

US EPA ARCHIVE DOCUMENT

S.F.



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

JUL 28 1987

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: FAP#7H5532 (RCB No. 2196) Metalaxyl (Ridomil®) on  
Hops - Evaluation of Analytical Method and Residue  
Data (Accession No. 401626)

FROM: Nancy D. Dodd, Chemist *Nancy Dodd*  
Tolerance Petition Section II  
Residue Chemistry Branch  
Hazard Evaluation Division (TS-769C)

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

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

and

Toxicology Branch  
Hazard Evaluation Division (TS-769C)

The petitioner, Ciba-Geigy Corporation, requests the establishment of 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-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester, each expressed as metalaxyl, in or on dry hops at 10.0 ppm and spent hops at 10.0 ppm.

Tolerances are established (40 CFR 180.408, 21 CFR 561.273, and 21 CFR 193.277) for metalaxyl on dry hops at 2 ppm (food additive tolerance) and green hops at 0.5 ppm (PP#1F2537/FAP# 1H5311). Metalaxyl tolerances are also established on a variety of other commodities at levels ranging from 0.02 to 20 ppm (see 40 CFR 180.408, 21 CFR 561.273, and 21 CFR 193.277). Tolerances are pending on some crops.

A screen has been conducted by RCB on this petition PP#7H5532 (N. Dodd, February 20, 1987) in which obvious deficiencies were listed.

This petition is submitted at the request of the West German government in order to allow importation of metalaxyl-treated hops into the USA. Higher tolerances are needed on hops imported from Germany since use patterns there differ from those in the USA.

A Registration Standard has been issued on metalaxyl (December 1981). A Final Regulatory Standard and Tolerance Reassessment (FRSTR) was due on June 26, 1987.

### Conclusions

1. The petitioner has submitted a list of ingredients in the formulas for Ridomil® plus 50WP and Ridomil® 5GR. This list is in the Confidential Appendix. All inerts have been cleared under 40 CFR 180.1001.
2. The petitioner should submit a revised Section B/label with the correct calculation of Ridomil plus from 19.8 kg/ha compound per year to 2.97 (not 3.48) kg/ha metalaxyl (ai) per year.
3. The nature of the residue in hops is adequately understood. The residues of concern in hops are the parent metalaxyl, its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester.
- 4a. The nature of the residue in meat and milk is adequately understood. Residues of concern in meat and milk are parent metalaxyl, its metabolites containing the 2,6-dimethylaniline moiety and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester.
- 4b. Since this use on hops does not involve poultry feed items, no poultry metabolism data are necessary.
5. Adequate analytical methods are available in the Pesticide Analytical Manual - Volume II (PAM-II) for enforcement of the proposed tolerances on dry hops and spent hops.
6. Storage stability data are adequate for hops samples which were stored for 18 months or less.

- 7a. RCB cannot determine from the available residue data whether the proposed 10 ppm tolerance for metalaxyl and its metabolites containing the 2,6-dimethyl-aniline moiety and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester is adequate to cover residues resulting from the proposed use. The methods used by the petitioner to obtain residue data on hops, REM 21/76 and REM 1/80, determine parent compound only. The petitioner should submit additional residue data on samples which are analyzed by the PAM-II procedure or another proven procedure that determines parent and the metabolites which are included in the U.S. tolerance expression. To use reanalyzed samples from the monitoring studies, RCB will need raw data including information such as application rates, sampling dates, sampling to analysis intervals, and storage conditions for the samples between sampling and analysis. If this information is not available or if the application rates/number of applications do not represent the heaviest uses, new residue studies would be needed since storage stability data have not been submitted to support use of samples obtained before 1986.
- 7b. RCB concludes that submission of dry hops samples analyzed by the PAM-II method, which involves refluxing in 80% (v/v) methanol/water for 2 hours, will resolve RCB's concern over extraction efficiency from dry hops.
- 7c. RCB concludes that storage intervals between sampling and analysis and storage conditions should be reported for all residue data.
- 7d. RCB concludes that the petitioner should identify the formulations which are referred to by the product codes A-6335A and A-6339A in Table 2, page 10, Volume 3 of 5, dated January 9, 1987.
- 8a. Pending resolution of issues discussed in No. 7a through 7d above, RCB tentatively concludes that the established tolerance of 0.02 ppm is adequate to cover residues in milk resulting from the proposed use. The established tolerances of 0.4 ppm for fat and liver and 0.05 ppm for meat and meat by-products of cattle, goats, hogs, horses, poultry, and sheep are also adequate.

