 and 115 days at pH 9), photolysis on water (half-life ≈400 days) and soil (no difference between irradiated or samples incubated in the dark) and does not volatilize appreciably. However, metalaxyl degrades moderately under aerobic aquatic (half-life ≈ 55 days) and anaerobic aquatic (half-life ≈30 days) conditions, which are probably the main routes of dissipation in aquatic systems together with leaching, surface mobility and plant uptake. Sensitized aqueous photodegradation may also be important in dissipation of metalaxyl and residues from aquatic systems.

Both laboratory and field studies indicate that metalaxyl is persistent and mobile and may leach in many soils; however, terrestrial and aquatic field studies demonstrate that the compound is less stable in the field than the laboratory data indicate, and it is also mobile under normal use conditions. For this reason, the December 1981 Registration Standard required the completion of ground-water monitoring studies for metalaxyl. In 1987, EPA recommended that retrospective studies be conducted for metalaxyl because of its long history of use and the potential for metalaxyl and its major degradate (CGA-62826) to reach groundwater. On March 9, 1993, EFED indicated to SRRD that sufficient information was available to regulate metalaxyl and that additional ground-water studies were not necessary at that time. The retrospective ground-water monitoring studies were placed on reserve in 1993.

Metalaxyl has been shown to exhibit the properties and characteristics associated with chemicals that have been detected in ground water. Metalaxyl is considered a persistent pesticide for ground water concerns with an aerobic soil metabolism half-life of approximately six weeks. In addition, metalaxyl is considered very mobile for ground water concerns with Kd values ranging from 0.43 to 1.40 L/kg in three different soils. Therefore, there is a strong possibility of movement to ground water, especially in vulnerable areas. This has been confirmed by the detections reported in the "Pesticides in Ground Water Database" (Hoheisel et al., 1992) which indicate that metalaxyl has had an impact on ground-water quality.

Monitoring data demonstrate that metalaxyl and its primary degradate (CGA-62826) have the potential to leach to groundwater. Metalaxyl has been detected in ground water in five states at levels typically ranging up to 3 ppb. Concentrations have been reported as high as 236 ppb, but are not likely to be the result of normal field use.

Although metalaxyl does not pose a threat to nontarget species, it does exceed the Level of Concern (LOC) for ground-water quality based on EFED's ground-water criteria for mobility and persistence.

Fish accumulation studies indicate that parent metalaxyl bioaccumulation factors (BCF) in whole fish of less than or equal to 7X were found when bluegill sunfish were exposed to 1 ppm ^{14}C-metalaxyl in a continuous flow-through system for 29 days.Fish accumulation did not exceed seven fold when fish were exposed to metalaxyl at 1 ppm in water, and residues were found to accumulate in the nonedible portions over the edible portions in a ratio of about 4:1 to 15:1. Residues declined rapidly during depuration. In addition, a separate fish accumulation study using catfish showed accumulation of one fold and rapid depuration.

b. Environmental Chemistry, Fate and Transport

(1) Hydrolysis (161-1)

Metalaxyl was found to be moderately stable to hydrolysis under normal environmental conditions. At 20°C, the calculated half-life was 200 days at pH 5 and 7 and 115 days at pH 9. (MRID # 00104493)

(2) Photodegradation in water (161-2)

^{14}C-Metalaxyl was photolytically stable in water when exposed to natural sunlight, with a half-life of 400 days. Less than 10 percent of the material photolyzed during the 28 day test period. CHA-62826, the major degradation product, was 5.7% of applied in the (day 14) irradiated sample and 6.1 percent in the (28 day) sample. Total radiocarbon remaining as metalaxyl was 88.5 percent for the irradiated samples and 89.9% for the dark controls. (MRID # 41156001)

(3) Photodegradation in soil (161-3)

Metalaxyl was stable to photodegradation on a silty loam soil exposed to a xenon arc lamp. The results indicated no difference between the degradation of the irradiated sample and the control sample (residues degraded at a rate comparable to the aerobic metabolism study). (MRID # 00100455)

(4) Aerobic soil metabolism (162-1)

The aerobic soil metabolism half-life of metalaxyl was determined to be about 40 days. The only major degradate was CGA-62826 which was identified as N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-L-alanine. This in turn breaks down to non-extractable material and CO_2. CGA-62826 accumulates to 53.6 percent of the applied at 66 days and thereafter degrades to 23 percent of the applied at 360 days. At 12 months, metalaxyl parent accounts for less than 2 percent of the applied and nonextractable residues account for 38.3 percent of the applied. (MRID # 00104494)

