FEB 18 1987

RCB

Rev. 4/14/82 Toxicology Branch/HED Review

Caswell No(s).: 375AA

To: Lois Rossi, Product Manager 21, Registration Division (TS-767C) File petition

Registration No(s).: 100-601

Pesticide Petition No(s).: 6F3387/6H5499

Chemical(s): Metalaxyl

Requested Action(s): Revised Section F for the above petitions to include 20 ppm on tomato pomace and 1.0 ppm on sugar beet molasses (see attached for previous request)

Recommendation: Assuming the existing tolerances on meat, milk, and eggs are adequate, there are adequate data available to support the proposed feed additive tolerances on tomato pomace (20 ppm) and sugar beet molasses (1 ppm). Remaing tolerances were previously approved September 5, 1986 (see attached review).
Inert(s) cleared 180.1001

% of ADI occupied: Existing: not applicable Resulting: not applicable

Resulting % increase in TMRC: not applicable

Data considered in setting the ADI: See Attached FR Notice dated December 4, 1985

Attached (?): ADI printout: YES ; TOX "one-liner": NO ; DER: NO

Existing regulatory actions against registration: None

RPAR status: None

New Data: NOne

Data gaps:

Comments:

Reviewer: Roger Gardner R. G.

Date: 2/17/87

REVIEWER

Rev. 4/14/82 Toxicology Branch/HED Review

SEP 5 1986 Caswell No(s).: 375AA

To: Henry Jacoby, Product Manager 21, Registration Division (TS-767C)

Registration No(s).: 100-601, 100-607, 100-629

Pesticide Petition No(s).: 6F3387/6H5499

Chemical(s): Metalaxyl

Requested Action(s): Tolerances of 1 ppm for Metalaxyl on fruiting vegetables (except cucurbits) and 0.1 ppm on sugar beets and sugar beet tops

Recommendation: There are adequate data to support the requested Tolerance

Inert(s) cleared 180.1001:

% of ADI occupied: Existing: 9.361 Resulting: 9.575

Resulting % increase in TMRC: 2.3

Data considered in setting the ADI: See Attached FR Notice dated December 4, 1985

Attached (?): ADI printout: YES ; TOX "one-liner": NO ; DER: NO

Existing regulatory actions against registration: None

RPAR status: None

New Data: None

Data gaps:

Comments:

Reviewer: Roger Gardner R. G. Date: 9/5/86 SEP 5 1986

ENVIRONMENTAL PROTECTION AGENCY

40 CFR PART 180

[PP 1F2537, 2F2743, 2F2762, 2F2764, 3F2788, 3F2816, 3F2827, 3F2847, 3F2848, 3F2918, 3F2919, 3F2955/R804; FRL-2934-3]

Pesticide Tolerances for Metalaxyl

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This rule establishes tolerances for the combined residues of the fungicide metalaxyl and its metabolites in or on certain raw agricultural commodities. This regulation to establish maximum permissible levels of residues of metalaxyl in or on the commodities, was requested through petitions submitted by Ciba-Geigy Corp. Elsewhere in this issue of the Federal Register, food and feed additive regulations for metalaxyl are also being established.

EFFECTIVE DATE: Effective on December 4, 1985.

ADDRESS: Written objections, identified by the document control number [PP 1F2587, 2F2743, 2F2762, 2F2764, 3F2788, 3F2818, 3F2827, 3F2847, 3F2848, 3F2918, 3F2919, 3F2955/R804] may be submitted to the:

Hearing Clerk (A-110), Environmental Protection Agency, Rm. M-3708, 401 M. St., SW., Washington, D.C. 20460.

FOR FURTHER INFORMATION CONTACT:

By mail: Henry M. Jacoby, Product Manager (PM) 21, Registration Division (TS-767C), Environmental Protection Agency, 401 M. St., SW., Washington, D.C. 20460.

Office location and telephone number: Rm. 227, CM#2 1921 Jefferson Davis Highway, Arlington, VA 22202 (703-557-1900).

SUPPLEMENTARY INFORMATION:

1. EPA issued notices, published in the Federal Register, which announced that Ciba-Geigy Corp., Agricultural Division, P.O. Box 11422, Greensboro, NC 27409, had submitted pesticide petitions (PP) to EPA requesting that the Administrator, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act, propose the establishment of tolerances for the fungicide metalaxyl [*N*-(2,6-dimethylphenyl)-*N*-(methoxyacetyl) alanine methyl ester] and its metabolites containing the 2,6-dimethyl aniline moiety and the *N*-(2-hydroxymethyl-6-methyl) moiety, expressed as metalaxyl.

The petitions, the Federal Register (FR) citations, the commodities included, and the tolerance limitations follow:

a. *PP 1F2537*. 46 FR 48755; October 2, 1981. Green hops at 0.2 part per million (ppm). Amended in 47 FR 30640; July 14, 1982 by increasing the proposed tolerance for green hops from 0.2 ppm to 0.5 ppm.

b. *PP 2F2743*. 47 FR 41654; September 22, 1982. Pineapples and pineapple fodder at 0.1 ppm. Amended in 47 FR 57128; December 22, 1982 by adding pineapple forage at 0.1 ppm.

c. *PP 2F2762*. 47 FR 53117; November 24, 1982. Broccoli, cabbage, and cauliflower at 1.0 ppm; head lettuce at 5.0 ppm, and spinach at 10.0 ppm. The tolerance request for broccoli, cabbage and cauliflower at 1.0 ppm was superceded and reproposed in PP 3F2955 (item 1.1).

d. *PP 2F2764*. 47 FR 53117; November 24, 1982. Soybean grain at 0.5 ppm; soybean forage and fodder at 7.0 ppm; wheat grain at 0.2 ppm; wheat forage and straw at 2.0 ppm. Amended in 48 FR 31082; July 6, 1983 by deleting soybean grain, soybean fodder, and soybean forage, and adding wheat fodder at 2.0 ppm.

e. *PP 3F2788*. 47 FR 57127; December 22, 1982. Citrus fruit at 1.0 ppm.

f. *PP 3F2818*. 48 FR 11155; March 16, 1983. Soybean fodder and soybean forage at 7.0 ppm, and soybean grain at 0.5 ppm. Ciba-Geigy subsequently amended PP 3F2818 by redesignating soybean fodder as soybean hay and increasing the proposed tolerances for soybean hay and soybean fodder to 8.0 ppm and soybean grain to 1.0 ppm.

g. *PP 3F2827*. 48 FR 11156; March 16, 1983. Brassica (cole) leafy vegetables, fruiting vegetables (cucurbits), fruiting vegetables (except cucurbits), leafy vegetables (except brassica), leaves of root and tuber vegetables, root and tuber vegetables, and sunflowers all at 0.1 ppm. Amended in 48 FR 31082; July 6, 1982 by changing the identity of fruiting vegetables (cucurbits) to cucurbit vegetables and increasing the proposed tolerance from 0.1 ppm to 1.0 ppm. Further amended in 48 FR 44267; September 28, 1983 by (1) deleting the proposed tolerances on fruiting vegetables (cucurbits), leaves and roots of tuber vegetables, and root and tuber vegetables; and (2) adding the fruiting vegetables group (except cucurbits and tomatoes), beets, beet tops, and sunflower forage at 0.1 ppm.

h. *PP 3F2847*. 48 FR 15980; April 20, 1983. Apples at 0.2 ppm.

i. *PP 3F2848*. 48 FR 15980; April 20, 1983. Raspberries at 0.5 ppm.

j. *PP 3F2918*. 48 FR 40452; September 7, 1983. Legume vegetable fodder at 3.0 ppm, legume vegetable forage at 5.0

ppm, and legume vegetable seeds at 0.2 ppm.

k. *PP 3F2919*, 48 FR 40432, September 7, 1983. Peanut fodder at 20.0 ppm, peanut nuts at 0.2 ppm, peanut shells at 2.0 ppm.

l. *PP 3F2955*, 48 FR 44904, September 30, 1983. Broccoli, cabbage, and cauliflower at 2.0 ppm.

There were no comments received in response to the notices of filing.

2. The data submitted in these petitions and other relevant material have been evaluated. The scientific data considered in support of these tolerances include:

a. A 3-month dietary study in rats with a no-observed-effect level (NOEL) at 12.5 mg/kg body weight/day (250 ppm).

b. A teratology study in rats with a NOEL of 400 mg/kg body weight (highest dose tested). Metalaxyl was not teratogenic, even in the presence of maternal toxicity.

c. A teratology study in rabbits with a NOEL of 300 mg/kg body weight (highest dose tested). Metalaxyl was not teratogenic, even in the presence of maternal toxicity.

d. A *Salmonella* mutagenicity study that was negative for reverse mutations with and without mammalian microsome activation.

e. A mouse dominant lethal study that was negative for mutagenicity.

f. A 3-generation rat reproduction study with a NOEL of 62.5 mg/kg body weight/day (1,250 ppm).

g. A 6-month dog feeding study with a NOEL of 6.3 mg/kg body weight (250 ppm).

h. A 2-year rat chronic feeding/oncogenic study with no compound-related oncogenic effects under the conditions of the study at dietary levels up to 1,250 ppm. The NOEL is 12.5 mg/kg body weight/day (250 ppm) based upon slight increases in liver weight to body weight ratios at 1,250 ppm.

i. A 2-year mouse oncogenic study with no compound-related oncogenic effects under the conditions of the study at dietary levels up to 1,250 ppm.

Because of concerns raised over some equivocal increases in tumor incidences in the male mouse liver and the male rat adrenal medulla, and the female rat thyroids, the two chronic feeding studies were submitted to Environmental Pathology Laboratories (EPL) for an independent reading of the microscopic slides. The new pathological evaluation by EPL and the original reports of the rat and mouse oncogenicity studies were then both submitted for review to EPA's Carcinogen Assessment Group (CAG). A final review of the oncogenicity studies and related material was performed by the peer review committee of the Toxicology Branch of the Office of Pesticide Program (OPP).

The four major issues evaluated by CAG and the peer review group included: (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) whether the highest dose tested (1,250 ppm) in the rat and mouse oncogenicity studies represented a maximum tolerated dose (MTD).

Regarding the thyroid tumors in female rats, the peer review group concluded that the increased incidences of thyroid tumors in females of treated groups were not compound-related. This conclusion was based on the following: (1) There was no progression of benign tumors (adenomas) to malignancy (carcinomas, (2) there was no increase in hyperplastic changes, (3) there was no dose-response relationship, and (4) the two re-evaluations of the microscopic slides by the pathologists at EPL and the Toxicology Branch in OPP further mitigated any apparent effect observed in the original report.

The issue concerning a possible treatment-related increase of adrenal medullary gland tumors, namely pheochromocytomas, in the male rat was also reassessed by both CAG and the peer review committee. Both concluded that the data, especially in view of the re-evaluation of the microscopic slides performed by EPL, did not support a compound-related increase of adrenal medullary tumors; the incidences of pheochromocytomas more accurately represented spontaneous variations of a common occurring tumor in the aged rat.

The analysis of the significance of the equivocal increase in the incidence of liver tumors in male mice was very similar to that performed for the rat thyroid and adrenal gland tumors. The original pathological reading of the tissue slides reported an elevated incidence of tumors in some treatment groups; however, these increases were not evident after a re-evaluation of the microscopic slides was performed by an independent pathologist at the EPL and by the readings of a CAG pathologist. The peer review committee concurred that the re-evaluation of the slides is reliable and does not show any compound related increase in the incidence of liver tumors in the mouse.

The issue of whether a maximum tolerated dose (MTD) of metalaxyl was used in the rat and mouse 2-year feeding studies was considered by CAG and the OPP peer review committee. Although increased liver weights and vacuolation of hepatocytes in the rat study and fatty infiltration of the liver in the mouse study indicated treatment-related effects, these weight and histologic changes in the liver suggest that a pharmacologic rather than a toxic response was observed at the highest dose tested (1,250 ppm). The pharmacologic response most often associated with these types of histologic and weight changes in the liver is the induction of the microsomal drug-metabolizing enzymes of the liver. A compound's self induction of these hepatic enzymes, which in turn leads to an acceleration of its own rate of metabolism, is the body's compensatory mechanism for handling excess exposure to a foreign chemical and may not in itself represent a minimal toxic effect.