However, if imported dried hops are extracted to produce hop extract for beer and spent hops which may be fed to animals, RCB foresees that the

established tolerance of 0.4 ppm should be raised to about 1.0 ppm for kidney of cattle, goats, hogs, horses, poultry, and sheep. However, it is our understanding that an agreement will be made with FDA and the hops importers to preclude the use of imported hops for the production of hops extract and spent hops. No increase in the kidney tolerance is needed because of the feeding of brewers' grain.

- 8b. Since there are no poultry feed items, no secondary residues are expected to occur in poultry and eggs as a result of this use. This use falls in category 3 of 40 CFR 180.6(a) with respect to poultry and eggs.
9. An International Residue Limits (IRL) Status sheet is attached. Codex has proposed a 10 mg/kg limit for metalaxyl per se on dry hops. Although this is numerically the same as the proposed tolerance of the U.S.A., the tolerance expression for the U.S.A. includes metabolites. There are no Canadian or Mexican proposals on hops.

#### Recommendations

1. At this time, RCB recommends against the proposed tolerances of 10 ppm for metalaxyl and its metabolites containing the 2,6-dimethylaniline moiety and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester in dry hops and spent hops for reasons given in Conclusions Nos. 2 and 7a through 7d above. The petitioner should be informed of Conclusion No. 8a.

2. The Federal Republic of Germany indicated that data would be submitted on the analyses of samples by two methods. One method was used to generate data for the parent compound only and one was used to analyze parent and metabolites. The residues of concern are parent, its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester. The FRG had some of these data at the 4/1/87 meeting with OPP. According to the 4/13/87 letter (from K.S. Stumpt-Ciba-Geigy to L.A. Rossi-EPA), additional analyses should have been completed in June 1987. Since these analyses should have been completed in June, RCB predicts that these analyses should be en route to RCB at this time. Therefore, RCB awaits this submission. In the meantime, the petitioner may resolve the remaining deficiencies outlined above which do not require additional experimental work. Thus, upon receipt of the data presumably finished in June 1987, RCB believes that a tolerance on dry and spent hops could be established.

Detailed ConsiderationsManufacture

The manufacturing process has been discussed in PP#1F2500 (see memorandum of P. Errico, March 9, 1982). RCB has previously concluded that impurities in the technical are not likely to present a residue problem (PP#8F2121, G. Makhijani, March 29, 1979).

Formulations

The formulations proposed for use on hops are Ridomil plus 50WP and Ridomil 5GR. Refer to the Confidential Appendix for a list of ingredients in the formulations. The inerts are cleared under 40 CFR 180.1001.

Proposed UseRidomil 5GR

Apply Ridomil 5GR after pruning when crowns are dry and corked, preferably before shooting of the hop. Apply to control early attack (primary infections) at the rate of 4 g Ridomil 5GR per plant (0.80 kg ai/ha; 0.7 lb ai/A). Do not make more than one application of Ridomil 5GR per year. If conditions are dry, cover the granules with soil.

Ridomil Plus 50WP

Apply Ridomil plus 50WP from the beginning of vegetation, or from the 2.5 to 3.0 m plant height if Ridomil Granule has been applied against primary infections. Apply at intervals of 14 days. Do not make more than six applications. Apply a 0.15 percent solution (150 g formulation/100 l water) as a high volume spray according to official recommendations.