(5) Anaerobic soil metabolism (162-2)

The aerobic soil degraded parent metalaxyl to 60 percent of the applied at 31 days, and then anaerobic conditions were established. After 66 days, the parent declined to 49.4 percent and after 89 days it had declined to 32.5 percent. The major degradation product was CGA-62826) which accumulated to 54.4 percent after 89 days. CO_2 was not a major degradate and non-extractables did not exceed 10 percent of the applied. (MRID # 00104494)

(6) Anaerobic aquatic metabolism (162-3)

Metalaxyl degraded in the anaerobic aquatic environment with a half-life of 26.9 days in soil with water, while the half-lives were 21.7 and 29.9 days, respectively, in the sediment and water phases. Metalaxyl accounted for 96.35 percent (1.72 ppm) at the start of the study and decreased to 1.25 percent (0.02 ppm) after 100 days post-treatment and was not detected after that time. CGA-62826 increased up to 85.53 percent at 265 days after treatment and then decreased to 48.07 percent by the termination of the study (day 385). The metabolite N-(3-hydroxy-2,6-dimethylphenyl)-N-(methoxyactyl)-L-alanine (CGA-119857) accounted for up to 16.25 percent at the end of the study, while CO_2 accounted for only 1.35 percent (0.02) ppm) of the initially-applied radioactivity. (MRID # 42259801)

(7) Aerobic aquatic metabolism (162-4)

Metalaxyl degraded in the aerobic aquatic environment with a half-life of 55.11 days in soil with water. The reported half-lives were $\approx$70 and $\approx$41 days, respectively, in the sediment and water phases. Parent metalaxyl (65.36%) and CGA-62826 (20.56%) were the only major metalaxyl residues found in soil/water extracts after 30 days of incubation. Unextractable residues accounted for 3.47 percent, while CO_2 was less than 0.5% of the applied radioactivity.

This study did not satisfy the data requirements because the registrant did not provide any data related to the concentration of metalaxyl in the sediment or water individually. The only data in the report was data related to the concentration of metalaxyl in the sediment/water combined. (MRID # 422590802)

(8) Leaching and adsorption/desorption (163-1)

In unaged leaching studies, parent ^{14}C-metalaxyl leached rapidly in sandy soil with up to 92 percent of the radioactivity recovered in the leachate. In the sandy clay loam and silt loam soils, the majority of the radioactivity was recovered in the 6 to-24 cm soil layers with less than 0.6 percent in the leachates.

In aged leaching studies, 79.2 percent of the applied radioactivity was found in the leachate and 16.1 percent remained in the soil in the sandy soil column. Of the activity found in the leachate, 56 percent was parent, 31 percent was CGA-62826, and 12 percent was unaccounted. In the silt loam soil, 48.7 percent was in the leachate and 34.9% remained in the column. Approximately 70 percent of the radioactivity found in the leachate was parent, 18 percent was CGA-62826 and 11 percent was unaccounted.

Adsorption/desorption studies using radiolabeled metalaxyl demonstrate K_{ads} values of 0.43, 0.48, 0.87 and 1.40 for sandy, sandy loam, silt loam and sandy clay loam soil. (MRID #s 00100464, 00100465, 00100466)

(9) Volatility (163-2)

Volatilization studies demonstrated that less than 5% of the applied metalaxyl would be lost due to volatilization, and that volatilization is not a major route of metalaxyl dissipation. (MRID # 00100455)

(10) Terrestrial Field Dissipation (164-1)

At the present time, none of the submitted field dissipation studies completely satisfy the data requirements for Field Dissipation For Terrestrial Uses. However, EFGWB believes that little further information will be gained from the submission of additional field dissipation studies. Sufficient data has been presented that demonstrates metalaxyl and its primary degradate CGA-62826, are capable of leaching to the 36 to 48 inch soil depth (which is further confirmed by groundwater and drinking water studies where metalaxyl and its degradate CGA-62826 were detected). Furthermore, there is sufficient data from the submitted studies that demonstrate that the route of dissipation is probably leaching, aerobic soil metabolism and plant uptake. The reported half-life of metalaxyl at the various field locations, where the studies were considered supplemental, varied from 14 to 56 days.