Nevertheless, the Agency believes that the data from the rat and mouse long-term studies are sufficient to support the conclusion that metalaxyl does not show an oncogenic potential in laboratory animals even though the MTD may not have been tested and that further testing is not warranted. This conclusion is supported by the following: (1) The doses tested in both the rat and mouse long term studies were high enough to produce compound-related changes in liver weight and/or histology, probably representing a pharmacologic response, (2) metalaxyl is not structurally related to known oncogens, (3) available mutagenic evidence indicates no potential genotoxic activity which correlates with the negative oncogenic potential demonstrated in long term testing, (4) under the conditions of the rat and mouse tests no indication of compound induced oncogenic effects were noted at any of the treatment doses, sexes, or species.

The acceptable daily intake (ADI), based on the 6-month dog feeding study (NOEL of 6.3 mg/kg body weight/day) and a 100-fold safety factor, is calculated to be 0.063 mg/kg/day. The maximum permitted intake (MPI) for a 60-kg human is calculated to be 3.8 mg/day. These tolerances and the established tolerances result in a theoretical maximum residue contribution (TMRC) of 0.378 mg/day (1.5 kg diet) for a 60-kg human and utilize 9.9 percent of the ADI.

The nature of the residue is adequately understood and the adequate analytical methods are available for enforcement purposes as follows: gas chromatography with alkali flame ionization detector (PP's 1F2537, 2F2743, 2F2762, 2F2764, 3F2786, 3F2818, 3F2847, 3F2848, 3F2918); radioactive

counting and gas chromatography (PP 3F2827); and capillary gas chromatography using a nitrogen/phosphorus detector (NPD) operating in the nitrogen-specific mode (PP's 3F2919, 3F2955).

The pesticide is considered useful for the purposes for which the tolerances are sought. Based on the information and data considered, the Agency concludes that the establishment of the tolerances would protect the public health. Therefore, the tolerances are established as set forth below.

Any person adversely affected by this regulation may, within 30 days after publication of this rule in the Federal Register, file written objections with the Hearing Clerk, at the address given above. Such objections should specify the provisions of the regulation deemed objectionable and the grounds for the objections. If a hearing is requested, the objections must state the issues for the hearing and the grounds for the objections. A hearing will be granted if the objections are supported by grounds legally sufficient to justify the relief sought.

Pursuant to the requirement of the Regulatory Flexibility Act (Pub. L. 96-354, 94 Stat. 1164, 5 U.S.C. 601-612), the Administrator has determined that regulations establishing new tolerances or raising tolerance levels or establishing exemptions from tolerance requirements do not have a significant economic impact on a substantial number of small entities. A certification statement to this effect was published in the Federal Register of May 4, 1981 (46 FR 24950).

The Office of Management and Budget has exempted this rule from the requirement of section 3 of Executive Order 12291.

List of Subjects in 40 CFR Part 180

Administrative practice and procedures, Agricultural commodities, Pesticides and pests.

Dated: November 22, 1985.

Steven Schatzow,

Director, Office of Pesticide Programs.

PART 180—[AMENDED]

Therefore, 40 CFR Part 180 is amended as follows:

1. The authority citation for Part 180 continues to read as follows:

Authority: 21 U.S.C. 346.

2. Section 180.408 is amended as follows:

a. By designating the existing text as paragraph (a), revising the list of commodities under paragraph (a) and adding paragraph (b) to read as follows:

§ 180.408 Metalaxyl; tolerances for residues.

(a) * * *

Commodities	Parts per million
Apples	0.2
Avocados	4.0
Beans	0.1
Beet, tops	0.1
Brassica (cole) leafy vegetables group (except broccoli, cabbage, and cauliflower)	0.1
Broccoli	2.0
Cabbage	2.0
Cattle, fat	0.4
Cattle, kidney	0.4
Cattle, meat	0.05
Cattle, mbyp (except kidney and liver)	0.05
Cauliflower	2.0
Citrus fruit	1.0
Cottonseed	0.1
Cucurbit vegetables group	1.0
Eggs	0.05
Fruiting vegetables (except cucurbits) group (except tomatoes)	0.1
Goats, fat	0.4
Goats, kidney	0.4
Goats, liver	0.4
Goats, meat	0.05
Goats, mbyp (except kidney and liver)	0.05
Grain, crops	0.1
Grasses, forage	0.1
Hogs, fat	0.4
Hogs, kidney	0.4
Hogs, liver	0.4
Hogs, meat	0.05
Hogs, mbyp (except kidney and liver)	0.05
Hops, green	0.5
Horses, fat	0.4
Horses, kidney	0.4
Horses, liver	0.4
Horses, meat	0.05
Horses, mbyp (except kidney and liver)	0.05
Leafy vegetables (except brassica) group	0.1
Legume vegetable forage	8.0
Legume vegetable group (dry or succulent)	0.2
Lettuce, head	5.0
Milk	0.02
Onions, dry bulb	3.0
Onions, green	10.0
Peanut, hay	20.0
Peanut, vines	20.0
Peanut, nuts	0.2
Peanut, shells	2.0
Pineapples	0.1
Pineapple, fodder	0.*
Pineapple, forage	0.1
Poultry, fat	0.4
Poultry, kidney	0.4
Poultry, liver	0.4
Poultry, meat	0.05
Poultry, mbyp (except kidney and liver)	0.05
Potatoes	0.5
Raspberries	0.5
Sheep, fat	0.4
Sheep, kidney	0.4
Sheep, liver	0.4
Sheep, meat	0.05
Sheep, mbyp	0.05
Soybean, grain	1.0
Spinach	10.0
Sunflowers	0.1
Sunflower, forage	0.1
Tomatoes	1.0

(b) Indirect or inadvertent tolerances. Tolerances are established for indirect or inadvertent residues of metalaxyl in or on the raw agricultural commodities when present therein as a result of the application of metalaxyl to growing crops listed in paragraph (a) of this section and other non-food crops to read as follows:

Commodities	Part per million
Wheat, fodder	2.0
Wheat, forage	2.0
Wheat, grain	0.2
Wheat, straw	2.0

[FR Doc. 85-28825 Filed 12-3-85; 8:45 am]

BILLING CODE 6560-50-M

TOXICOLOGY BRANCH ADI PRINTOUT Date: 09/05/86

Metalaxyl 6m feeding- dog ADI = 0.060000 mg/kg/day
Caswell #375AA NOEL = 6.2500 mg/kg Safety Factor = 100
CFR No. 180.408 LEL = 25.0000 mg/kg
Status: TOX ADI complete 5/23/86. ORD verified 7/8/86.

DRAFT

RESIDUE CONTRIBUTION OF PUBLISHED TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
6	Avocados	4.000		0.03	0.001800
41	Cottonseed (oil)	0.100		0.15	0.000225
47	Cucumbers, not inc. pickles	1.000		0.34	0.005100
54	Eggs	0.050		2.77	0.002078
64	Grain crops	0.100		13.79	0.020685
90	Meat, red	0.400		10.81	0.064860
92	Melons	1.000		2.00	0.030000
93	Milk and dairy products	0.020		28.62	0.008586
106	Onions, dry bulb	3.000		0.72	0.032400
107	Onions, green	10.000		0.11	0.016500
115	Peanuts	0.100		0.36	0.000540
127	Potatoes	0.500		5.43	0.040725
128	Poultry	0.400		2.94	0.017640
143	Seed and Pod vegetables	0.100		3.66	0.005490
163	Tomatoes	1.000		2.87	0.043050
191	Squash	1.000		0.11	0.001650
203	Kidney	0.400		0.03	0.000180
211	Liver	0.400		0.03	0.000180

TMRC % ADI
0.004861 mg/kg/day (60kg BW, 1.5kg diet) 8.102458

RESIDUE CONTRIBUTION OF TOX-APPROVED TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
5	Asparagus	7.000	6F3330	0.14	0.014700000
67	Grapes, not including raisins	2.000	6F3362	0.45	0.013500000
134	Raisins	6.000	6F3362	0.04	0.003600000
152	Strawberries	5.000	6F3337	0.18	0.013500000

TMRC % ADI
0.005616 mg/kg/day (60kg BW, 1.5kg diet) 9.360792

RESIDUE CONTRIBUTION OF NEW (PENDING) TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
53	Eggplant	1.000	6F3387	0.03	0.000450000
120	Peppers	1.000	6F3387	0.12	0.001800000
154	Sugar, cane and beet	0.100	6F3387	3.64	0.005460000

TMRC	% ADI
0.005745 mg/kg/day (60kg BW, 1.5kg diet)	9.574958

End Of Document

Copies to TOX, RCB 2/12

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

FEB 11 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Expedited Review for Ciba-Geigy - Metalaxyl on Sugar Beets and Fruiting Vegetables

FROM: Edwin F. Tinsworth, Director
Registration Division (TS-767C)

TO: John W. Melone, Director
Hazard Evaluation Division (TS-769C)

I am requesting an expedited review of data related to pending petitions on the fungicide metalaxyl. These actions are new food and feed uses for the chemical. Ciba-Geigy has responded directly to HED reviews of data previously submitted to the Agency. This new information may allow the Agency to approve the registration of metalaxyl for these uses during the upcoming growing season.

I am requesting that HED complete its review of these data by February 24, 1987 and return the completed reviews to Lois Rossi, Product Manager 21.

Requested DDL of 3/2/87 (Quick- Mayer 2/13/87)

Date _____

REQUEST FOR EXPEDITE REVIEW

PM: 21 CHEMICAL: METALAXYL

EPA IDENTIFICATION NUMBER(S): 6F3387

TOX RECORD # 189306 20131

RCB RECORD # 189306 "

DATE(S) SENT TO HED: 2/10/87

HED BRANCH(ES) REQUIRED TO RESPOND TO EXPEDITE: TOX

RCB

EXPEDITE DUE DATE: 2/24/87

SPECIAL INSTRUCTIONS TO HED BRANCH(ES):

End Of Document

Copies to
1) Schmitt TOX, RCB 2/12

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

EXPEDITE

2) Quick.

FEB 11 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Please Expedite
Get extension
if needed, let
me know new
date

2/18

MEMORANDUM

SUBJECT: Expedited Review for Ciba-Geigy - Metalaxyl on Sugar Beets and Fruiting Vegetables

FROM: Edwin F. Tinsworth, Director
Registration Division (TS-767C)

TO: John W. Melone, Director
Hazard Evaluation Division (TS-769C)

I am requesting an expedited review of data related to pending petitions on the fungicide metalaxyl. These actions are new food and feed uses for the chemical. Ciba-Geigy has responded directly to HED reviews of data previously submitted to the Agency. This new information may allow the Agency to approve the registration of metalaxyl for these uses during the upcoming growing season.

I am requesting that HED complete its review of these data by February 24, 1987 and return the completed reviews to Lois Rossi, Product Manager 21.

3/2

Note Quick
get extension
to 3/2

Date _____

REQUEST FOR EXPEDITE REVIEW

PM: 21 CHEMICAL: METALAXYL

EPA IDENTIFICATION NUMBER(S): 6F3387

TOX RECORD # 189306

RCB RECORD # 189306

DATE(S) SENT TO HED: 2/10/87

HED BRANCH(ES) REQUIRED TO RESPOND TO EXPEDITE: TOX

RCB

EXPEDITE DUE DATE: 2/24/87

SPECIAL INSTRUCTIONS TO HED BRANCH(ES):

End Of Document

Agricultural Division

CIBA-GEIGY Corporation
P.O. Box 18300
Greensboro, North Carolina 27419
Telephone 919 292 7100

CIBA-GEIGY

EVPRESS

To Dick Griffith
for review on 2/13/87.

