UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 20-SEP-1999

SUBJECT: PP#2F04155 Myclobutanil in/on the Cucurbit Crop Group. **Amendment of 2/8/93. Evaluation of Storage Stability and Magnitude of Residue Data.** MRID# 445114-01 and 446798-05. Barcode D251635. Chemical 128857. Case 284006. Submission S551678.

FROM: Jennifer E. Rowell, Chemist
Registration Action Branch 1
Health Effects Division (7509C)

THROUGH: George F. Kramer, Ph.D., Chemist
Melba Morrow, D.V.M., Branch Senior Scientist
Registration Action Branch 1
Health Effects Division (7509C)

TO: Mary Waller, PM Team 21
Registration Division (7505C)

Rohm and Haas Company requests the establishment of a permanent tolerance for the combined residues of myclobutanil, (α-butyl-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile) and its metabolite, α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile (free and bound) in or on the cucurbit crop group at 0.5 ppm.

REGULATORY BACKGROUND

The following terms, as defined below, are used interchangeably throughout this review:
(i) **myclobutanil**: RH-3866; α-butyl-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile; and
(ii) **alcohol metabolite**: RH-9090; α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile.

Permanent tolerances are currently established for the combined residues of myclobutanil and its RH-9090 metabolite (free and bound) in/on a variety of agricultural commodities at levels ranging from 0.02 to 25.0 ppm and in meat, milk, poultry, and eggs at levels ranging from 0.02 to 1.0 ppm [40 CFR §180.443(a)].

Section 18 tolerances (with expiration dates) have been established for: artichokes (1.0 ppm; expires 7/31/00); asparagus (0.02 ppm, expires 7/31/00); caneberries (1.0 ppm; expires 12/31/99); cucurbit vegetable group (0.3 ppm, expires 5/30/00); hops, dried (5.0 ppm; expires 12/31/99); peppermint (2.5 ppm, expires 1/31/00); peppers, bell and non-bell (1.0 ppm, expires 7/31/00); spearmint (2.5 ppm, expires 1/31/00); strawberries (0.5 ppm; expires 3/31/00); tomatoes (0.3 ppm, expires 7/28/98); tomato paste (1.2 ppm, expires 7/28/98); and tomato puree (0.6 ppm, expires 7/28/98) [40 CFR §180.443(b)].

The current amendment addresses deficiencies identified in HED's previous review (Memo, D. Davis 2/8/93, Barcode D183273).

Executive Summary of Chemistry Deficiencies

- Revised Section F.

RECOMMENDATIONS

Provided Section F is revised as specified in Conclusion 1b, RAB1 concludes there are no residue chemistry data requirements that would preclude the establishment of the following permanent tolerance for the combined residues of the myclobutanil and its metabolite RH-9090 (free and bound):

cucurbit crop group	0.2 ppm

A human-health risk assessment will be prepared as a separate document.

CONCLUSIONS

OPPTS GLN 860.1500: Crop Field Trials

1a. Sixteen field trials have been conducted: 5 cucumber trials in Regions 1 (1 trial), 2 (1 trial), 3 (1 trial), and 5 (2 trials); 5 muskmelon trials in Regions 5 (1 trial), 6 (2 trials) and 10 (2 trials); and 6 summer squash trials in Regions 1 (2 trials), 3 (1 trial), 6 (2 trials), and 10 (1 trial). According to the current guidance (Table 1 of OPPTS 860.1500), for the establishment of a tolerance on the cucurbit crop group, a minimum of 17 trials should be conducted on the following commodities: 6 cucumber trials in Regions 2 (2 trials), 3 (1 trials), 5 (2 trials), and 6 (1 trial); 6 muskmelon trials in Regions 2 (1 trial), 5 (1 trial), 6 (1 trial), and 10 (3 trials); and 5 summer squash trials in Regions 1 (1 trial), 2 (1 trial), 3 (1 trial), 5 (1 trial), and 10 (1 trial). HED has determined that the submitted trial data are adequate to support a permanent registration for the use of myclobutanil on the cucurbit crop group.

1b. The combined residues of myclobutanil and its metabolite RH-9090 in/on the cucurbit crop group treated at application rates of 0.6 - 0.75 lb. a.i./A and harvested at 0-day PHIs ranged from 0.004-0.105 ppm. The available data indicate that the combined residues of myclobutanil and its metabolite RH-9090 will not exceed 0.2 ppm in/on the cucurbit crop

group. **Therefore, the appropriate tolerance level for the combined residues of myclobutanil and its metabolite RH-9090 is 0.2 ppm. A revised Section F should be submitted.**

DETAILED CONSIDERATIONS

Deficiency - Conclusion 2 (from Memo, D. Davis 2/8/93)

2. CBTS concludes that the proposed use labels for Rally 40W and Nova® 40W are adequate provided additional residue data are generated to reflect application intervals of less than 7 days. If no additional data are generated, the suggestion to reduce the application interval to less than 7 days should be removed from the label.