The field dissipation half-lives determined from four previously reviewed unacceptable field dissipation studies were ≈27, 36, 148 and 296 days (although the data in the latter two studies were too variable to accurately assess the dissipation).

Three other field dissipation studies produced the following results:

1. In one study, metalaxyl dissipated with a half-life of 56 days from the upper 6 inches of bareground plots of loamy sand soil in California after a broadcast application of metalaxyl (Ridomil 2E, 2 lbs/gallon EC) at 8 lbs AI/acre. The degradate, CGA-62826, was detected in the 0- to 6-inch soil depth at all sampling intervals. Metalaxyl and CGA-62826 leached to the 36- to 48-inch soil depth; leaching correlated with significant amounts of irrigation water applied to the plots. This study is scientifically sound, but is not acceptable because adequate freezer storage stability data were not provided. (MRID# 41765001)

2. In the 2nd study, metalaxyl dissipated with a half-life of 50 days from the upper 6 inches of plots of sandy loam soil planted to young citrus in California following the last of three applications (3-month intervals) of metalaxyl (Ridomil 2E, 2 lb/gallon EC) at 4.4 lbs ai/A (13.2 lbs ai/A total). The degradate, CGA-62826, was detected in the 0- to 6-inch soil depth at most sampling intervals. Metalaxyl leached to the 24- to 36-inch soil depth and CGA-62826 leached to the 36- to 48-inch soil depth. This study is scientifically sound, but is not acceptable because adequate freezer storage stability data were not provided. (MRID # 41765002)

3. In the last study, metalaxyl dissipated with half-lives of 38 to 39 days from the upper 6 inches of bareground and cropped (tobacco) plots of loamy sand soil in North Carolina after a single broadcast application of metalaxyl (Ridomil 2E, 2 lb/gallon EC) at 4.3 lbs ai/A. The degradate, CGA-62826, was detected in the 0 to 6 inch soil depth at most sampling intervals. Metalaxyl and CGA-62826 leached to the 36 to 48 inch soil depth; however, leaching patterns were confounded with apparent contamination during sampling. This study is scientifically sound, but is not acceptable because the patterns of leaching of metalaxyl and CGA-62826 were confounded by an apparent problem with contamination during sampling; and adequate freezer storage stability data were not provided. (MRID # 41809301)

(11) Aquatic field dissipation (164-2)

Metalaxyl dissipated from rice paddy water with calculated half-lives of 5 and 20 days and from soil with half-lives of 11 and 24 days. The studies were not acceptable because soil samples containing metalaxyl and its major degradate, CGA-62826, were stored frozen for up to 436 days before analysis; however, storage stability experiments with soil was performed for only up to 180 days. Therefore, the registrant should

provide data that show metalaxyl and CGA-62826 are stable when stored frozen for up to 436 days to upgrade the study to acceptable. (MRID #s 42259803, 422590804)

(12) Accumulation in fish (165-4)

Parent metalaxyl bioaccumulation factors (BCF) in whole fish of less than or equal to 7X were found when bluegill sunfish were exposed to 1 ppm ^{14}C-metalaxyl in a continuous flow-through system for 29 days. Bioaccumulation in edible and non-edible tissues ranged from 0.60 to 0.98 and 3.25 to 14.65, respectively. Residues declined rapidly during depuration. In another fish accumulation study with catfish, BCFs were below 1X in the edible, non-edible and whole fish portions at all exposure sampling times. Greater than 80 percent of the residues were recovered after 14 days of depuration. (MRID #s 00100468, 00100470)

(13) Droplet size spectrum and field drift

No studies are required based on the moderate toxicity of metalaxyl.

2. Ecological Effects

a. Ecological Effects Risk Assessment

Metalaxyl is registered for numerous use sites. Exposure to non-target organisms may result from direct applications, spray drift and/or runoff from treated areas.

(1) Risk to Terrestrial Animals

(A) Nontarget insects

Nontarget insects will be exposed to metalaxyl based on the end-use product's terrestrial food and nonfood use patterns. For nontarget insects, the honeybee or *Apis mellifera* is the representative test species; with an acute contact LD_{50} value of greater than 100 ug/bee, metalaxyl is practically nontoxic to honeybees.