January 30, 1987

Ms. Lois A. Rossi
Acting Product Manager (21)
Registration Division (TS-767C)
Office of Pesticide Programs
U.S. Environmental Protection Agency
401 M. Street, S.W.
Washington, D.C. 20460

RH

Dear Ms. Rossi:

SUBJECT: TECHNICAL METALAXYL - EPA REG. NO. 100-601
PP6F3387/FAP6H5499
FRUITING VEGETABLES/SUGAR BEETS
RESPONSE TO YOUR LETTER OF NOVEMBER 25, 1986

This letter and the enclosures will address the deficiencies noted in the Residue Chemistry Branch review of September 26, 1986 regarding the subject petition. A copy of this review was received with your letter of November 25, 1986.

The following are enclosed:

1. A revised section B including a seven day pre-harvest interval for tomatoes and peppers. (Located in Volume 1 of 1)

2. A revised Section F combining tolerances for wet and dry tomato pomace into one requested tolerance at 20 ppm. The revised Section F also now proposes a feed additive tolerance for sugar beet molasses at 1.0 ppm. (Located in Volume 1 of 1)

   This tolerance is proposed at this time to meet the immediate needs of the sugar beet industry. As you may be aware, discussions regarding the need for a processing study in sugar beets, as asked for in the RCB review of September 26, 1986, have taken place with Mr. Charles Trichilo of RCB and Mr. Phil Hundemann of your office.

   Much of this discussion has been handled by Mr. Jerome Rockwell of Gustafson, Inc. on behalf of CIBA-GEIGY. Gustafson's interests in the seed treatment market prompted them to hold a meeting in the latter part of 1986 with EPA officials regarding the need for certain data requirements for minor use seed treatment crops. Mr.

Rockwell attended this meeting and was well prepared to enter into the discussions regarding the processing study for sugar beets.

As CIBA-GEIGY now understands it, the processing study will still be required. However, in the interest of meeting the needs of the sugar beet industry, EPA is agreeable in setting an interim tolerance based upon the maximum concentration of molasses from sugar beets.

To that end, Mr. Rockwell contacted the Beet Sugar Development Foundation and obtained a letter stating the maximum concentration that has been found based on their experience is 7X. The proposed tolerance for sugar beets and sugar beet tops is 0.1 ppm. Using a 7X concentration factor, a tolerance in sugar beet molasses is therefore proposed at 1.0 ppm. A copy of the aforementioned letter is enclosed for your information.

I might mention that CIBA-GEIGY is completing a processing study in sugar beets for a proposed soil treatment use of metalaxyl. The treatment regime used to generate residue samples for analysis was conducted at much higher rates than would be used for seed treatment. It is CIBA-GEIGY's opinion that such a study would also meet the requirement for a processing study for seed treatment uses. We trust the Agency will concur with our position. The study should be available in early spring for Agency review. In the meantime, it is hoped an interim tolerance can be established in sugar beets to help meet the needs of this industry.

3. A revised Section G with rationale for the proposed tolerance in sugar beet molasses and transfer of residues to beef and dairy cattle and poultry.

4. Five copies of revised labeling incorporating the 7-day PHI under Peppers and Tomatoes and adding a statement cautioning the user when tank mixing with any chemical for any crop on the Ridomil 2E label, to check the other product label to make certain the use is labeled and that use patterns are compatible.

5. Chromatograms as requested on page 11 of the RCB review for tomatoes and peppers. (Located in Volumes 2 of 3 and 3 of 3 of the data accompanying this submission.)

Also enclosed is a completed EPA Form 8570-1.

We trust that with the submission of the above, the subject petition can move forward with the establishment of the requested tolerances.

By copy of this letter to Mr. Rick Tinsworth, CIBA-GEIGY

requests the Agency expedite the review of this data. On behalf of Gustafson and the sugar beet industry, we certainly appreciate any effort the Agency can make to resolve this situation in a timely manner.

Sincerely,

Karen S. Stumpf

Karen S. Stumpf
Regulatory Specialist
Regulatory Affairs

Enclosures

cc: Mr. Rick Tinsworth
Director, Registration Division, EPA

Mr. Charles Trichilo, Chief, Residue Chemistry Branch, EPA

Mr. Jerome Rockwell
Gustafson, Inc.

End Of Document

RCB
Griffith
File petition

Rev. 4/14/82 Toxicology Branch/HED Review

SEP 5 1986

Caswell No(s).: 375AA

To: Henry Jacoby, Product Manager 21, Registration Division (TS-767C)

Registration No(s).: 100-601, 100-607, 100-629

Pesticide Petition No(s).: 6F3387/6H5499

Chemical(s): Metalaxyl

Requested Action(s): Tolerances of 1 ppm for Metalaxyl on fruiting vegetables (except cucurbits) and 0.1 ppm on sugar beets and sugar beet tops

Recommendation: There are adequate data to support the requested Tolerance

Inert(s) cleared 180.1001:

% of ADI occupied: Existing: 9.361 Resulting: 9.575

Resulting % increase in TMRC: 2.3

Data considered in setting the ADI: See Attached FR Notice dated December 4, 1985

Attached (?): ADI printout: YES ; TOX "one-liner": NO ; DER: NO

Existing regulatory actions against registration: None

RPAR status: None

New Data: NOne

Data gaps:

Comments:

Reviewer: Roger Gardner R. G.

Date: 9/5/86 SEP 5 1986

Section Head: Jane C Harris 9/5/86

Branch Chief: 9/5/86

ENVIRONMENTAL PROTECTION AGENCY

40 CFR PART 180

[PP 1F2537, 2F2743, 2F2762, 2F2764, 3F2786, 3F2818, 3F2827, 3F2847, 3F2848, 3F2918, 3F2919, 3F2955/R804; FRL-2934-3]

Pesticide Tolerances for Metalaxyl

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This rule establishes tolerances for the combined residues of the fungicide metalaxyl and its metabolites in or on certain raw agricultural commodities. This regulation, to establish maximum permissible levels of residues of metalaxyl in or on the commodities, was requested through petitions submitted by Ciba-Geigy Corp. Elsewhere in this issue of the Federal Register, food and feed additive regulations for metalaxyl are also being established.

EFFECTIVE DATE: Effective on December 4, 1985.

ADDRESS: Written objections, identified by the document control number [PP 1F2587, 2F2743, 3F2762, 2F2764, 3F2786, 3F2818, 3F2827, 3F2847, 3F2848, 3F2918, 3F2919, 3F2955/R804] may be submitted to the:

Hearing Clerk (A-110), Environmental Protection Agency, Rm. M-3708, 401 M St., SW., Washington, D.C. 20460.

FOR FURTHER INFORMATION CONTACT:

By mail: Henry M. Jacoby, Product Manager (PM) 21, Registration Division (TS-767C), Environmental Protection Agency, 401 M. St., SW., Washington, D.C. 20460.

Office location and telephone number: Rm. 227, CM#2 1921 Jefferson Davis Highway, Arlington, VA 22202 (703-557-1900).

SUPPLEMENTARY INFORMATION:

1. EPA issued notices, published in the Federal Register, which announced that Ciba-Geigy Corp., Agricultural Division, P.O. Box 11422, Greensboro, NC 27409, had submitted pesticide petitions (PP) to EPA requesting that the Administrator, pursuant to section 409(d) of the Federal Food, Drug, and Cosmetic Act, propose the establishment of tolerances for the fungicide metalaxyl [*N*-(2,6-dimethylphenyl)-*N*-(methoxyacetyl) alanine methyl ester] and its metabolites containing the 2,6-dimethyl aniline moiety and the *N*-(2-hydroxymethyl-6-methyl) moiety, expressed as metalaxyl.

The petitions, the Federal Register (FR) citations, the commodities included, and the tolerance limitations

a. *PP 2F2537*. 46 FR 48755; October 2, 1981. Green hops at 0.2 part per million (ppm). Amended in 47 FR 30640; July 14, 1982 by increasing the proposed tolerance for green hops from 0.2 ppm to 0.5 ppm.

b. *PP 2F2743*. 47 FR 41654; September 22, 1982. Pineapples and pineapple fodder at 0.1 ppm. Amended in 47 FR 57128; December 22, 1982 by adding pineapple forage at 0.1 ppm.

c. *PP 2F2762*. 47 FR 53117; November 24, 1982. Broccoli, cabbage, and cauliflower at 1.0 ppm; head lettuce at 5.0 ppm, and spinach at 10.0 ppm. The tolerance request for broccoli, cabbage and cauliflower at 1.0 ppm was superceded and reproposed in PP 3F2955 (item 1.1).

d. *PP 2F2764*. 47 FR 53117; November 24, 1982. Soybean grain at 0.5 ppm; soybean forage and fodder at 7.0 ppm; wheat grain at 0.2 ppm; wheat forage and straw at 2.0 ppm. Amended in 48 FR 31082; July 6, 1983 by deleting soybean grain, soybean fodder, and soybean forage, and adding wheat fodder at 2.0 ppm.

e. *PP 3F2786*. 47 FR 57127; December 22, 1982. Citrus fruit at 1.0 ppm.

f. *PP 3F2818*. 48 FR 11155; March 16, 1983. Soybean fodder and soybean forage at 7.0 ppm, and soybean grain at 0.5 ppm. Ciba-Geigy subsequently amended PP 3F2818 by redesignating soybean fodder as soybean hay and increasing the proposed tolerances for soybean hay and soybean fodder to 8.0 ppm and soybean grain to 1.0 ppm.

g. *PP 3F2827*. 48 FR 11156; March 16, 1983. Brassica (cole) leafy vegetables, fruiting vegetables (cucurbits), fruiting vegetables (except cucurbits), leafy vegetables (except brassica), leaves of root and tuber vegetables, root and tuber vegetables, and sunflowers all at 0.1 ppm. Amended in 48 FR 31082; July 6, 1982 by changing the identity of fruiting vegetables (cucurbits) to cucurbit vegetables and increasing the proposed tolerance from 0.1 ppm to 1.0 ppm. Further amended in 48 FR 44267; September 28, 1983 by (1) deleting the proposed tolerances on fruiting vegetables (cucurbits), leaves and roots of tuber vegetables, and root and tuber vegetables; and (2) adding the fruiting vegetables group (except cucurbits and tomatoes), beets, beet tops, and sunflower forage at 0.1 ppm.

h. *PP 3F2847*. 48 FR 16980; April 20, 1983. Apples at 0.2 ppm.

i. *PP 3F2848*. 48 FR 16980; April 20, 1983. Raspberries at 0.5 ppm.

j. *PP 3F2918*. 48 FR 40452; September 7, 1983. Legume vegetable fodder at 3.0

ppm, and legume vegetable seeds at 0.2 ppm.

k. *PP 3F2918*. 48 FR 40432; September 7, 1983. Peanut fodder at 20.0 ppm, peanut nuts at 0.2 ppm, peanut shells at 2.0 ppm.

l. *PP 3F2955*. 48 FR 44904; September 30, 1983. Broccoli, cabbage, and cauliflower at 2.0 ppm.

There were no comments received in response to the notices of filing.

2. The data submitted in these petitions and other relevant material have been evaluated. The scientific data considered in support of these tolerances include:

a. A 3-month dietary study in rats with a no-observed-effect level (NOEL) at 12.5 mg/kg body weight/day (250 ppm).

b. A teratology study in rats with a NOEL of 400 mg/kg body weight (highest dose tested). Metalaxyl was not teratogenic, even in the presence of maternal toxicity.

c. A teratology study in rabbits with a NOEL of 300 mg/kg body weight (highest dose tested). Metalaxyl was not teratogenic, even in the presence of maternal toxicity.

d. A *Salmonella* mutagenicity study that was negative for reverse mutations with and without mammalian microsome activation.

e. A mouse dominant lethal study that was negative for mutagenicity.

f. A 3-generation rat reproduction study with a NOEL of 62.5 mg/kg body weight/day (1,250 ppm).

g. A 6-month dog feeding study with a NOEL of 6.3 mg/kg body weight (250 ppm).

h. A 2-year rat chronic feeding/oncogenic study with no compound-related oncogenic effects under the conditions of the study at dietary levels up to 1,250 ppm. The NOEL is 12.5 mg/kg body weight/day (250 ppm) based upon slight increases in liver weight to body weight ratios at 1,250 ppm.

i. A 2-year mouse oncogenic study with no compound-related oncogenic effects under the conditions of the study at dietary levels up to 1,250 ppm.