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\* The petitioner calculates application rates based on the following estimated application rates of water, which depend on the growth stage of the plants:

| <u>Application No.</u> | <u>Liters Water Applied/Hectare</u> |
|------------------------|-------------------------------------|
| 1                      | 1000                                |
| 2                      | 1500                                |
| 3                      | 2100                                |
| 4                      | 2300                                |
| 5                      | 2300                                |
| 6                      | 4000                                |

Depending on plant growth stages\*, this application rate ranges from 1.5 to 6.0 kg Ridomil plus 50WP/ha (1.3 to 5.4 lb Ridomil plus/A/application; 0.2 to 0.8 lb ai/A/application). If lower spray volumes are used, the rate of product should be increased according to the reduction of the spray volume. Apply in sufficient water to obtain good and even wetting of the hops. Observe a 10-day PHI.

Ridomil plus is compatible with Elocron, Ultacron, and zinc sulfate. The company does not assume liability for tank mixtures since it cannot test all possible tank mixtures.

The petitioner has submitted a revised Section B/label dated April 13, 1987 in response to RCB's screen of PP#7H5532 dated February 20, 1987. This revised label indicates that Ridomil Granular and Ridomil plus can be applied at rates of 0.80 and 3.48 kg ai/ha/yr, totaling 4.28 kg ai/ha/yr for the total of one granular application plus six applications of Ridomil plus. However, the calculation for Ridomil plus from 19.8 kg formulation/ha/yr to kg ai/ha/yr is incorrect; instead of 3.48, the number should be 2.97 kg ai/ha/yr.

RCB concludes that the petitioner should submit a revised Section B/label with the correct calculation of Ridomil plus from 19.8 kg/ha compound per year to 2.97 (not 3.48) kg/ha metalaxyl (ai) per year.

### Nature of the Residue

#### Plants

No metabolism studies are submitted with this petition. Metabolism studies on lettuce (PP#2F2762, K. Arne, January 6, 1983 and PP#1F2500, P. Errico, March 9, 1982), potatoes (PP#1F2500, P. Errico, March 9, 1982 and PP#8G2121, G. Makhijani, March 29, 1979), and grapes (PP#1F2500, P. Errico, March 9, 1982) have previously been reviewed. The metabolism in potatoes was also discussed in the Metalaxyl Registration Standard (December 1983). Plant metabolism was summarized in RCB's review of PP#6F3337 (M. Firestone, February 21, 1986) as follows:

"Metabolism of metalaxyl in plants involves oxidation of the ring methyl to benzyl alcohol and/or 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. Based on these studies, RCB has previously concluded that the nature of the residue in plants is adequately understood and the residues of concern consist of the parent metalaxyl and its metabolites (free plus conjugates) containing the 2,6-dimethylaniline

moiety, and N-[(2-hydroxymethyl)-6-methylphenyl]-N-(methoxyacetyl)alanine, methyl ester." (See PP#2F2762, K. Arne, January 6, 1983).

RCB concludes that the nature of the residue in hops is adequately understood. The residues of concern in hops are the parent metalaxyl, its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester.

#### Animals

No new animal metabolism studies have been submitted with this petition. Animal metabolism studies on rats and goats have previously been reviewed (PP#8G2121, G. Makhijani, March 29, 1979 and PP#1F2500, P. Errico, July 16, 1982). RCB has previously concluded in PP#2F2762 (K. Arne, January 6, 1983) that residues of concern in meat and milk are the same as those of concern in plants.

No poultry metabolism studies are available. However, since this use on hops does not involve any poultry feed items, no poultry metabolism data are necessary at this time.

RCB concludes that the nature of the residue in meat and milk is adequately understood. Residues of concern in meat and milk are parent metalaxyl, its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester. Since this use on hops does not involve poultry feed items, no poultry metabolism data are necessary.

#### Analytical Methods

The petitioner has submitted methods REM 21/76 ("CGA 48988, Gas Chromatographic Determination of Residues in Hops and Tobacco," dated December 23, 1976) and REM 1/80 ("CGA 48988, Gas Chromatographic Determination of Residues in Wine and Beer," dated January 15, 1980).