(B) Avian and mammalian species

Avian and mammalian species will be exposed to metalaxyl through the consumption of insect and plant food material containing metalaxyl residues. The criterion for the presumption of high risk from exposure for acute avian and mammalian species is a value greater than or equal to 0.5 for the quotient of the

estimated environmental concentration (EEC) divided by the lowest LD_{50} value for birds and mammals--this is known as the risk quotient (RQ).

Acute RQ = EEC/LC50 ≥ 0.5 for birds and mammals

(i) Avian Acute Oral and Subacute Dietary Effects

Metalaxyl has been characterized as being practically non-toxic to avian species on a dietary basis and slightly toxic on an acute,single dose basis. Metalaxyl may be used in granular form or as a liquid formulation. As a liquid formulation, the risk quotient of Metalaxyl is the expected environmental concentration (EEC) divided by the dietary LC_{50}. For a granular formulation, the risk quotient is the LD_{50} per square foot.

1) Granular Formulation (LD_{50}/sq ft)

To calculate maximum mg ai/ft^2 for a granular formulation with a maximum application rate of 6.0 lbs AI/acre, where 454,598 is the number of milligrams per pound, and 43,560 are the number of square feet per acre:

6.0 lb ai/A x 454,590 mg/lb x 1 A/43,560 ft^2 = 62.62 mg/ft^2

The LD_{50} for the mallard duck is 1466 mg/kg. According to Dunning (1984), the average weight of a mallard duck is 1.082 kg. To calculate the LD_{50} per square foot:

$$\frac{62.62 \text{kg mg/ft}^2}{1466 \text{mg/kg}(1.082)} = 0.039 \ LD_{50}/\ ft^2$$

The risks to birds from exposure to granular Metalaxyl was analyzed by the above method, LD_{50} per square foot, to characterize acute risk. When the LD_{50} per square foot value equals or exceeds 0.5, then the pesticide is said to pose a high acute risk to birds. As the calculated value is only 0.039, the risk from granular metalaxyl to exposed birds is minimal.

2) Nongranular Formulations (EEC/LC_{50})

Metalaxyl is registered as nongranular formulations for numerous use sites. Exposure to nontarget organisms may result from direct application spray drift and/or runoff from treated areas. The maximum expected terrestrial residues based on a single application at different application rates and on different categories of avian food items is presented in the following table.

Application Rate (lbs AI/A)	Short Grass (ppm)	Long Grass (ppm)	Leaves and Leafy Crops (ppm)	Forage and Insects (ppm)	Seeds (ppm)	Fruits (ppm)
0.14[1]	34	15	18	8	2	1
0.33[2]	79	36	42	19	4	2
0.90[3]	216	99	113	52	11	6
1.0[4]	240	110	125	58	12	7
1.35[5]	324	149	169	78	16	10
1.5[6]	360	165	188	87	18	11
2.0[7]	480	220	250	116	24	14
3.0[8]	720	330	375	174	36	21
4.0[9]	960	440	500	232	48	28
6.0[10]	1440	660	750	348	72	42
7.2[11]	1728	792	900	418	86	50
8.0[12]	1920	880	1000	464	96	56

1. broccoli, cabbage, cauliflower, cotton, cucumbers, melons, squash, onions, alfalfa, buckwheat, dill, cucumber 2. beans, lentils, potatoes, avocados, raspberries, cotton, onions, cucurbits, barley, cole crops 3. hops, peas, soybeans, melons, ornamental turf, cotton, forage and hay, brassica, spinach, rice, blueberries, tobacco 4. lettuce, peanuts, squash, ornamental plants, hops, strawberries 5. soybeans, tomatoes, ornamental plants, cotton, vegetable bedding plants, onions, legume vegetables, lawn and turf 6. apples, curcubits, grapes, avocado, asparagus 7. spinach, pineapple, citrus, tomatoes, lettuce, legume vegetables, peanuts 8. tobacco, citrus, grapes, herbaceous plants 9. apples, citrus, grapes, herbaceous plants 10. stone fruit, conifer trees, shrubs and vines 11. pome fruit, citrus trees
12. apples, citrus, stone fruit