Because of concerns raised over some equivocal increases in tumor incidences in the male mouse liver and the male rat adrenal medulla, and the female rat thyroids, the two chronic feeding studies were submitted to Environmental Pathology Laboratories (EPL) for an independent reading of the microscopic slides. The new pathological evaluation by EPL and the original reports of the rat and mouse oncogenicity studies were then both submitted for review to EPA's Carcinogen Assessment Group (CAG). A final review of the oncogenicity studies and related material was performed by the peer review committee of the Toxicology Branch of the Office of Pesticide Program (OPP).

The four major issues evaluated by CAG and the peer review group included: (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) whether the highest dose tested (1,250 ppm) in the rat and mouse oncogenicity studies represented a maximum tolerated dose (MTD).

Regarding the thyroid tumors in female rats, the peer review group concluded that the increased incidences of thyroid tumors in females of treated groups were not compound-related. This conclusion was based on the following: (1) There was no progression of benign tumors (adenomas) to malignancy (carcinomas, (2) there was no increase in hyperplastic changes, (3) there was no dose-response relationship, and (4) the two re-evaluations of the microscopic slides by the pathologists at EPL and the Toxicology Branch in OPP further mitigated any apparent effect observed in the original report.

The issue concerning a possible treatment-related increase of adrenal medullary gland tumors, namely pheochromocytomas, in the male rat was also reassessed by both CAG and the peer review committee. Both concluded that the data, especially in view of the re-evaluation of the microscopic slides performed by EPL, did not support a compound-related increase of adrenal medullary tumors; the incidences of pheochromocytomas more accurately represented spontaneous variations of a common occurring tumor in the aged rat.

The analysis of the significance of the equivocal increase in the incidence of liver tumors in male mice was very similar to that performed for the rat thyroid and adrenal gland tumors. The original pathological reading of the tissue slides reported an elevated incidence of tumors in some treatment groups; however, these increases were not evident after a re-evaluation of the microscopic slides was performed by an independent pathologist at the EPL and by the readings of a CAG pathologist. The peer review committee concurred that the re-evaluation of the slides is reliable and does not show any compound related increase in the incidence of liver tumors in the mouse.

The issue of whether a maximum tolerated dose (MTD) of metalaxyl was used in the rat and mouse 2-year feeding studies was considered by CAG and the OPP peer review committee. Although increased liver weights and vacuolation of hepatocytes in the rat study and fatty infiltration of the liver in the mouse study indicated treatment-related effects, these weight and histologic changes in the liver suggest that a pharmacologic rather than a toxic response was observed at the highest dose tested (1,250 ppm). The pharmacologic response most often associated with these types of histologic and weight changes in the liver is the induction of the microsomal drug-metabolizing enzymes of the liver. A compound's self induction of these hepatic enzymes, which in turn leads to an acceleration of its own rate of metabolism, is the body's compensatory mechanism for handling excess exposure to a foreign chemical and may not in itself represent a minimal toxic effect.

Nevertheless, the Agency believes that the data from the rat and mouse long-term studies are sufficient to support the conclusion that metalaxyl does not show an oncogenic potential in laboratory animals even though the MTD may not have been tested and that further testing is not warranted. This conclusion is supported by the following: (1) The doses tested in both the rat and mouse long term studies were high enough to produce compound-related changes in liver weight and/or histology, probably representing a pharmacologic response. (2) metalaxyl is not structurally related to known oncogens. (3) available mutagenic evidence indicates no potential genotoxic activity which correlates with the negative oncogenic potential demonstrated in long term testing. (4) under the conditions of the rat and mouse tests no indication of compound induced oncogenic effects were noted at any of the treatment doses, sexes, or species.

The acceptable daily intake (ADI), based on the 6-month dog feeding study (NOEL of 6.3 mg/kg body weight/day) and a 100-fold safety factor, is calculated to be 0.063 mg/kg/day. The maximum permitted intake (MPI) for a 60-kg human is calculated to be 3.8 mg/day. These tolerances and the established tolerances result in a theoretical maximum residue contribution (TMRC) of 0.378 mg/day (1.5 kg diet) for a 60-kg human and utilize 9.9 percent of the ADI.

The nature of the residue is adequately understood and the adequate analytical methods are available for enforcement purposes as follows: gas chromatography with alkali flame ionization detector (PP's 1F2537, 2F2743, 2F2782, 2F2784, 3F2786, 3F2816, 3F2847, 3F2848, 3F2918); radioactive

counting and gas chromatography (PP 3F2827); and capillary gas chromatography using a nitrogen/phosphorus detector (NPD) operating in the nitrogen-specific mode (PP's 3F2819, 3F2955).

The pesticide is considered useful for the purposes for which the tolerances are sought. Based on the information and data considered, the Agency concludes that the establishment of the tolerances would protect the public health. Therefore, the tolerances are established as set forth below.

Any person adversely affected by this regulation may, within 30 days after publication of this rule in the Federal Register, file written objections with the Hearing Clerk, at the address given above. Such objections should specify the provisions of the regulation deemed objectionable and the grounds for the objections. If a hearing is requested, the objections must state the issues for the hearing and the grounds for the objections. A hearing will be granted if the objections are supported by grounds legally sufficient to justify the relief sought.

Pursuant to the requirement of the Regulatory Flexibility Act (Pub. L. 96-354, 94 Stat. 1164, 5 U.S.C. 601-612), the Administrator has determined that regulations establishing new tolerances or raising tolerance levels or establishing exemptions from tolerance requirements do not have a significant economic impact on a substantial number of small entities. A certification statement to this effect was published in the Federal Register of May 4, 1981 (46 FR 24950).

The Office of Management and Budget has exempted this rule from the requirement of section 3 of Executive Order 12291.

List of Subjects in 40 CFR Part 180

Administrative practice and procedures, Agricultural commodities, Pesticides and pests.

Dated: November 22, 1985.

Steven Schatzow,

Director, Office of Pesticide Programs.

PART 180—[AMENDED]

Therefore, 40 CFR Part 180 is amended as follows:

1. The authority citation for Part 180 continues to read as follows:

Authority: 21 U.S.C. 346.

2. Section 180.408 is amended as follows:

a. By designating the existing text as paragraph (a), revising the list of commodities under paragraph (a) and adding paragraph (b) to read as follows:

§ 180.408 Metalaxyl; tolerances for residues.

(a) * * *

Commodities	Parts per million
Apples	0.2
Avocados	4.0
Beans	0.1
Beet, tops	0.1
Brassica (cole) leafy vegetables group (except broccoli, cabbage, and cauliflower)	0.1
Broccoli	2.0
Cabbage	2.0
Cattle, fat	0.4
Cattle, kidney	0.4
Cattle, meat	0.05
Cattle, mbyp (except kidney and liver)	0.05
Cauliflower	2.0
Citrus fruit	1.0
Cottonseed	0.1
Cucurbit vegetables group	1.0
Eggs	0.05
Fruiting vegetables (except cucurbits) group (except tomatoes)	0.1
Goats, fat	0.4
Goats, kidney	0.4
Goats, liver	0.4
Goats, meat	0.05
Goats, mbyp (except kidney and liver)	0.05
Grain, crops	0.1
Grasses, forage	0.1
Hogs, fat	0.4
Hogs, kidney	0.4
Hogs, liver	0.4
Hogs, meat	0.05
Hogs, mbyp (except kidney and liver)	0.05
Hops, green	0.5
Horses, fat	0.4
Horses, kidney	0.4
Horses, liver	0.4
Horses, meat	0.05
Horses, mbyp (except kidney and liver)	0.05
Leafy vegetables (except brassica) group	0.1
Legume vegetable forage	8.0
Legume vegetable group (dry or succulent)	0.2
Lettuce, head	5.0
Milk	0.02
Onions, dry bulb	3.0
Onions, green	10.0
Peanut, hay	20.0
Peanut, vines	20.0
Peanut, nuts	0.2
Peanut, shells	2.0
Pineapples	0.1
Pineapple fodder	0.1
Pineapple forage	0.1
Poultry, fat	0.4
Poultry, kidney	0.4
Poultry, liver	0.4
Poultry, meat	0.05
Poultry, mbyp (except kidney and liver)	0.05
Potatoes	0.5
Raspberries	0.5
Sheep, fat	0.4
Sheep, kidney	0.4
Sheep, liver	0.4
Sheep, meat	0.05
Sheep, mbyp	0.05
Soybean, grain	1.0
Spinach	10.0
Sunflowers	0.1
Sunflower, forage	0.1
Tomatoes	1.0

(b) Indirect or inadvertent tolerances. Tolerances are established for indirect or inadvertent residues of metalaxyl in or on the raw agricultural commodities when present therein as a result of the application of metalaxyl to growing crops listed in paragraph (a) of this section and other non-food crops to read as follows:

Commodities	Parts per million
Wheat, fodder	2.0
Wheat, forage	2.0
Wheat, grain	0.2
Wheat, straw	2.0

[FR Doc. 85-28825 Filed 12-3-85; 8:45 am]

BILLING CODE 6560-50-M

TOXICOLOGY BRANCH ADI PRINTOUT Date: 09/05/86

Metalaxyl 6m feeding- dog ADI = 0.060000 mg/kg/day
Caswell #375AA NOEL = 6.2500 mg/kg Safety Factor = 100
CFR No. 180.408 LEL = 25.0000 mg/kg
Status: TOX ADI complete 5/23/86. ORD verified 7/8/86.

DRAFT

RESIDUE CONTRIBUTION OF PUBLISHED TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
6	Avocados	4.000		0.03	0.001800
41	Cottonseed (oil)	0.100		0.15	0.000225
47	Cucumbers, not inc. pickles	1.000		0.34	0.005100
54	Eggs	0.050		2.77	0.002078
64	Grain crops	0.100		13.79	0.020685
90	Meat, red	0.400		10.81	0.064860
92	Melons	1.000		2.00	0.030000
93	Milk and dairy products	0.020		28.62	0.008586
106	Onions, dry bulb	3.000		0.72	0.032400
107	Onions, green	10.000		0.11	0.016500
115	Peanuts	0.100		0.36	0.000540
127	Potatoes	0.500		5.43	0.040725
128	Poultry	0.400		2.94	0.017640
143	Seed and Pod vegetables	0.100		3.66	0.005490
163	Tomatoes	1.000		2.87	0.043050
191	Squash	1.000		0.11	0.001650
203	Kidney	0.400		0.03	0.000180
211	Liver	0.400		0.03	0.000180

TMRC % ADI
0.004861 mg/kg/day (60kg BW, 1.5kg diet) 8.102458

RESIDUE CONTRIBUTION OF TOX-APPROVED TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
5	Asparagus	7.000	6F3330	0.14	0.014700000
67	Grapes, not including raisins	2.000	6F3362	0.45	0.013500000
134	Raisins	6.000	6F3362	0.04	0.003600000
152	Strawberries	5.000	6F3337	0.18	0.013500000

TMRC % ADI
0.005616 mg/kg/day (60kg BW, 1.5kg diet) 9.360792

RESIDUE CONTRIBUTION OF NEW (PENDING) TOLERANCES

	CROP	TOLERANCE (PPM)	PETITION NUMBER	FOOD FACTOR	MG/DAY
53	Eggplant	1.000	6F3387	0.03	0.000450000
120	Peppers	1.000	6F3387	0.12	0.001800000
154	Sugar, cane and beet	0.100	6F3387	3.64	0.005460000

TMRC	% ADI
0.005745 mg/kg/day (60kg BW, 1.5kg diet)	9.574958

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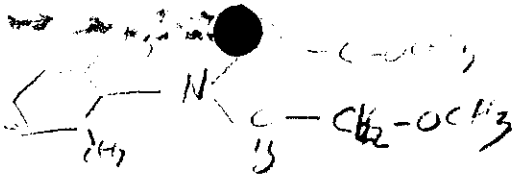

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

SEP 26 1986

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

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

FROM: Francis D. Griffith, Jr., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

TO: Henry M. Jacoby, PM 21
Fungicide-Herbicide Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

Ciba-Geigy Corporation proposes tolerances for residues of the fungicide metalaxyl, trade named Ridomil® and Apron® [N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine, methyl ester] and its metabolites containing the 2,6-dimethylaniline moiety and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl) alanine, methyl ester, each expressed as metalaxyl in or on the following raw agricultural commodities (RAC's):

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

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

Dry Tomato Pomace at 20.0 ppm.