Petitioner's Response: A revised label with the statement "If environmental conditions favor heavy disease development, reduce application interval" removed from the use recommendations.

RAB1's Conclusion: The requested revised label has been provided. This deficiency is now resolved.

Deficiency - Conclusion 6a (from Memo, D. Davis 2/8/93)

6a. The acceptance of the residue data reviewed in this memorandum is contingent upon the satisfactory resolution of the questions raised in this review (see Magnitude of the Residue - Plants section of this review). If the petitioner is unable to provide the supporting data needed to resolve the issues raised, new field trials will be needed to replace those previously submitted.

1986 Crop Field Trials: *Additional information on the field portion of the three field trials is needed to adequately evaluate the applicability of the results to the establishment of a permanent tolerance. The petitioner is requested to supply the following supporting data. Information on retreatment intervals should be provided for the cantaloupe and squash trials. Additionally, clarification is requested as to the number of plots involved in each of the trials. For each trial, residue levels are reported for three samples at each harvesting interval. Were three plots treated at each site and sampled, or was a single plot treated and three samples taken? Following harvest, how were cantaloupe and cucumber samples treated/stored? The petitioner is requested to supply information on sample processing and sample storage.*

Additional supporting data is requested from the petitioner on the analytical portion of these field trials. Dates of extraction and conditions of extract storage should be elucidated. The petitioner should explain why the RH-3866 and RH-9090 residues found in all three trials were corrected for 90% and 70% average recovery, respectively, when the fortification data provided do not support these averages. From the residue data reported, it is apparent that fortified samples were not injected with each set of field samples injected. Were field samples extracted with fortified samples and controls as a quality assurance measure, if not, what quality control mechanism was in place to insure the analytical integrity of the field residues reported? The petitioner is asked to comment on the following analytical concern in the squash field trial results. Chromatograms of samples injected on 02/20/87 and 02/19/87 show a large "interference" peak at a retention time close to RH-3866. Later samples do not show the same peak. Was the peak due to contamination picked up during the extraction process or was it a column or detector contamination problem? Was a confirmatory technique run on a representative sample to be sure that the peak was not a residue of interest? What impact did the interference have on quantitation of RH-3866 or the method sensitivity?

The fungicide use pattern employed to generate the residue data in these studies did not emulate the proposed use pattern in this petition. In the cantaloupe and squash trials, the fungicide was applied at the maximum label rate, but the maximum seasonal maximum rate was not applied to the crop. Myclobutanil was applied at twice the proposed use rate in the cucumber trial, but again, the maximum seasonal rate was not applied to the crop. Given the fact that the data must be extrapolated to estimate residues which would be present on the RAC at the time of harvest as a result of the proposed use; this data will be considered as supporting data only, and will not be considered as stand alone data on which to base the establishment of a permanent tolerance.

1990 Crop Field Trials: *Sufficient raw data has been supplied to verify the field portion of the 1990 crop field trials, however additional information needs to be supplied for the analytical phase of the study. Information to be supplied by the petitioner includes sample extraction dates and extract storage conditions. The petitioner is asked to explain why residues of RH-3866 and RH-9090 were corrected for an average recovery of 90% and 85%, respectively, when the results of actual fortifications do not support these averages. Additionally, the petitioner is asked to explain why the detector response as indicated by several "curved" standard curves was not linear for all runs. The method clearly states that given the concentrations injected and the injection volume, the detector response should be linear over the range of standard concentrations.*

Only residue levels generated from the 2X application will be considered as stand alone data on which to base the establishment of a permanent tolerance level since the maximum seasonal rate was reached. Data from plots treated at the lower rate (1X) will only be considered as supporting data which can be extrapolated to estimate the residue levels expected in the RAC at the time of harvest based on the proposed use contained in this petition.

Aerial vs. Ground Bridging Study: *Adequate information has been supplied by the petitioner to confirm all aspects of the field portion of this trial. The analytical portion has been adequately supported by the raw data submitted, however, the petitioner is asked to explain why average recoveries of 90% for RH-3866 and 85% for RH-9090 were used to correct residues found. Results should have been corrected using the results of the fortifications run concurrently with the field samples. The petitioner should explain why the detector response for RH-9090 was not linear during several runs.*

Petitioner's Response: The following information was provided by the petitioner (Correspondence, S. Longacre 10/30/98):

The extraction and analysis dates are listed on the run sheets in the raw data for each study. The extraction date was most frequently the same as the day of analysis. In some cases analysis took place the day after extraction, or three days later (i.e., extracted Friday and analyzed Monday). The sample extracts were stored in the freezer until analysis.