Acute dietary risk to birds from nongranular metalaxyl were analyzed by comparing EEC's to the LC_{50} values. When the risk quotient (EEC/LC_{50}) is at least equal to 0.2, the chemical is a candidate for Restricted Use classification. When the quotient is at least 0.5, the chemical is said to be a high acute risk to birds. The EEC value for short grass based on the maximum application rate is 1920 ppm. The LC_{50} from the avian dietary studies were shown to be in excess of 10,000 ppm. If the LC_{50} were estimated as 5 times the no mortality level (criteria for no risk is based on an EEC less than the $LC_{50}/0.2$), then the estimated LC_{50} would be 50,000 ppm. The quotient of the EEC/LC_{50} (1920 ppm/50,000 ppm) is significantly less 0.2 and 0.5. Therefore, it can be concluded that there are minimal risks to birds from dietary exposure to Metalaxyl.

(ii). Avian - Chronic Risk

Chronic risk cannot be determined as there are no avian reproduction studies for metalaxyl. Due to its widespread use (registered on over 100 agricultural crops), multiple applications and persistence in the field these studies are needed.

(iii). Mammalian Risk

1) Nongranular Formulation

An acute exposure for mammals may be estimated by converting an experimental mammalian (eg. rat or mouse) LD_{50} to an estimated LC_{50} value. The following calculation estimates the LC_{50} using the actual LD_{50} value. Estimates of body weight, weight eaten per day and food consumed per day follows Davis and Golly (1963), Principles of Mammology, Reinhold Corp. NY. This mammalian acute risk assessment is based on the lowest average LD_{50} of 1250 mg/kg for rats.

LC_{50}/day = Lowest LD_{50} mg/kg X Body Weight (gms)/ Weight Consumed (gms)

SMALL MAMMAL FOOD CONSUMPTION IN PARTS PER MILLION (PPM)				
SMALL MAMMAL	BODY WEIGHT (gms)	WEIGHT EATEN/DAY (%)	FOOD CONSUMED/ DAY(gms)	LC_{50}(ppm)
Meadow vole (herbivore)	46	61	28.1	2046
Field mouse (granivore)	13	16	2.1	7738
Least Shrew (insectivore)	5	110	5.5	1136

The following table presents risks to small mammals in relation to application rates (4 and 8 lbs AI/acre), with maximum and typical expected residues on the main food item for each class of mammal and their associated Risk Quotients (RQ). Please note that this model assumes that each mammal feeds only on its preferred food item contaminated with metalaxyl.

Mammal	Appl. rate (lbs AI/A)	Max residue	RQ	Typical residue	RQ
Herbivore (short grass)	4	960	**0.45**	500	**0.25**
	8	1920	**0.90**	1000	**0.49**
Granivore (grain)	4	48	**0.06**	12	**0.002**
	8	96	**0.12**	24	**0.004**
Insectivore (small insects)	4	232	**0.20**	132	**0.12**
	8	464	**0.41**	264	**0.23**

The Level of Concern (LOC) for acute high risk to small mammals is a RQ of 0.5. When application rates exceed 4 lbs AI/acre there is a predicted high risk only to herbivorous small mammals when the estimated metalaxyl residues are based on maximum exposure rates. However, when typical residue levels are used for estimates, the RQ for herbivores is below the LOC for high risk. The RQs for granivorous and insectivorous mammals based on maximum and typical residue levels do not exceed the LOC.

High risks to meadow voles and related herbivorous mammals are only predicted when the chemical is applied to the crop at high rates by methods such as foliar or surface spray or drenching that are likely to contaminate nearby short grasses or grass-like application sites. Soil or incorporated methods of application will not place these mammals at risk. However, these risks are not expected to occur under natural or field conditions. Metalaxyl has an inherently low toxicity to rats. Mammals would need to consume very large amounts of contaminated vegetation to generate toxic symptoms. As mammals consume a variety of foods, not all of which will be contaminated with metalaxyl, the likelihood of adverse effects to mammals from exposure to metalaxyl is minimized.

2) Granular Formulations

The same formula and method of calculating risk using the index of LD_{50}'s/square foot are used for mammals as well as birds. The calculated amount of Metalaxyl in a square foot area is 62.62 mg/sq ft. Using the rat LD_{50} of 1250 mg/kg and an average weight of 0.4 kg the mammalian LD_{50}/sq ft is:

$$\frac{62.62 \text{ mg/sq ft}}{(1250 \text{ mg/kg}) \times 0.4 \text{ kg}} = 0.13 \ LD_{50}/\text{sq ft}$$

This value is below the LOC of 0.5 LD_{50}/sq ft indicating low risk to mammals exposed to granular metalaxyl.