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

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

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

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

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

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

Conclusions

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

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

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

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

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

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

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

Tomato Pomace (wet or dry) 20 ppm.

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

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

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

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

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

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

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

Recommendation

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

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

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

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

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

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

Detailed Considerations

Manufacture and Formulation

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

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

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

Proposed Uses

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

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

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

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

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

Apron® 25 is proposed as a fungicide seed treatment chemical to control systemic downy mildew, seed rot, and damping-off. Apron® is to be used only by commercial seed treaters. Apron® is to be applied to sugar beet seed as a water based slurry at a rate of two ounces (0.5 oz ai)/ 100 lbs of seed. The label has the following restriction: Use with an EPA approved dye that imparts an unnatural color to the seed. Seed treaters are warned that any bags of treated seed must contain the following statement "This seed

has been treated with metalaxyl fungicide. Do not use for feed, food, or oil purposes. Store away from feeds and foodstuffs."

Nature of the Residue

Plant Metabolism

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

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

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

Animal Metabolism

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

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

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

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

Analytical Methods

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

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

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

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

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

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

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

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

Briefly, method AG-330 involves blending 15 grams of tomatoes in 300 mL of methanol/water (4/1) for ten minutes. An aliquot (one or five gms) is evaporated on a roto-evaporator to < 5 mL but not dryness. The sample is refluxed 16 hours in 85 percent H_3PO_4 and one gram of $CaCl_3.6H_2O$. After cooling,

the solution is made basic with 200 mL of 25 percent NaOH to a pH > 5. The 2,6-dimethylaniline is steam distilled into 15 mL of hexane. The steam distillation apparatus is a modification of the equipment proposed by Veith and Kiwus. The distillation time is approximately 1 1/4 hours. The hexane is drawn off, dried over anh. Na_2SO_4. 100 uL of trichloroacetylchloride is added to form the derivative. The derivative is washed 2 x 25 mL 5 percent $NaHCO_3$ then cleaned up on an alumina column, Woelm, basic, grade V. The derivative is eluted off the column in the 150 mL hexane fraction then the hexane is rotoevaporated to dryness in a water bath no higher than 30 °C. The sample is made to 5.0 mL volume in acetone then analyzed by GC. The instrument used was a Tracor Gas Chromatograph, model 200, equipped with an alkali flame detector and a 1.2 m x 4 mm(id) glass column packed with 3 percent Dexsil-300 on Gas Chrom Q operated at 155 °C and a He carrier gas at 60 mL/min. The limit of detection is 0.05 ppm to 0.1 ppm. Quantitation is either peak height or peak area comparison of the unknown to knowns on a standard curve. Samples were corrected for recovery and a factor of 1.053 is used to connect residues of TCA-DMA detected to metalaxyl equivalents. With n = 31 metalaxyl recoveries in tomatoes ranged from 30 percent to 137 percent at spike levels of 0.05 ppm to 0.8 ppm. The median metalaxyl recovery in tomatoes is 58 percent and the mode recovery was 50 percent $\pm$ 1 percent.

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

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

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

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

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

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

Residue Data

Storage Stability

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

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

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

Tomatoes

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

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

six foliar applications total metalaxyl residues on tomatoes at zero day PHI ranged from < 0.06 ppm to 0.71 ppm of which parent only residues ranged from < 0.05 ppm to 0.46 ppm, and five-day PHI total metalaxyl residues ranged from < 0.05 ppm to 0.29 ppm of which parent only residues ranged from < 0.05 ppm to 0.13 ppm.

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

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

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

Tomato Processing Study

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

In this petition the registrant wants to raise the established dry tomato pomace tolerance from 16 ppm to 20 ppm. This proposal is consistent with RCB's policy of feed additive tolerances being based on the proposed RAC tolerance x the concentration factor and our desire to avoid "fractional"

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

Tomato Pomace (wet or dry) 20 ppm

Residue Data for Tomatoes and Peppers From Metalaxyl Seed Treatment

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

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

Peppers

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

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

of two lbs metalaxyl at planting then two applications of one lb ai each at a 30-day interval, metalaxyl residues on peppers at seven days PHI ranged from 0.17 ppm to 0.90 ppm, at 14 days PHI metalaxyl residues ranged from 0.19 ppm to 0.98 ppm, and at 21 days PHI metalaxyl residues ranged from 0.14 ppm to 0.64 ppm.

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

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

Sugar Beets and Sugar Beet Tops

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

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

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

However, the petitioner has presented no data to show whether or not these residues concentrate if the sugar beets are processed into molasses, sugar, and dehydrated pulp. RCB suggests the petitioner conduct such a processing study using field incurred metalaxyl residues that result from

the proposed use. After the completion of the proposed study the petitioner may need to revise his Section F with additional food and feed additive tolerances.

Residues in Meat, Milk, Poultry and Eggs

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

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

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

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

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

Other Considerations

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

Attachment 1: International Residue Limit Status Sheet

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

INTERNATIONAL RESIDUE LIMIT STATUS

6/30/86

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

CCPR NO. 138

f. Keves 7/1/86

Codex Status

☐ No Codex Proposal Step 6 or above

Proposed U. S. Tolerances

40 CFR 180.408 a,d
40 CFR 180.561.273

Residue (if Step 9): _____
parent only

Residue: metalaxyl and its metabolites *

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

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

CANADIAN LIMIT

Residue: _____
parent only 1/

MEXICAN TOLERANCIA

Residue: _____

Crop	Limit (ppm)
none (on above items)	

Crop	Tolerancia (ppm)
none	

1/ On 0.1 ppm negligible residue limit for potatoes

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

Notes:

End Of Document

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

MAR 13 1987

EXPEDITE

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#6F3387/6H5499 Metalaxyl on Fruiting Vegetables (except Curcurbits), Sugar Beets and Sugar Beet Tops. Evaluation of February 26, 1987, Amendment. (No Assession Number) [RCB #1996 and #2013]

FROM: Francis D. Griffith Jr., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

TO: Lois A. Rossi (Acting PM-21)
Fungicide-Herbicide Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

The review of this amendment is being expedited at the request of Edwin F. Tinsworth, Director of the Registration Division in his memorandum dated February 11, 1987, to John W. Melone, Director of the Hazard Evaluation Division.

Ciba-Geigy Corporation, Agricultural Division has submitted this amendment consisting of a supplementary Section D (a summary of a sugar beet processing study) and revised Section F (new tolerance proposals). The amendment has been submitted in response to a deficiency outlined in our reviews of metalaxyl (trade named Ridomil® and Apron®) in fruiting vegetables and sugar beets by F. D. Griffith, Jr. on September 26, 1986 and February 27, 1987. The deficiency is listed below as it appeared in the September 1986, review followed by the petitioner's response, then RCB comments and conclusions.

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

Petitioner's Response

The petitioner has submitted the results of a sugar beet metalaxyl processing study. The title of the report is "Total Metalaxyl Residues in Sugar Beet Fractions Following Applications of Ridomil® 2E and Ridomil MZ 58". The report was cooded ABR-87009, dated February 25, 1987, under the direction of M.W. Cheung with approval of L. G. Ballantine, Manager of Advanced Product Chemistry. The report is stamped DRAFT thus RCB awaits the final completed report.

RCB Comments

An overall review of the document suggest it is a summary document not a complete study report. The petitioner states several times in this report that additional information is in Ciba-Geigy's AG-A9908,01 document. Perhaps the following RCB concerns could be resolved if we are able to review this document.

Sugar beets were planted at the petitioner's test plot in Fresno, CA, on November 9, 1985, and harvested as mature beets on Aguust 21, 1986. This is a growing season of 286 days. Field information has not been provided but is available. The petitioner should be encouraged to supply this information. There is no proposed or registered use for metalaxyl on sugar beets using ground or foliar applications. RCB observes this use is quite similar to the metalaxyl potato and onion uses. The petitioner applied metalaxyl five times to sugar beets first at 2.0 lbs a.i./acre as a broadcast spray just prior to planting. The next Ridomil® application was on July 1, 1986, with other applications at 14 days repeat application intervals and harvest was seven days after the last application. The four foliar applications in July and August were at 1.16 lbs a.i./acre. This treatment regime is designated as the 1X rate for a total of 6.64 lbs a.i. metalaxyl/acre/season. At the same time the petitioner conducted a 2X field trial for a total of 13.28 lbs a.i. metalaxyl/acre/season. Dates of the 2X trial are the same as the 1X trial.

The formulation used at planting was Ridomil® 2E (EPA Reg #100-607) an emulsifiable concentrate containing 2.0 lbs a.i. per gallon (25.1% a.i.). The formulation used for foliar application was Ridomil MZ58 (EPA Reg #100-629) containing 10% a.i. metalaxyl and 48% a.i. mancozeb.

Beet roots were harvested on August 21, 1986, and shipped frozen to Spreckels Sugar Division in Woodland, CA for processing. No details of harvesting were provided. The petitioner provided No description of the sugar beet processing. RCB can not judge the adequacy of this study without details of how the beets were processed and how and why deviations, if any, were made in this study from standard commerical sugar beet processing. The petitioner claims environmental conditions and raw data for this test are available in Ciba Geigy document AG-A9908,01. The petitioner should be encouraged to present this document to resolve RCB concerns.

The sugar fractionation samples were received in Greensboro, N.C. (on dry ice) from CA on October 4, 1986. All analysis were completed within 4 months. All samples were stored in a freezer at -15°C until analysis. RCB concludes there is adequate storage stability data for metalaxyl to support the sugar beet metalaxyl processing study.

The petitioner maintains method AG-395 was used to determine metalaxyl residues. This method has been previously submitted and reviewed in detail in the September 1986, review (which see). However, the petitioner's summary is too vague for RCB to ascertain if modifications have been made for analysis of sugar beets, sugar, molasses and dehydrated beet pulp. The petitioner should provide details for the method as modified for each commodity. The petitioner provided No method validation data for sugar beets and its three processed commodities. The petitioner provided No supporting chromatographic data. With the limited number of analyses involved the petitioner should supply legible photocopies of all chromatograms. In the petitioner's discussion of analytical reference standards the reference standards were used to prepare solutions for fortification of recovery samples and for the quantitation of the GC results; thus, the data needed by RCB are available and should be presented.

RCB declines judgement on this method to generate reliable metalaxyl residue data on sugar beets, sugar molasses, and dehydrated beet pulp until we are given more complete details of the analytical method, provided with method validation data for each commodity, and review all supporting chromotographic data.

Metalaxyl and its metabolites were not detected in sugar beets at the petitioner's 1X use rate to the claimed limit of method detection of <0.05 ppm. Sugar beets from the 2X application rate have total metalaxyl residue of 0.08 ppm. Sugar and dehydrated pulp from sugar beets at the 1X and 2X application rates had no total metalaxyl residue above the limit of detection i.e., <0.05 ppm. RCB tentatively concludes depending on successful resolution of our three method concerns that metalaxyl does not concentrate in sugar or dehydrated pulp. Metalaxyl food and feed additive tolerance are probably not necessary for sugar and dehydrate beet pulp. RCB does not require metalaxyl residue data or tolerances on slices of sugar beets; ie, the cossettes.

