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

OPP OFFICIAL RECORD  
HEALTH EFFECTS DIVISION  
SCIENTIFIC DATA REVIEWS  
EPA SERIES 361

6 AUG 1987

**SPECIAL**MEMORANDUMOFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: FAP#7H5532 (RCB #2196). Metalaxyl (Ridomil®) on Hops.  
Addendum to RCB's 7/28/87 Review. (No Accession #).

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and

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Introduction

RCB has been requested by Registration Division to estimate the ratio of total residues to parent metalaxyl from available data on the 2E formulation.

Conclusions

1. RCB can calculate from available data on the 2E formulation that total residues of parent plus metabolites on dry hops and spent hops are not likely to exceed parent residues by more than a factor of 10 when the 2E formulation is applied. Since the proposed use is for the 5GR and 50WP formulations instead of the 2E formulation and the use patterns are different, the 10X factor is only an estimate for the proposed use. RCB will reconsider this estimate upon receipt of additional analyses of samples with residues resulting from use of the 5GR and 50WP formulations and the proposed uses.

2. The petitioner should propose a 50 ppm tolerance for dry hops in 21 CFR 193.277 for human consumption and for spent hops in 21 CFR 561.273 for animal feeds to cover total residues of parent and metabolites.

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3. The deficiencies which were detailed by RCB in the 7/28/87 review of FAP#7H5532 remain outstanding.

#### Recommendations

RCB would have no objection to the establishment of a tolerance of 50 ppm with an expiration date of one year for metalaxyl on dry hops and spent hops provided that the following deficiencies are addressed during that time period:

1. The petitioner should submit a revised Section B/label with the correct calculations of Ridomil plus from 19.8 kg/ha formulation per year to 3.18 kg/ha metalaxyl (ai) per year.
2. 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.
3. 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.
4. RCB concludes that storage intervals between sampling and analysis and storage conditions should be reported for all residue data.
5. 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.

#### Basis for Recommendations

A summary and tables for parent metalaxyl compared with "total" metalaxyl (including parent and metabolites determined as 2,6-dimethylaniline) on hops are available for the 2E formulation. The studies were submitted in PP#1F2537 for metalaxyl on U.S.A.-grown hops. These tabular data do not reflect the proposed use in PP#7H5532 with regard to formulation, application rates, and number of applications, but offer only a comparison of levels of parent metalaxyl to total residues. The two tables are attached.

The method for total residues is "Analytical Method for the Determination of Total Residues of Metalaxyl in Crops as

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2,6-Dimethylaniline", AG-348. The method was found acceptable by EPA although recoveries for N-(2-hydroxymethyl-6-methylphenyl)-N-(methoxyacetyl)alanine methyl ester are 50% by the method as determined in an EPA method trial (K. Arne, 12/28/82).

The issue of parent vs. total residues was discussed as Deficiency #7a of RCB's 7/28/87 review of FAP#7H5532 (N. Dodd) as follows:

"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 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."

Tables I and II indicate that the residue level of parent plus metabolites can be 0.95X to 9.6X the level of parent alone. [This is based on the no detectable residue ( $<0.05$  ppm) of metalaxyl being calculated as 0.05 ppm (ie.  $0.48 \div 0.05 = 9.6$ ). For detectable residues of parent, the highest ratio of total residues to parent residues was 8.1 ( $1.3 \div 0.16$ ).]

RCB has been requested by the Registration Division to estimate the ratio of total residues to parent. RCB can estimate from the available data that total residue levels of parent plus metabolites are not likely to exceed parent residues by more than a factor of 10. RCB understands that additional analyses for parent plus metabolites will be submitted for review as described under Recommendation #2 of RCB's 7/28/87 review. Upon receipt of this additional data, RCB will reconsider this estimate.

The deficiencies which were detailed by RCB in the 7/28/87 review of FAP#7H5532 remain outstanding.

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Attachments 1 and 2: Tables

cc with Attachments: SF, Circu., RF, Reviewer-N. Dodd, FAP#7H5532,  
PM#21, TOX, PMSD/ISB-Eldredge  
RDI:M. Kovacs:8/5/87:RDSchmitt:8/6/87  
TS-769:RCB:CM#2:RM800:X1681:N.Dodd:N.Dodd:8/6/87

TABLE I. RESIDUES IN HOPS RESULTING FROM A SINGLE SOIL DRENCH APPLICATION OF METALAXYL

Test No. Location	Formu- lation	Type of Application	GPA	Rate lbs. ai/A	Number of Applications	Application Dates	PHI	Substrate	Rep	Residue (ppm)	
										Metalaxyl	"Total"
6156 OR	2E	Ground	20	0.5	1	4/17/80	139	Dry Cones	I	<0.05	0.36
									II	<0.05	0.45
6157 OR	2E	Ground	20	0.5	1	4/17/80	139	Dry Cones	I	0.18	1.1
									II	0.18	0.40
6158 WA	2E	Ground	20	0.5	1	4/29/80	111	Dry Cones	I	<0.05	0.42
									II	<0.05	0.48
6159 ID	2E	Ground	20	0.5	1	4/30/80	111	Dry Cones	I	0.22	0.69
									II	0.07	0.14
							108	Wet Cones	I	0.06	0.18
									II	0.47	1.2
							108	Dry Cones	I	—	—
									II	0.21	0.20
							108	Wet Cones	I	0.21	0.20
									II	1.4	3.6

Value in parenthesis indicates relationship to maximum use rate.

\*Residues of metalaxyl and metabolites determined as 2,6-dimethylaniline and expressed as metalaxyl equivalents.

TABLE II. RESIDUES IN HOPS RESULTING FROM SOIL PLUS FOLIAR APPLICATION OF METALAXYL

Test No. Location	Formu- lation	Type of Application	GPA	Rate lbs. ai/A	Number of Applications	Application Dates	PHI	Substrate	Rep	Residue (ppm)	
										Metalaxyl	Total**
6158 WA	2E	Ground	20 (Soil) 50 (Foliar)	0.5 (S)	1 + 2 (S) (F)	4/29/80 (S) 6/10/80 (F) 7/11/80 (F)	38	Dry Cones	I	0.32	1.0
				+ 0.2 (F) + 0.2 (F)					II	0.25	0.46
				1.0 (S)			38	Dry Cones	I	0.57	1.4
				+ 0.4 (F) + 0.4 (F)					II	--	--
				0.5 (S)			35	Wet Cones	I	0.11	0.17
				+ 0.2 (F) + 0.2 (F)					II	<0.05	0.18
6159 ID	2E	Ground	20 (Soil) 50 (Foliar)	0.5 (S)	1 + 2 (S) (F)	4/30/80 (S) 6/10/80 (F) 7/12/80 (F)	35	Dry Cones	I	0.16	1.3
				+ 0.2 (F) + 0.2 (F)					II	0.21	1.0
				1.0 (S)			35	Wet Cones	I	0.28	0.71
				+ 0.4 (F) + 0.4 (F)					II	0.31	0.89
				0.5 (S)			35	Dry Cones	I	0.87	4.6
				+ 0.2 (F) + 0.2 (F)					II	0.87	3.0

NOTE: The proposed label does not include foliar applications. These data are provided to assist in evaluating parent:"total" and green:dry ratios.

\*Residues of metalaxyl and metabolites determined as 2,6-dimethylaniline and expressed as metalaxyl equivalents.