(2) Aquatic Risk

Estimated aquatic environmental concentrations were calculated and are presented in the following table.

Application Rate (lbs AI/acre)	EEC Ground[1] Application (ppb)	EEC Aerial[2] Application (ppb)	EEC Direct[3] Application (ppb)
0.14	0.85	0.94	8.54
0.33	2.01	2.23	20.13
0.90	5.49	6.04	54.90
1.0	6.10	6.71	61.00
1.4	8.24	9.06	82.35
1.5	9.15	10.07	91.50
2.0	12.2	13.2	122.0
3.0	18.3	20.1	183.0
4.0	24.4	26.8	244.0
6.0	36.6	40.3	366.0
7.2	43.9	48.3	439.2
8.0	48.8	53.7	488.0

1. The total aquatic EEC from a 10-acre field treated by un-incorporated ground application and draining into a 6-foot deep one acre water body. 2. The total loading from both runoff (1%) and drift (5%) of a 10-acre field treated by aerial application and draining into a 6 foot deep one acre water body. Aerial application includes mist blowers. 3. A single inadvertent direct application to a 6 foot deep one acre water body.

(A) Aquatic - Acute Risk

The Risk Quotients (RQ) are calculated by comparing the EEC values for ground and aerial applications to the lowest LC_{50} values for freshwater and estuarine fish and invertebrates for technical and formulated metalaxyl. When the RQ's equal or exceed the levels of concern (LOC) the associated risk can be presumed:

LOC	Risk Presumption
0.5	high acute risk
0.1	Restricted Use
0.05	risk to endangered species

The following RQ's were calculated for ground and aerial applications for freshwater and estuarine fish and invertebrates.

Organism	Ground appl.	Aerial appl.
Freshwater fish		
technical	0.0004	0.0004
formulate	0.003	0.003
Daphnia		
technical	0.002	0.002
formulate	0.004	0.005
Mysid		
technical	0.002	0.002
formulate	0.008	0.009
Oyster		
formulate	0.011	0.012

As the RQ's are below the levels of concern, there are minimal risks to non-endangered and endangered freshwater and estuarine species.

(B) Aquatic - Chronic Risk

When the risk quotient of the EEC/NOEC is less than 1.0, it is presumed that the chemical will not pose a high chronic risk. Metalaxyl can be applied on many of the registered crops up to four times per season. As it is persistent, the maximum residues from ground and aerial application are 0.193 ppm ground application and 0.213 ppm aerial application. As these residue levels are below the NOEC of 9.1 mg/L from the fathead minnow chronic study, chronic risks to freshwater fish are minimal.

(3) Plants

The risk to aquatic plants is determined by comparing the EEC's from ground and aerial applications to the EC_{50} values for duckweed and algae. As the highest EEC's, 48.8 ppb and 53.7 ppb, respectively, are less than the EC_{50} values of 92 and 140 ppm, metalaxyl is not expected to adversely affect aquatic plants.

(4) Endangered Species

The registered uses of metalaxyl do not present a hazard to endangered terrestrial and aquatic animals or plant species.

b. Ecological Effects Data

The ecotoxicological data base is adequate to characterize the toxicity of metalaxyl to nontarget terrestrial and aquatic organisms when used on terrestrial food, feed and nonfood sites.

(1) Terrestrial Animal Data

(A) Nontarget Insect Toxicity

The minimum data required to establish the acute toxicity to honey bees is an acute contact LD_{50} study with the technical material.

Nontarget Insect Acute Contact Toxicity Findings			
Species	**% Test Material**	**LD_{50}**	**Conclusion**
Apis mellifera	27.0	>100ug/bee	practically non-toxic

There is sufficient information to characterize metalaxyl as practically non-toxic to bees. The guideline requirement is fulfilled. (MRID# 00402767).

(B) Avian Acute Toxicity

In order to establish the toxicity of metalaxyl to birds, the following tests are required using the technical grade material: one avian single-dose oral (LD_{50}) study on one species (preferably mallard or bobwhite quail); two subacute dietary studies (LC_{50}) on one species of waterfowl (preferably the mallard duck) and one species of upland game bird (preferably bobwhite quail or ring-necked pheasant).