When the sugar beets containing 0.08 ppm were processed into molasses the total metalaxyl residues are 0.42 ppm for a 5.25X concentration factor. Sugar beets from the 1X level containing no detectable total metalaxyl residue above 0.05 ppm were processed into molasses and had 0.32 pm metalaxyl residue. Since in the second case the raw agricultural commodity (rac) contained no detectable residue the processing study results indicate that the minimum concentration factor is a ratio of the concentration in the processed commodity (0.31 ppm) to the limit of detection (0.05 ppm) or 6.2X. Before deciding on the appropriateness of a 1 ppm metalaxyl FAT for molasses RCB needs to evaluate all chromatographic data to determine the potential level of residue in sugar beets in order to determine the appropriate concentration factor. In this case it may be possible to estimate the residue level from the chromatograms where it is below the limit of sensitivity or reliable quantification, but above a limit of detection thus indicates of a "true" residue and a more accurate concentration factor than the 6.2X factor. RCB thus declines to judge the adequancy of the concentration factor and the proposed metalaxyl food additive tolerance until we have reviewed the supporting chromatographic data.

RCB Conclusions (for Sugar Beet Processing Study)

RCB declines to judge the adequacy of the metalaxyl sugar beet processing study and the proposed food additive metalaxyl tolerance (FAT) on molasses until the petitioner resolves the following four concerns:

1. Submit a complete description of the analytical method used to generate the metalaxyl residue data on sugar beets, sugar, molasses, and dehydrated pulp. The summary is not sufficiently complete to judge the method.

2. The petitioner needs to provide a complete set of metalaxyl validation data using method AG-395 for sugar beets, sugar, molasses, and dehydrated beet pulp.

3. The petitioner needs to supply all supporting chromatographic data in order for RCB to determine the appropiate concentration factor thus judge the adequacy of the proposed food additive metalaxyl tolerance (FAT) for molasses.

4. RCB can not judge any results of the metalaxyl sugar beet processing study until the petitioner has provided a complete description (including flow chart, if applicable) of the actual process and, if appropriate, describe how and why it differs from the standard commercial sugar beet process. It is possible most, if not all, of the information RCB needs to complete its review of the study from planting of seeds to review of metalaxyl results in the processed commodities is in Ciba-Geigy document coded AG-A 9908,01. The petitioner is encouraged to submit this document for review.

Other Considerations

An updated International Residue Limit (IRL) status sheet is attached to this amendment review. There continues to be no problems of compatibility with Mexican or Canadian metalaxyl tolerances for fruiting vegetables (except cucurbits), sugar beets and sugar beet tops, tomato pomace (wet or dry) and sugar beet processed commodities (sugar, molasses, and dehydrate pulp) as those countries have not established metalaxyl tolerances for these commodities. There are Codex tolerances for parent only metalaxyl on tomatoes at 0.5 ppm and sugar beets at 0.05 ppm. There are no Codex metalaxyl tolerances for tomato processed commodities and sugar beet processed commodities; thus no compatability problems exist for these U.S. processed commodity tolerances.

In 1987 Codex will consider a definition of residue change to now include metalaxyl metabolites with the 2,6-dimethylaniline moiety as a result of U.S. interventions. Inclusion of the hydroxy metalaxyl metabolite is not in the proposed Codex change. While the U.S.A. plans to propose an additional metalaxyl residue definition to include the hydroxyl metabolite it is unlikely Codex will accept the change in 1987. It is not possible at this time for the U.S. to change its definition of metalaxyl residues as the present enforcement methods recovers and calculate all residues as metalaxyl. Also the hydroxyl metabolites are a significant portion of the total residue and thus warrant regulation.

RCB Recommendation

RCB reiterates its previous conclusion in the February 27, 1987, memorandum concerning metalaxyl residues on the fruiting vegetables group as follows:

RCB can recommend for the proposed metalaxyl tolerance of 1 ppm on the crop group Fruiting Vegetables (except Curcurbits) being established. RCB can also recommend that the proposed metalaxyl tolerance of 20 ppm on tomato pomace (wet or dry) be established. Both of these tolerances need TOX Branch and Exposure Assessment Branch concurrance before being established.

RCB can not recommend for the requested sugar beets and sugar beet tops, and molasses metalaxyl tolerances, at this time, for the reasons cited in our conclusions one through four above.

For further consideration of the metalaxyl on sugar beets and sugar beet tops, and molasses tolerances the petitioner should be advised to do the following:

1. Submit a complete description of the analytical method used to generate the metalaxyl residue data on sugar beets, sugar, molasses and dehydrated beet pulp. The summary is not sufficiently complete to judge the method.

2. The petitioner needs to provide a complete set of metalaxyl validation data using method AG-395 for sugar beets, sugar, molasses, and dehydrated beet pulp.

3. The petitioner needs to supply all supporting chromatographic data in order for RCB to determine the appropriate concentration factor thus judge the adequacy of the proposed food additive metalaxyl tolerance (FAT) for molasses.

4. RCB can not judge any results of the metalaxyl sugar beet processing study until the petitioner has provide a complete description (including flowchart, if applicable) of the actual process and, if appropriate, describe how and why it differs from the standard commercial sugar beet process. It is possible that most, if not all, of the information RCB needs to complete its review of the study from planting of seeds to review of metalaxyl results in the processed commodities is in Ciba-Geigy document coded AG-A 9908,01. The petitioner is encouraged to submit this document for review.

Attachment: International Residue Limit Status Sheet

TS-769C:RCB:Reviewer(FDG):vg:CM#2:Rm814B:557-0826:3/11/86:edited:fdg:3/
cc: RF., Circu., PP#6F3387/6H5499, TOX, FDA, EAB, EEB
PM-21, Reviewer, ISB/PMSD
RDI:Section Head:R.S.Quick:3/9/87:R.D.Schmitt:3/9/87

INTERNATIONAL RESIDUE LIMIT STATUS

Fred Griffith 3/6/87

CHEMICAL Metalaxyl (Ridomil®)

CODEX NO. 138

CODEX STATUS:

☑ No Codex Proposal Step 6 or above

Residue(if Step 8): _____

Metalaxyl

Crop(s)	Limit (mg/kg)
Fruiting veg.: Tomatoes	0.5
Sugar beets	0.05**

PROPOSED U.S. TOLERANCES:

Petition No. 6F3387/6H5499

RCB Reviewer F.D. Griffith Jr. 4/6/87

Residue: Metalaxyl and its Metabolites*

40CFR 180.408 and 21CFR 561.273

Crop(s)	Limit (mg/kg)
Fruiting Vegetables (except Cucurbits)	1.0 ppm
Tomato Pomace (Wet or Dry)	20.0 ppm
Sugar Beets and Sugar Beet Tops	0.1 ppm
Sugar Beet Molasses	1.0 ppm
Sugar Beet Sugar	
Dehydrated Sugar Beet Pulp	

CANADIAN LIMITS:

☑ No Canadian limit (as above)

Residue: _____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

☑ No Mexican limit

Residue: _____

Crop(s)	Limit (mg/kg)

** at or about limit of determination

‡ Currently the definition is parent only. This year Codex will consider parent plus metabolites (with 2,6 dimethyl aniline moiety based on U.S. interpretations (see note).

NOTES:

* N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester and its metabolites containing the 2,6 dimethyl aniline moiety and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl) alanine methyl ester

Form revised 1986

End Of Document

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

23 MAR 1987

EXPEDITE

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#6F3387/6H5499 Metalaxyl on Fruiting Vegetables (except Curcurbits), Sugar Beets and Sugar Beet Tops. Evaluation of March 6 and 10, 1987, Amendments. (No Assession Number) [RCB #2037 and #2039]

FROM: Francis D. Griffith Jr., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

TO: Lois A. Rossi (Acting PM-21)
Fungicide-Herbicide Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

The review of these amendments are being expedited at the request of Edwin F. Tinsworth, Director of the Registration Division in his memorandum dated February 11, 1987, to John W. Melone, Director of the Hazard Evaluation Division.

Ciba-Geigy Corporation, Agricultural Division has submitted these amendments consisting of cover letters and a supplementary Section D (a description of the sugar beet processing study with results, the analytical method, validation data, and chromatographic data). The amendments have been submitted in response to deficiencies outlined in our review of metalaxyl (trade named Ridomil® and Apron®) in fruiting vegetables and sugar beets by F. D. Griffith, Jr. on March 13, 1987. The deficiencies are listed below as they appeared in the March 1987, review followed by the petitioner's responses then RCB comments and conclusions.

Deficiency 1. Submit a complete description of the analytical method used to generate the metalaxyl residue data on sugar beets, sugar, molasses and dehydrated beet pulp. The summary is not sufficiently complete to judge the method.

Petitioner's Response

In Volume 4 of 4 this submission the petitioner has submitted an updated description of analytical method for metalaxyl.

RCB Comments

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

In summary, method AG-395, dry crop version, involved refluxing ten grams of sugar beets and sugar beet processed products for two hours in 100 mL of methanol/water (80/20, v/v). Filter through Whatman 2V filter paper then remove a two gram aliquot equivalent. Rotoevaporate to dryness then dissolve the residue in one mL H_2O and ten mL of methanesulfonic acid. Reflux for 15 minutes. The petitioner cautions a 20 minute reflux will degrade 2,6-dimethyl-aniline. Cool, then add 15 mL hexane and 25 mL of 25 percent NaOH through the top of the condenser. Be sure the pH > 8.0. The steam distillation apparatus is a modification of the equipment proposed by Veith and Kiwus and is commerically available from Ace Glass Co.(telcon EPA-Ciba,March 16, 1987). The distillation time is approximately 1 1/4 hours. The solution is then frozen. Cleanup is by silica SepPak®. The hexane is poured off the frozen water into the syringe then force through the SepPak® at a rate < 5 ml/min. The 2,6-dimethylaniline is recovered from the SepPak® with 18 mL CH_2Cl_2. The derivative is formed by adding 200 uL of trifluoroacetic acid (TFA), then rotoevaporate in a 15 °C, not 18 °C or 20 °C, water bath to just dryness. Dryness is essential as traces of TFA will cause losses. Take up in 2.0 mL tolune and transfer the tolune to a HP autosampler vial. The instrument used was a Hewlett Packard (HP) gas chromatograph, model 5880,

equipped with a N/P detector and a capillary column. The columns were either a fused silica 0.25 um coating of SE-54 in a 0.2 mm x 25 m column or a wide bore 0.32 mm x 30 m fused silica column with a 0.25 um coating of DX-4. The petitioner has adequate run tables and used suitable temperature programming.

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

The limit of metalaxyl sensitivity or reliable quantification is < 0.05 ppm. Quantitation is by the HP-1000 Lab Automation computer system. An electronic calculator such as a TI-55 is also adequate. The peak heights are used for comparison of standards in a range from 0.04 ng to 2.0 ng to unknowns for software calculations. Corrections are made for recoveries but not controls; and a factor 1.188 is used to convert DMA-TFA detected to metalaxyl equivalents. The petitioner has now provided all of the necessary details for RCB to judge the method.

RCB Conclusion

The written description of the method plus a Telcon (F.D. Griffith, EPA - L.G. Ballantine, Ciba) on March 16 have provided RCB with a complete description of the analytical method.

Deficiency one is now resolved.

Deficiency 2. The petitioner needs to provide a complete set of metalaxyl validation data using method AG-395 for sugar beets, sugar, molasses,and dehydrated beet pulp.

Petitioner's Response

In Volume 2 of 4 of this submission the petitioner has provided validation data. This part of the submission also included Ciba-Geigy document AG-A 9908. The title of the report is "Total Metalaxyl Residues in Sugar Beet Fractions Following Application of Ridomil® 2E and Ridomil MZ58 (Magnitude of Residues)" by B. Gold and dated February 25, 1987.