#### REM 21/76

The hops or tobacco is extracted with acetone. After filtration and evaporation, the residue is redissolved in methanol. The interfering coextractives are precipitated with Celite<sup>®</sup> and FeCl<sub>3</sub>/CuSO<sub>4</sub> solutions. After addition of sodium chloride, the residue is partitioned into toluene. After evaporation of the toluene, the residue is cleaned up by alumina column chromatography. Residues of CGA 48988 are analyzed by gas chromatography using either an alkali flame ionization detector (AFID) or a nitrogen specific Hall electrolytic conductivity detector (HECD). The limit of



detection for CGA 48988 is 0.1 ppm, except for a limit of detection of 0.2 ppm for hops using the AFID. Recoveries for green cones fortified at 0.2 and 2.0 ppm were 106 to 298 percent and 74 to 125 percent, respectively. Recoveries for dry cones in the monitoring study which were fortified at 1.0 and 5.0 mg/kg were 132 and 102 percent, respectively. Recoveries for beer fortified at 0.02 and 0.2 ppm were 121 and 107 percent, respectively.

Note: In a letter to L. Rossi of EPA dated April 13, 1987, Ciba-Geigy indicated that the method REM 21/77/IA2 is REM 21/76 and method IA2 (a method to analyze copper). This information satisfies a question raised in RCB's screen of PP#7H5532 (N. Dodd, February 20, 1987) concerning the identity of the method.

#### REM 1/80

A wine or beer sample is cleaned up by partition chromatography with n-hexane on an Extrelut<sup>®</sup> column. The residue is cleaned up further on an alumina column. The residue is analyzed by gas chromatography using a nitrogen specific detector. The limit of determination is 0.005 mg/kg. Recovery for beer fortified at 0.1 ppm was 117 percent.

Analytical methods are available in the Pesticide Analytical Manual-Volume II for analysis of metalaxyl, its metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester in several crops (Method I) and in animal tissues, milk, and eggs (Method II). Residues are extracted from crops with methanol-water (8 + 2). Cottonseed extracts are partitioned between acetonitrile and hexane to remove interfering oils and fats. The extract is refluxed overnight with phosphoric acid in the presence of cobalt chloride. The solution is made alkaline. The 2,6-dimethylaniline is steam distilled and derivatized with trichloroacetyl chloride. The derivative is cleaned up on an alumina column. Cottonseed samples are additionally cleaned up on a silica gel column. The derivative is determined by gas liquid chromatography (GLC) with alkali flame ionization detection (AFID) or by GLC with mass spectrometry. The method for animal tissues, milk, and eggs is the same as that for crops except for the extraction step. Milk and eggs are extracted with acetonitrile. Tissues are extracted with acetonitrile-water (8 + 2). Fat is extracted with hexane. The extract is partitioned between acetonitrile and hexane to remove interfering oils and fats. Liver and kidney samples are further cleaned up on a silica gel column before GLC analysis.

Satisfactory method tryouts have been conducted on Method I (on cottonseed) and on Method II (on beef liver and milk).

RCB concludes that adequate analytical methods are available in the Pesticide Analytical Manual-Volume II for enforcement of the proposed tolerances on dry hops and spent hops.

### Residue Data

#### Storage Stability

Storage stability data for strawberries stored 1 to 14 months (PP#6F3337, M. Firestone, February 21, 1986) and for potatoes and tobacco stored at least 18 months (PP#1F2500, P. Errico, March 9, 1982) indicate that residues of metalaxyl and its metabolites determined as 2,6-dimethylaniline are stable for at least 18 months when stored at 5°F. This indicates that storage stability data are adequate for hops samples which were stored for 18 months or less.