Avian Acute Oral Toxicity Findings			
Species	**% Test Material (TGAI)**	**LD_{50}**	**Conclusions**
Mallard duck	96.9	1466 mg/kg	slightly toxic

These results show that metalaxyl is slightly toxic to birds on an acute basis. The guideline requirement for the avian acute oral LD_{50} study is fulfilled. (MRID# 00236854)

(C) Avian Subacute Dietary Toxicity

Avian Subacute Dietary Toxicity Findings			
Species	**% Test Material**	**LC_{50}**	**Conclusions**
Bobwhite Quail	96.9	>10,000 ppm	practically nontoxic
Mallard Duck	96.9	>10,000 ppm	practically nontoxic
Japanese Quail	tech.	>10,000 ppm	practically nontoxic

On a subacute dietary basis, metalaxyl has been characterized as being practically non-toxic to avian species. (MRID#s 00077335; 00063989; 00234439).

(D) Avian Reproduction

Avian reproduction studies are required when birds may be exposed repeatedly or continuously through persistence, bioaccumulation, or multiple applications, or if mammalian reproduction tests indicate reproductive hazard. Present product labeling of metalaxyl allows several applications of the end-use product per growing season.

There are no avian reproduction studies in the current metalaxyl database. These studies are required to assess the chronic risk of metalaxyl to birds.

(E) Toxicity to Nontarget Mammals

Mammalian Acute Oral Toxicity Findings		
Species	**LD_{50}(mg/kg)**	**Conclusion**
Rat	1250 ppm	slightly toxic

The available mammalian data indicate that metalaxyl is slightly toxic to small mammals on an acute basis. (OPPTS Pesticide Fact Sheet 540/FS-88-116, 1988.

(2) Aquatic Animal Data

(A) Freshwater Fish Toxicity

(i) Acute testing with the TGAI

In order to establish the toxicity of a pesticide to freshwater fish, the minimum data required on the technical grade of the active ingredient are two freshwater fish toxicity studies. One study should use a coldwater species (preferably the rainbow trout), and the other should use a warmwater species (preferably the bluegill sunfish).

Freshwater Fish Acute Oral Toxicity Findings			
Species	**% Test Material (TGAI)**	**LC_{50}**	**Conclusions**
Rainbow trout (2 studies)	95.1 94.4	132 mg/L 130 mg/L	practically non-toxic
Bluegill sunfish (2 studies)	94.4 95.1	150 mg/L 139 mg/L	practically non-toxic

The results of the 96-hour acute toxicity studies indicate that metalaxyl can be characterized as being practically non-toxic to both cold and warm water fish. The guideline requirement for acute toxicity testing of the technical on freshwater fish is fulfilled. (MRID #s 00071303, 00100447, 00236854, 00071302)

(ii) Acute testing with the formulated product

Formulated product testing was required on fish by the Guidance for the Reregistration of Pesticide Products Containing Metalaxyl as the Active Ingredient (1988).

Freshwater Fish Acute Testing with the Formulated Product			
Species	**% A.I.**	**Result EC50**	**Conclusion**
Bluegill TEP	27.9	27 mg/L	slightly toxic
Rainbow trout	27.9	18.4 mg/L	slightly toxic

The results of the 96-hour EC50 studies indicate that metalaxyl can be characterized as slightly toxic to freshwater fish. These data fulfill the data requirements for establishing the toxicity of formulated metalaxyl to fish. (MRID#s 00071301;00072396).

(iii) Chronic Test-Early Life Stage

The fish early life stage is required to support reregistration of Metalaxyl as its presence in water is likely to be continuous, recurrent or persistent, and multiple applications of the chemical may occur. The minimum data required to establish chronic toxicity of Metalaxyl to fish is the early life stage toxicity test based on survival of fish embryos and post-hatch larvae.

Chronic Test-Early Life Cycle		
Species	**% A.I.**	**NOEC**
Fathead minnow	90.1	9.1 mg/L

The highest concentration tested was 9.1 mg/L. Due to 90-199% survival the NOEC was established at 9.1 mg/L. These data fulfill the minimum data requirements for establishing the chronic toxicity of metalaxyl to fish. (MRID# 00071308).