RCB Comments

Sugar Beet Roots control sample was spiked with 0.2 ppm metalaxyl and a recovery of 97% using method AG-395 (discussed above) was obtained. In the telcon (ibid) RCB learned there are additional metalaxyl recovery data on sugar beets with spikes ranging from 0.05 ppm to 0.5 ppm and corresponding recoveries ranging from 75% to 97%. Sugar beet pulp control sample was spiked with 0.1 ppm metalaxyl and had a recovery of 91%. Sugar control sample was spiked with metalaxyl at 0.05 ppm with recovery of 71%. Molasses control sample was spiked at 0.1 ppm. The 56% recovery is somewhat lower then RCB generally accepts but considering the matrix RCB will accept the data.

The petitioner also provided metalaxyl recovery data from cossettes. At the 0.1 ppm fortification level recoveries were 40% and 55%. RCB can not explain these recoveries in view of the 97% recovery on sugar beets, per se. In the telcon (ibid) the petitioner is aware of the problem and, at this time, could not offer an explanation, but is working to resolve the problem prior submission of any additional metalaxyl residue data on sugar beets.

RCB does not need additional method validation data for metalaxyl on sugar beets and sugar beet commodities to judge the proposed tolerances.

RCB Conclusion

The petitioner has provided a complete set of metalaxyl recovery/validation data using method AG-395 for sugar beets, sugar, molasses, and dehydrated beet pulp.

Deficiency two is thus resolved.

Deficiency 3. The petitioner needs to supply all supporting chromatographic data in order for RCB to determine the appropriate concentration factor thus judge the adequacy of the proposed food additive metalaxyl tolerance (FAT) for molasses.

Petitioner's Response

In the March 10, 1987, amendment the petitioner supplied the requested supporting chromatographic data.

RCB Comments

The petitioner supplied twelve photocopies of chromatograms for metalaxyl derivatized standards ranging from 0.02 ng to 0.5 ng. Copies of four control sample chromatograms were presented. RCB concludes there are no unidentified analytical responses (UAR's) where metalaxyl-TFA elutes. Metalaxyl spikes at various fortification levels in the control samples could be quantatated. In both the controls and spike samples UAR's are not a problem. Likewise in the eight field incured residue sample chromatograms UAR's are not a qualitative or quantitative problem. RCB observes the limit of detection is closer to 0.01 ppm and the limit of sensitivity or reliable quantification is <0.05 ppm. The petitioner provided no copies of sugar chromatograms. In the telcon (ibid) RCB was assured sugar chromatograms contained lower and smaller UAR's. This is as RCB expects, thus no additional chromatograms for metalaxyl in sugar are necessary. Reviewing the chromatogram for sugar beet sample, 2 - 1AB, RCB observes metalaxyl being present at a 0.035 ppm level. Using the 0.035 ppm as the indication of the "true" residue level in the rac the concentration factor is 10X. Thus the highest concentration factor for metalaxyl in sugar beets processed into molasses is 10X, and not 5.25X.

For this petition RCB needs no additional supporting chromatographic data to determine the appropriate concentration factors for the proposed food additive metalaxyl tolerances. The petitioner's 1.0 ppm metalaxyl in molasses is adequate.

RCB Conclusion

The petitioner has presented the requested supporting chromatographic data. The appropriate concentration factor for metalaxyl from sugar beets to molasses to 10X. The proposed FAT for metalaxyl in molasses at 1.0 ppm is adequate. RCB now concludes the petitioner has presented a well described, validated analytical method with supporting chromatograms and this method is suitable to gather the metalaxyl residue data on sugar beets and sugar beet commodities molasses, dehydrated beet pulp, and sugar.

Deficiency 3 is thus resolved

Deficiency 4. RCB can not judge any results of the metalaxyl sugar beet processing study until the petitioner has provided a complete description (including flowchart, if applicable) of the actual process and, if appropriate, describe how and why it differs from the standard commerical sugar beet process. It is possible that most, if not all,

of the information RCB needs to complete its review of the study from planting of seeds to review of metalaxyl results in the processed commodities is in Ciba-Geigy document coded AG-A 9908,01. The petitioner is encouraged to submit this document for review.

Petitioner Response

The petitioner provided a description of the sugar beet processing study and a flow chart of the process used to generate the commodities in this study.

RCB Comments

The raw sugar beets were shipped to Spreckels Sugar Division of Amstar Corporation. The samples were held three to five days in cold storage prior to processing. The beets were processed in batches of 260 lbs. each. The sugar beet processing is summarized as follows:

The beets were first thoroughly washed then sent to the slicer. The whirling knives sliced the beets into thin strips called cossettes. The cossettes were then fed into the diffuser where the hot water removes the sugar. This solution is called raw juice. The raw thin juice is purified in the Dorr Carbonater where lime and CO_2 are added to remove/precipitate impurities. This solution is called thin juice. After filtration the thin juice underwent a second purification step in the lab prior to evaporation.

In the commerical process there were two evaporation steps to form a thick juice. RCB does not consider this change between lab processing and commerical processing significant enough to change residue results. A final filtration removes all solid particles. Sugar is formed by boiling the juice under vacuum. The resulting mass of crystals and liquid is called fillmass. The fillmass is then spun and washed in a centrifuge. The crystals left are white and are now "pure" sugar (sucrose). The separated liquid is the molasses. The commerical process takes the raw sugar and drys it by tumbling in warm air in a rotating drum called a granulator.

At the diffuser the mass left over after removing the raw juice is the wet beet pulp. In this process the wet pulp is sent to a press. The press water is added to the raw juice. The remaining pulp is then dried. The commerical beet pulp can be a livestock feed either wet or dried. Occasionally some of the molasses is added back into the pulp prior to final drying and distribution into livestock feed channels.

RCB considers there are no significant differences between commercial sugar beet processing and the processing of these test metalaxyl treated sugar beets into sugar, molasses, and dehydrated beet pulp. RCB found the petitioner's flow chart a valuable aid in understanding how his sugar beets were processed in the lab.

RCB now has the suggested description of the sugar beet processing. The sugar beet processed commodities were prepared by an acceptable process.

RCB Conclusion

RCB concludes the petitioner has conducted an acceptable metalaxyl in sugar beets processing study and generated valid residue data using approved methods.

RCB concludes that a FAT is appropriate only for molasses. The metalaxyl concentration factor for sugar beets to molasses is 10X. The petitioner has proposed metalaxyl tolerances for sugar beets and sugar beet tops at 0.1 ppm from a seed treatment use. The petitioner has proposed a FAT of 1.0 ppm metalaxyl in molasses from sugar beets seeds treated with metalaxyl. Metalaxyl FAT's are not necessary for sugar and dehydrated sugar beet pulp. RCB does not expects the proposed tolerances to be exceeded.

Deficiency 4 is thus resolved.

Other Considerations

In our original review dated September 26, 1986 (which see) RCB determined there was adequate metalaxyl storage stability data to support this petition.

Volume 3 of 4 of this submission contains additional storage stability data for metalaxyl. The title of the study is "Stability and Accountability of Residues of Metalaxyl and Selected Metabolites Using Analytical Method AG-395 (Storage Stability)" by B. Gold and dated May 28, 1986. Ciba's code for this study is ABR-86044.

The petitioner prepared homogenous samples of apples, cabbage, lettuce, potatoes and strawberries. Samples of each of these substrates were fortified separately with 1.0 ppm of metalaxyl; and the metabolites CGA-62862 [N-2,6-dimethyl-phenyl)-N-(methoxyacetyl) alanine], CGA-67869 [N-(2,6-dimethyl-phenyl)-N-(hydroxyacetyl) alanine methyl ester], CGA-107955 [N-(2,6-dimethylphenyl)-N-(hydroxyacetyl) alanine], CGA-37734 [N-(2,6-dimethylphenyl)-2-hydroxyacetamide], and CGA-94689 [N-[-2-(hydroxymethyl)-6-methylphenyl]-N-(methyloxyacetyl)

alanine methyl ester]. The parent metalaxyl and each metabolite was added to the samples in an acetone solution. The acetone was allowed to evaporate, then the jars were sealed and stored in a freezer at - 15°C.

Samples were analyzed at zero day, six months, and at twelve months. The petitioner used the wet crop version of method AG-395 to gather the residue data (see memo dated September 26, 1986). Duplicate stored samples plus a control sample and a fortified sample were analyzed as a set.

Metalaxyl recovery results at a zero day storage period were all 1.0 ppm, at six months storage metalaxyl ranged from 0.93 ppm to 1.1 ppm, and at twelve months storage ranged from 0.98 ppm to 1.3 ppm. Metalaxyl at 1 ppm is stable for at lease twelve months in apples, cabbage, lettuce, potatoes and strawberries.

Metabolite CGA-62862 recovery results at zero day storage were all 1.0 ppm, at six months storage ranged from 0.94 ppm to 1.2 ppm, and at twelve months ranged 0.96 ppm to 1.1 ppm. CGA-62862 at 1.0 ppm is stable for at least twelve months in apples, cabbage, lettuce, potatoes, and strawberries.

Metabolite CGA-67869 recovery results at zero day storage were all 1.0 ppm, at six months storage ranged from 0.86 ppm to 1.2 ppm, and at twelve months storage ranged from 0.90 ppm to 1.2 ppm. CGA-67869 at 1 ppm is stable for at least twelve months in apples, cabbage, lettuce, potatoes and strawberries.

Metabolite CGA-107955 recovery results at zero day storage were either 0.99 ppm or 1.0 pm, at six months storage ranged from 0.84 ppm to 1.3 ppm and at twelve months storage ranged from 0.86 ppm to 1.0 ppm. CGA-107955 at 1 ppm is stable for at least twelve months in apples, cabbage, lettuce, potatoes, and strawberries.

Metabolite CGA-37734 recovery results at zero day storage were at the 1 ppm level, at six months storage results ranged from 0.77 ppm to 1.4 ppm and at twelve months results ranged from 0.91 ppm to 1.3 ppm. CGA-37734 at 1 ppm is stable for at least twelve months in apples, cabbage, lettuce, potatoes, and strawberries.

Metabolite CGA-94689 recovery results at zero days storage were 0.98 ppm to 1.0 ppm, at 6 months results ranged from 0.67 ppm to 1.1 ppm, and at twelve months storage results ranged 0.72 ppm to 1.1 ppm. RCB notes that metabolite CGA-94689 storage stability results are less in cabbage, lettue, and potatoes than in strawberries and apples. RCB does not consider the metabolite CGA-94689 storage stability results

in cabbage, lettuce, and potatoes to warrant correction as only one recovery was less the 70% (at 67%). Thus RCB concluded metabolite CGA-94689 at 1 ppm is stable for at least twelve months in apples and strawberries; and stable for twelve months in cabbage, lettuce, and potatoes.

The petitioner has provided supplementary storage stability data for metalaxyl and five of its metabolites in a variety of matrices. Method AG-395 gives acceptable accountability for these six compounds in the five matrices during the period of freezer storage. RCB concludes metalaxyl and five of its metabolites are stable at -15°C for at least twelve months in apples, cabbage, lettuce, potatoes, and strawberies.

An updated Interational Residue Limit (IRL) status sheet was attached to the March 13, 1987, amendment review.

RCB Recommendation

There being no further residue chemistry deficiencies associated with this petition RCB makes the following recommendations; TOX Branch and EAB considerations permitting:

Since residues are not expected to exceed the proposed tolerance under the proposed conditions of use RCB recommends for the 1.0 ppm metalaxyl tolerance on the crop group Fruiting Vegetables (except Cucurbits) and recommends for the Feed Additive Tolerance of 20 ppm metalaxyl on tomato pomace (wet or dry).

Since residues are not expected to exceed the proposed tolerance under the proposed condition of use RCB recommends for the 0.1 ppm metalaxyl tolerance on sugar beets and sugar beet tops, and recommends for the FAT of 1.0 ppm metalaxyl in sugar beet molasses.