Twenty-eight studies were conducted in Germany from 1977 to 1983. Metalaxyl was applied as a foliar spray with copper and/or folpet. Metalaxyl was also applied to the soil as a granular formulation. In 16 of the studies, 12 to 14 foliar applications of Ridomil plus 50WP, A-6335A, or A-6339A were made at the rates of 150 to 900 g ai/ha (0.13 to 0.8 lb ai/A). Residues of parent were determined in green cones, dry cones, and beer as follows:

| No. of Appl. | Application Rate<br>g ai/ha | Residues of Metalaxyl in mg/kg after the Preharvest Interval (Days) |                   |                  |       |         |                   |        |
|--------------|-----------------------------|---|-------------------|------------------|-------|---------|-------------------|--------|
|              |                             | Green Cones   |                   |                  |       |         | Dry Cones         | Beer   |
|              |                             | 0   | 2 - 3             | 4 - 6            | 7 - 8 | 10 - 12 | 7 - 12            |        |
| 12           | 248 - 900                   | 17.2  | 3.7               | 3.5              |       |         | 1.8               | < 0.05 |
| 12           | 248 - 900                   | 5.4   | 2.1               | 1.5              |       |         | 0.5               | < 0.05 |
| 12           | 248 - 900                   | 1.9   | 6.0               | 2.7              |       |         | 1.7               | 0.05   |
| 12           | 248 - 900                   | 14.0  | 1.2               | 1.7              |       |         | 3.4               | 0.03   |
| 12           | 248 - 900                   | 29.0 <sup>3</sup>   | 11.0 <sup>3</sup> | 6.8 <sup>3</sup> |       |         | 12.0 <sup>4</sup> | 0.08   |
| 12           | 248 - 900                   | 22.0  | 5.6               | 4.4              |       |         | 2.2               | < 0.01 |
| 12           | 220 - 800                   | 3.76  | 1.64              | 0.69             | 0.59  | 0.70    | 1.17              | 0.01   |
| 12           | 220 - 800                   | 2.91  | 0.90              | 0.54             | 0.80  | 0.56    | 1.38              | 0.01   |
| 12           | 150 - 800                   | 15.1  | 3.04              | 4.11             | 3.68  | 1.94    | 2.24              | 0.04   |
| 14           | 200 - 700                   | 11.2  | 9.0               | 7.7              | 4.8   | 1.4     | 2.5               | 0.02   |
| 14           | 200 - 700                   | 4.7   | 1.90              | 0.94             | 0.90  | 0.39    | 0.79              | < 0.02 |
| 12           | 200 - 800                   | 2.32  | 1.85              | 0.78             | 0.75  | 0.31    | 0.95              | < 0.01 |
| 12           | 200 - 800                   | 10.3  | 4.8               | 2.6              | 4.6   | 1.19    | 1.47              | < 0.01 |
| 12           | 150 - 800                   | 17.0  | 5.0               | 3.0              | 4.0   | 1.6     | 2.0               | 0.05   |
| 12           | 220 - 800                   | 6.27  | 2.28              | 0.85             | 1.3   | 0.33    | 0.80              | 0.03   |
| 12           | 220 - 800                   | 12.0  | 1.1               | 0.79             | 0.80  | 0.69    | 1.40              | 0.02   |

3/ Control sample contaminated: 0.61 mg/kg.

4/ Control sample contaminated: 2.9 mg/kg.

In 12 of the studies, 1 or 2 soil applications of Ridomil 5G were made at rates of 0.2 to 0.4 g ai/plant (0.04 to 0.07 lb ai/A). Residues of parent were determined in green cones, dry cones, and beer as follows:

| No. of Appl. | Application Rate g ai/plant | Residues of Metalaxyl in mg/kg after the Preharvest Interval (Days) |           |           |         |           |        |
|--------------|-----------------------------|---|-----------|-----------|---------|-----------|--------|
|              |                             | Green Cones   |           |           |         | Dry Cones | Beer   |
|              |                             | 80 - 87   | 90 - 94   | 114-135   | 146-153 | 87 - 153  |        |
| 1            | 0.2                         |   |           |           | < 0.2   | < 0.1     | <0.005 |
| 1            | 0.2                         |   |           |           | < 0.1   | < 0.1     | <0.005 |
| 1            | 0.2                         |   |           |           | < 0.1   | 0.18      |        |
| 2            | 0.2 + 0.4                   | 0.38-0.72   |           |           |         | 0.34*     | 0.006  |
| 2            | 0.2 + 0.4                   | < 0.1   |           |           |         | < 0.1     | <0.005 |
| 2            | 0.2 + 0.4                   |   | 0.45-0.12 |           |         | 0.15*     |        |
| 2            | 0.3                         | <0.1-0.27   |           |           |         | 0.26*     | <0.005 |
| 2            | 0.3                         | 0.18-<0.1   |           |           |         | 0.48*     | <0.005 |
| 2            | 0.3                         |   | 0.26-0.09 |           |         | 0.11      |        |
| 1            | 0.4                         |   |           | 0.67-0.25 |         | 0.18      | <0.01  |
| 1            | 0.4                         |   |           | 0.21-<0.1 |         | 0.22      | <0.01  |
| 1            | 0.4                         |   |           | 0.18-0.54 |         | 0.93      | <0.01  |