(B) Freshwater Invertebrate Toxicity

(i) Acute testing with the TGAI

The minimum testing required to assess the hazard of a pesticide is a freshwater aquatic invertebrate toxicity test, preferably using first instar *Daphnia magna* or early instar amphipods, stoneflies, mayflies, or midges.

Freshwater Invertebrate Toxicity Findings			
Species	**% Test Material (TGAI)**	**LC_{50}**	**Conclusions**
Daphnia magna	95.1 96.9 94.4	121 mg/L 29 mg/L 28 mg/L	slightly toxic slightly toxic slightly toxic

There is sufficient information to characterize metalaxyl as slightly toxic to aquatic invertebrates. The guideline requirement is fulfilled. (MRID #s 00244183,00234439,00236854)

(ii) Acute testing with the formulated product

The minimum data requirement to establish acute toxicity of the formulated product to freshwater invertebrates is a 48-hour acute study.

Acute Toxicity Findings on the End-Use Formulation			
Species	**% A.I. formulated**	**LC50**	**Conclusion**
Daphnia magna	27	12 mg/L	slightly toxic

There is sufficient information to characterize the formulated product of metalaxyl as slightly toxic to freshwater aquatic invertebrates. The minimum data requirements for establishing the toxicity of the formulated product of metalaxyl are fulfilled. (MRID # 00244184)

(iii) Chronic Test-life cycle

The Daphnia Life Cycle is required to support reregistration of metalaxyl as its presence in water is likely to be continuous, recurrent or persistent, and multiple applications of the chemical may occur. The minimum data required

to establish chronic toxicity of metalaxyl to invertebrates if the Daphnia life cycle test based on reproduction, growth and survival.

Chronic Test-Life Cycle		
Species	**% A.I.**	**Results**
Daphnia magna	90.1	NOEC 1.27 mg/L LOEC 2.70 mg/L MATC 1.85 mg/L

Based on the data submitted, the No Observable Effect Concentration (NOEC) was established at 1.27 mg/L; the Lowest Observable Effect Concentration (LOEC) at 2.70 mg/L; and the Maximum Allowable Tolerated Concentration (MATC) at 1.85 mg/L. These data fulfill the minimum data requirements for establishing the chronic toxicity of metalaxyl to invertebrates. (MRID # 0071307)

(C) Estuarine/Marine Toxicity

Acute toxicity testing with estuarine and marine organisms is required when an end-use product is intended for direct application to the marine/estuarine environment or is expected to reach this environment in significant concentrations.

The requirements under this category include a 96-hour LC_{50} for an estuarine fish, a 96-hour LC_{50} for shrimp, and either a 48-hour embryo-larvae study or a 96-hour shell deposition study with oysters.

Estuarine/Marine Acute Toxicity Findings			
Species	**% Test Material (TGAI)**	**LC_{50}**	**Conclusions**
Mysidopsis bahia (shrimp)	96.1	25.7 ppm	slightly toxic
Crassostrea virginica	96.1	4.6 ppm	moderately toxic
Mysidopsis bahia	25.0	5.98 ppm	moderately toxic
Crassostrea virginica	25.0	4.4 ppm	moderately toxic

There is sufficient information to characterize the TGAI of metalaxyl as slightly toxic to mysid shrimp and the formulated product or metalaxyl as moderately toxic to mysid shrimp. Both the formulated product and TGAI are moderately toxic to the Eastern oyster. The guideline requirement is fulfilled. (MRID #s 00412881,00412881,00423375,00423781)

(3) Aquatic Plant Data

The minimal data required to establish toxicity to nontarget aquatic plants evaluate the effect of maximum exposure level of these plants. The preferred test species are: the algae, *Selenastrum capricornutum* and the duckweed, *Lemna gibba*.

Aquatic Plant Toxicity Findings		
Species	% A.I.	EC_{50}
Selenastrum capricornutum	90	140 ppm
Lemna gibba	90	92 ppm

Metalaxyl with an EC50 of 140 ppm (cells/ml) is not expected to exert a detrimental effect on the alga *Selenastrum* at application rates up to 3.0 lbs AI/acre. Metalaxyl with an EC50 of 92 ppm (frond counts) is not expected to exert a detrimental effect on Duckweed at application rates up to 3.0 lbs AI/acre. The minimum data requirements for establishing the toxicity of metalaxyl to aquatic plants are fulfilled. (MRID #s 00257626,00257626)