TS-769C:RCB:F.D.Griffith:vg:CM#2:Rm814B:557-0826:3/20/87:edited:fdg:3/23
cc: RF, SF, PP#6F3387, Reviewer, PMSD/ISB, TOX, EAB, EEB, FDA
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WASHINGTON, D.C. 20460

FEB 27 1987

EXPEDITE

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#6F3387/6H5499 Metalaxyl on Fruiting Vegetables (except Curcurbits), Sugar Beets and Sugar Beet Tops. Evaluation of January 30, 1987, Amendment. (Assession Numbers 400661-1 and 400661-2) [RCB #1916]

FROM: Francis D. Griffith Jr., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

TO: Lois A. Rossi (Acting PM-21)
Fungicide-Herbicide Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

The review of this amendment is being expedited at the request of Edwin F. Tinsworth, Director of the Registration Division in his memorandum dated February 11, 1987, to John W. Melone, Director of the Hazard Evaluation Division.

Ciba-Geigy Corporation, Agricultural Division has submitted this amendment consisting of a cover letter, a revised Section B (new label), supplementary Section D (additional chromatographic data), a revised Section F (new tolerance proposals) and a supplementary Section G (rationale for a sugar beet molasses metalaxyl tolerance without a processing study). The amendment has been submitted in response to several deficiencies outlined in our review of metalaxyl (trade named Ridomil® and Apron®) in fruiting vegetables and sugar beets by F. D. Griffith, Jr. on September 26, 1986. The deficiencies are listed below in the order they appeared in the September 1986, review followed by the petitioner's response, then RCB comments and conclusions.

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

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

Petitioner's Response

The petitioner has submitted a revised label (Section B).

RCB Comments

The petitioner has added the seven day pre-harvest interval to the label for fruiting vegetables. In the General Information Section of the label the petitioner cautions producers that before tank mixing metalaxyl with other registered chemicals for any use on the label, producers should read all labels of the tank mix partners to ascertain if the partner is labeled for use on the particular crop and that use patterns are compatible with those of metalaxyl.

RCB Conclusion

Deficiencies 1a and 1b are resolved.

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

Petitioner's Response

The petitioner has submitted photocopies of 33 chromatograms showing metalaxyl standards and metalaxyl residues on tomatoes, tomato juice, and tomato pomace. The petitioner also submitted photocopies of 14 chromatograms showing metalaxyl standards, spikes, and metalaxyl residues on peppers.

RCB Comments

The petitioners presented six chromatograms of metalaxyl standards ranging from 0.04 ng to 1.0 ng metalaxyl run using the instrumentation described for method AG-395. Two chromatograms of pepper blanks showed no crop coextractives interfering where metalaxyl eluted. Recovers of matalaxyl spikes in these samples showed quantitative separation of metalaxyl from the background. Three chromatograms showed field incured residues of metalaxyl on peppers ranging from 0.13 ppm to 0.37 ppm. The chromatogram for a clean field sample showed no metalaxyl above 0.02 ppm. The petitioner has presented sufficient chromatographic supporting data for method AG-395 used in this petition. An adequate analytical method was used to generate the metalaxyl on peppers residue data.

Twelve chromatograms of metalaxyl standards ranging from 0.25ng to 8.0ng metalaxyl were run using the instrumentation described for methods AG-330 and AG-348. For the raw tomato extracts the crop blank or control samples had crop coextractives but none showed where metalaxyl eluted. A 0.05 ppm metalaxyl spike in this sample could recover 0.03 ppm metalaxyl. Four chromatograms of tomato extracts using method AG-330 had two results at 0.05 ppm-0.06 ppm metalaxyl and two residues were less than 0.05 ppm. RCB will not pursue how valid is the number for metalaxyl below 0.05 ppm. We recognize that apparent real residues at 0.01-0.03 ppm level are difficult to confirm. Using method AG-348 RCB noted a large late eluting coextractive that could interfere.

The determination of metalaxyl residues with the unidentified analytical response (UAR) requires a skilled residue analyst. Metalaxyl spikes in the control sample could be recovered at 0.03 ppm and at 0.49. Two chromatograms for treated tomatoes extracts showed metalaxyl residues of 0.14 pm and 0.62 pm. The manner in which the petitioner drew his baseline for the 0.62 ppm sample does not appear to be consisted with other sample calculations. However RCB will not pursue this point as our estimate of the answer will not materially increase the residue results. The petitioner presented a blank tomato juice chromatogram plus two chromatograms showing metalaxyl spikes at 0.03 ppm and 0.33 ppm. While numerous crop coextratives are present these UAR's do not present a problem for a skilled residue analyst.

The chromatograms of tomato juice from metalaxyl tomatoes are acceptable. The recovery samples for metalaxyl in tomato pomace show recoveries at 0.02 ppm and 0.4 ppm with potential UAR interference. RCB notes the higher the metalaxyl residue the less of a problem the UAR's becomes. The petitioner has presented sufficient chromatographic supporting data for methods AG-330 and AG-348 used in this petition. Adequate analytical methods were used to generate the metalaxyl on tomatoes residue data.

RCB Conclusion

Deficiency 3b is resolved.

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

Petitioner's Response

The petitioner presented the following revised tolerance proposal:

We hereby request a tolerance for combined residues of the fungicide, metalaxyl [N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester], and its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxy-methyl-6-methyl-phenyl)-N-(methoxyacetyl) alanine methyl ester, each expressed as metalaxyl, in or on the following raw agricultural commodities:

Fruiting Vegetables (except Cucurbits) - 1.0 ppm
Sugar Beets - 0.1 ppm
Sugar Beet Tops - 0.1 ppm

PROPOSED FEED ADDITIVE TOLERANCES

We hereby request feed additive tolerances for combined residues of the fungicide, metalaxyl [N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester], and its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxy-methyl-6-methylphenyl)-N-(methoxyacetyl) alanine methyl ester, each expressed as metalaxyl, in or on the following feed additive commodities:

Tomato Pomace (wet or dry) - 20.0 ppm
Sugar Beet Molasses - 1.0 ppm

RCB Comments

The petitioner has submitted the suggested tomato pomace metalaxyl tolerance. RCB will comment on the proposed sugar beet molasses metalaxyl tolerance in our discussion of the supplementary Section G (see comments following on deficiency 4F).

RCB Conclusion

Deficiency 4b is resolved. RCB notes there are no other Residue Chemistry deficiencies related to establishing a metalaxyl crop group tolerance for fruiting vegetable (except cucurbits).

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

Petitioner's Response

The petitioner did not present results of the suggested processing study. The petitioner has provided a supplementary Section G which contains the rationale for the proposed sugar beet molasses metalaxyl tolerance, a letter from Gustafson, Inc., requesting a waiver for the suggested sugar beet processing study, and letter with supporting documentation from the Beet Sugar Development Foundation detailing how a 7X concentration factor from sugar beet to sugar beet molasses is appropriate.

RCB Comments

RCB reiterates its previous conclusion that while metalaxyl residues on sugar beets and sugar beet tops are not expected to exceed the proposed 0.1 ppm tolerance under the conditions of the proposed use, the petitioner needs to conduct a sugar beet processing study using field incurred metalaxyl residues and process those beets into molasses, sugar, and dehydrated pulp. Metalaxyl residues data are needed for each of these commodities, and if metalaxyl residue concentration is shown on any of these commodities, then the petitioner should propose the appropriate food or feed additive tolerances.

In the cover letter the petitioner states a sugar beet processing study is near completion. RCB should be able to review the results of the metalaxyl sugar beet processing study from a soil treatment use in February, 1987. We defer judgement on the adequacy of this study to address our concerns until we have actually reviewed the entire study results.

In the revised Section G the petitioner proposes a 7X concentration factor (theoretical) based on data from the Beet Sugar Development Corporation. No mention is made of sugar or dehydrated pulp. The petitioner will have to consider the question food/feed additive tolerances for metalaxyl in sugar, pulp, and molasses further, during the sugar beet processing study.

A letter from the Beet Sugar Development Foundation in Fort Collins, Colorado, dated December 19, 1986, signed by Stephen Reynolds provides information on molasses production from sugar beets. RCB notes that molasses production from sugar beets was 4% to 6% in straight houses and 5% to 7% in Steffen houses. If all of the sugar beets had 0.1 ppm metalaxyl and all of this metalaxyl went into molasses then RCB estimates a 20X concentration factor. Presumeably the appropriate concentration factors will be determined in the requested sugar beet processing study.

Gustafson, Inc. of Dallas, Texas, in a letter dated December 12, 1986, and signed by J. C. Rockwell requests EPA reconsider the imposition of the requirement of a processing study for sugar beets. Three arguments were presented to back up the the waiver request. The first argument centers on a use rate of metalaxyl per acre for seed treatment. RCB points out this is not a soil application use but a seed treatment use and essentially all of the ^{14}C-residue on the seed appeared in the beet. The second argument centers on this is a minor use pattern. Sugar beets are not a minor crop. Considering the acreage involved and the amount of seed treated, this is minor use on a major crop. The third argument centers on potential crop loss. This is not an argument in RCB preview; thus no comments will be made.

RCB Conclusions

Deficiency 4f is not resolved. RCB reiterates its conclusion of the September 26, 1986, review. The petitioner needs to complete a sugar beet processing study using field incurred metalaxyl residues at the proposed tolerance and process these beets into sugar, molasses and dehydrated pulp. Residues data are needed for each of the commodities. If metalaxyl concentrates in any of these commodities appropriate food and/or feed additive tolerances should be proposed. Deficiency 4f is the only unresolved deficiency remaining in this petition.

RCB Recommendation

RCB can recommend for the prorposed metalaxyl tolerance of 1 ppm on the crop group fruiting vegetables (except Curcurbits) being established. RCB can also recommend that the proposed metalaxyl tolerance of 20 ppm on tomato pomace (wet or dry) be established. Both of these tolerances need TOX Branch and Exposure Assessment Branch concurrance before being established.

RCB can not recomend for the requested metalaxyl tolerance in sugar beets and sugar beet tops at this time for the reason cited in our conclusion 4f above.

For further consideration of the metalaxyl in sugar beets and sugar beet tops tolerances the petitioner should complete and submit the sugar beet processing study now in progress, report the results to RCB, and propose the appropriate food or feed additive tolerance as necessary. The beet processing study should include analyses for sugar, dehydrated beet pulp, and for beet molasses.

The product Manager should note that Section G in this submission states that the results of the sugar beet processing study will be submitted to the Agency in February, 1987. The Product Manager should be on the look out for this action when it arrives in RD.

RCB:TS-769C:Reviewer(FDG):CM#2:Rm814B:557-0826:vg:2/25/87:edited:fdg:2/26
cc: RF, PP#6F3387,SF,PM-21,PMSD/ISB, Reviewer, TOX, EAB, EEB, FDA, Circu.
RDI:Section Head:R.S.Quick:2/19/87:R.D.Schmitt:2/20/87

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Memo of Telephone Conversation on February 25, 1987

Between: Robert Quick, Chemist
Residue Chemistry Branch
Hazard Evaluation Division

And: Ms. Karen Stumpf
Ciba Geigy Corp.

Subject: PP#6F3387. Metalaxyl on fruiting vegatables and sugar beets.

I was requested by R.D. P.M. 21 (Lois Rossi) to contact Ms. Stumpf regarding our RCB review of this petition and specifically our RCB request for a metalaxyl sugar beet processing study.

Ms. Stumpf said that the processing study is completed and that the data submission to EPA is being typed. She read the residue results to me over the phone. She said that residues concentrated only in molasses. Pulp and sugar were also analyzed but showed no residue concentration.

Mr. Conn of Ciba is delivering a copy of the processing study to the Agency on 2/26/87. The formal submission will be sent to the Agency the week of 3/2/87.

I discussed briefly with Ms. Stumpf the rationale that went into our RCB data request.

The conversation ended.

cc: PP#6F3387, R.F., Circu., R.S. Quick, P.M. 21, Griffith
RDI:R.S. Quick:2/26/87:R.D.Schmitt:2/26/87
TS-769:R.S. Quick:2/26/87:mt:CM#2:Rm.810:557-7324:2/27/87

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HED File Code	**11500 Petition Files Chemistry**
Memo Date:	**11/23/2004**
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