\*Maximum residues of two samples.

RCB has previously indicated (screen of PP#7H5532 dated February 20, 1987) that the petitioner should provide specific information on how dried hops were actually reconstituted (volume of water, soaking time) prior to extraction with organic solvent. In a letter to L. Rossi of EPA dated April 13, 1987, Ciba-Geigy indicates the following:

" . . This requirement would seem to be irrelevant because a recovery of 81 percent was shown in a hops sample fortified with 0.2 ppm metalaxyl (Figure 2, REM 21/76). However, with analysis of reserve hops samples according to the PAM II, CIBA-GEIGY

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Analytical Method AG-395, this concern should be resolved because according to this method, dry hops are extracted by refluxing with 80% (V/V) methanol/water for two hours."

Thus, RCB awaits submission of samples analyzed by the PAM-II method to resolve this concern.

In a 1986 monitoring study, residues in dried hops after one to three applications of Ridomil plus applied according to "good agricultural practices" were determined. Residues (not corrected for recoveries) for preharvest intervals of 39 to 107 days were 1.4 to < 0.5 mg/kg.

In a letter to L. Rossi of EPA dated April 13, 1987, Ciba-Geigy indicated that reserve samples were available for reanalysis from the 1986 monitoring study.

RCB cannot determine from the available residue data whether the proposed 10 ppm tolerance for metalaxyl and its metabolites containing the 2,6-dimethylaniline moiety and N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester is adequate to cover residues resulting from the proposed use. The methods used by the petitioner to obtain residue data on hops, REM 21/76 and REM 1/80, determine parent compound only. The petitioner should submit additional residue data on samples which are analyzed by the PAM-II procedure or another proven procedure that determines parent and the metabolites which are included in the tolerance expression. To use reanalyzed samples from the monitoring studies, RCB will need raw data including information such as application rates, sampling dates, sampling to analysis intervals, and storage conditions for the samples between sampling and analysis. If this information is not available or if the application rates/number of applications do not represent the heaviest uses, new residue studies would be needed since storage stability data are not available to support use of samples obtained before 1986.

RCB also concludes that submission of dry hops samples analyzed by the PAM-II method, which involves refluxing in 80% (v/v) methanol/water for 2 hours, will resolve RCB's concern over extraction efficiency from dry hops.

RCB also concludes that storage intervals between sampling and analysis and storage conditions should be reported for all residue data.

Finally, RCB concludes that the petitioner should identify the formulations which are referred to by the product codes A-6335A and A-6339A in Table 2, page 10, Volume 3 of 5, dated January 9, 1987.

Meat, Milk, Poultry, and Eggs

Feeding studies are available on cows at levels of 0.5 to 15 ppm for 40 days and 75 ppm ( $^{14}\text{C}$ ) for 28 days. Residues in cows were as high as 0.22 ppm in liver and 0.83 ppm in kidney resulting from the 15 ppm feeding level. No detectable residues were found in meat ( $< 0.05$  ppm) or milk ( $< 0.01$  ppm) (PP#1F2500, P. Errico, March 9, 1982; PP#1G2532/FAP#1H5314, R. Loranger, February 5, 1982; PP#3F2847, M. Nelson, July 7, 1983).

Spent hops are an animal feed item comprising up to 5 percent of the diet in beef and dairy cattle. The residue ingestion level of cattle from the proposed crop tolerance is  $< 0.5$  ppm (10 ppm tolerance  $\times$  5% of the feed). Brewers' grain, the by-product of the beer brewing industry which includes hops, is also an animal feed.

Present U.S. tolerances for metalaxyl are established on meat and milk at the following levels:

- 0.4 ppm fat, kidney, and liver of cattle, goats, hogs, horses, poultry, and sheep;
- 0.05 ppm meat and meat byproducts (except kidney and liver) of cattle, goats, hogs, horses, poultry, and sheep; and
- 0.02 ppm in milk.

Pending resolution of issues discussed in the Residue Data section, RCB tentatively concludes that the established tolerance of 0.02 ppm is adequate to cover residues in milk resulting from the proposed use. The established tolerances of 0.4 ppm for fat and liver and 0.05 ppm for meat and meat by-products of cattle, goats, hogs, horses, poultry, and sheep are also adequate.

However, if imported dried hops are extracted to produce hop extract for beer and spent hops which may be fed to animals, RCB foresees that the established tolerance of 0.4 ppm should be raised to about 1.0 ppm for kidney of cattle, goats, hogs, horses, poultry, and sheep. However, it is our understanding that an agreement will be made with FDA and the hops importers to preclude the use of imported hops for the production of hops extract and spent hops. No increase in the kidney tolerance is needed because of the feeding of brewers' grain.

Since there are no poultry feed items, no secondary residues are expected to occur in poultry and eggs as a result of this use.

Other Considerations

An International Residue Limits (IRL) Status sheet is attached. Codex has proposed a 10 mg/kg limit for metalaxyl

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per se on dry hops. Although this is numerically the same as the proposed tolerance of the U.S.A., the tolerance expression for the U.S.A. includes metabolites. There are no Canadian or Mexican proposals on hops.

Attachment I: International Residue Limit Status Sheet  
Attachment II: Confidential Appendix

cc with Attachment I only: SF, Circu  
cc with Attachments I and II: RF, Reviewer - N. Dodd, FAP#7H5532,  
PM#21, TOX, PMSD/ISB - Eldredge

RDI:JHOnley:7/8/87:RDSchmitt:7/8/87  
TS-769:RCB:CM#2:RM800:X1681:N.Dodd:Kendrick & Co.:7/15/87

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL metaxyl  
 CODEX NO. 738

*J. Wes*  
*6/25/87*

CODEX STATUS:

No Codex Proposal  
 Step 6 or above

PROPOSED U.S. TOLERANCES:

Petition No. 745532

RCB Reviewer Nancy Daddel

Residue(if Step 8): \_\_\_\_\_  
Metaxyl per se

Residue: metaxyl\* and  
metabolites\*\*

| <u>Crop(s)</u>   | <u>Limit (mg/kg)</u> |
|------------------|----------------------|
| <u>Hops, dry</u> | <u>10</u>            |

| <u>Crop(s)</u>    | <u>Limit (mg/kg)</u> |
|-------------------|----------------------|
| <u>dry hops</u>   | <u>10.0</u>          |
| <u>spent hops</u> | <u>10.0</u>          |

CANADIAN LIMITS:

No Canadian limit (on hops)  
 Residue: \_\_\_\_\_

MEXICAN LIMITS:

No Mexican limit ~~to~~  
 Residue: \_\_\_\_\_

| <u>Crop(s)</u> | <u>Limit (mg/kg)</u> |
|----------------|----------------------|
|----------------|----------------------|

| <u>Crop(s)</u> | <u>Limit (mg/kg)</u> |
|----------------|----------------------|
|----------------|----------------------|

NOTES:

\* N-(2,6-dimethylphenyl)-N-(methoxyacetyl) alanine methyl ester Page 1 of 1  
 \*\* metabolites containing the 2,6-dimethylaniline moiety, and N-(2-hydroxymethyl-6-methylphenyl)-N- Form revised 1986