Historical recoveries (i.e., the average recoveries from one to two years of analyses), rather than each individual study's fortification recoveries, were used routinely for studies conducted at this time to minimize the variation of individual study fortification recoveries. This is a less relevant issue today, because current guidelines specify that residue values should by reported uncorrected for fortification recovery. Therefore, the reported residue values in the reviewed studies are actually greater than would by reported by today's standards. The residue values, whether corrected or not corrected for fortification recovery, are all well under the proposed 0.5 ppm tolerance for the cucurbit crop group.

The contract analytical laboratory (Centry Analytical Laboratories) used a Restex Meagbor RTX-35 column and a Capillary Thermionic Specific (NPD) detector for both the RH-3866 and RH-9090 analyses. Use of this detector very frequently results in a

nonlinear response due to the need to constantly adjust to optimize the response. The regression used to fit the standard curve was quadratic throughout the study, even in cases where the response appeared "linear," in order to maintain consistency.

RAB1's Conclusion: The requested information has been provided for the 1990 field trials only. Therefore, the data from these 7 residue trials will be used to determine the appropriate tolerance for the cucurbit crop group.

Deficiency - Conclusions 6b-6c (from Memo, D. Davis 2/8/93)

6b. A sufficient number of crop field trials have not been submitted to support the establishment of a permanent tolerance for a crop grouping. The petitioner should conduct at least seven new field trials on representative crops to provide sufficient residue data for evaluation of the appropriateness of setting a tolerance for the cucurbit crop group (see Magnitude of the Residue -Plants section of this review for details).

6c. Determination of the adequacy of the geographical representation of the residue data will be withheld until CBTS is in receipt of all the studies required. Further, an evaluation of the appropriateness of 0.5 ppm as the tolerance level for residues of myclobutanil in or on the cucurbit crop group will be made when the petitioner has submitted all the residue data needed to properly evaluate a request for a permanent tolerance.

Petitioner's Response: Submission of the following crop field trial study:

RH-3866 40W Field Residue Trials in Cucurbits: RAR 94-0091, 94-0105, 94-0106, 94-0109, 94-0110, 94-0126, 94-0159, 94-0160, 94-0177. MRID# 445114-01.

Residue data were submitted depicting the magnitude of residue of myclobutanil in/on the cucurbit crop group. Nine field trials (2 cucumber trials, 3 muskmelon trials, 4 summer squash trials) were conducted in the following states: CA(1), FL(2), IN (1), NY(2), and TX(3). Six to eight applications of Rally® 40W were applied at intervals of 7-10 days, beginning approximately 4 weeks after planting. Each application was made by either ground (with a hollowcone multinozzle or flat fan sprayer) or hand (with a hollowcone nozzle) at a rate of 0.1 lb a.i./A (1.6x) for a total application rate of 0.6 - 0.8 lb. ai./A/season. The samples were harvested on the final day of application (0-day PHI) after sufficient time was allowed for the application to air dry. Samples were either immediately frozen or shipped fresh via overnight to Rohm and Haas Research Laboratories, where they were stored frozen until analysis. All samples were processed, then 10g of each were analyzed for RH-3866 and RH-9090 using the following reference method with minor modifications: TR 34S-88-10 Systhane Total Residue Analytical Method for Parent and Metabolites (MRID# 40803302). For both analytes the limit of quantitation (LOQ) is 0.01 ppm and the method limit of detection (LOD) is 0.003 ppm. At the 0.6 lb a.i./A/season application rate, total residues (RH-3866 and RH-9090) ranged from 0.004 to 0.105 ppm. A summary of the residues are listed in Table 1.

Table 1. Cucurbit Residue Data Summary: Treatment to Harvest Interval = 0-Day

Site	Variety	Total Application Rate (lb. ai/A)	SAI[1] (days)	Uncorrected Residues (ppm)		
				RH-3866	RH-9090	Total
Waller, TX (R6)	Squash/ Table King	0.6	431, 439	0.100 <LOD	0.0055 0.0063	**0.105** 0.0060
	Watermelon/ Jubilee	0.8	425, 427	<LOD <LOD	0.0043 <LOD	0.0040 <LOD
Fresno, CA (R10)	Zucchini/ Ambassador	0.6	403, 421	0.0047 0.0055	0.0058 0.0134	0.0102 0.0182
Westfield, NY (R1)	Cucumber/ Marketmore	0.6	387, 405	0.0324 <LOD	0.0051 <LOD	0.0372 <LOD
	Squash/ Multipick	0.6	387, 405	0.0248 <LOD	0.0083 <LOD	0.0326 <LOD
Noblesville, IN (R5)	Cantaloupe/ Iriquois	0.6	367, 385	0.0455 <LOD	<LOD <LOD	0.0455 <LOD
Zellwood, FL (R3)	Squash/ Dixie Hybrid	0.6	280, 282	0.0279 0.0050	0.0065 0.0069	0.0340 0.0114
	Cucumber/ Poinsett 76	0.6	280, 282	0.0417 0.0150	<LOD <LOD	0.0417 0.0150
Waller, TX (R6)	Cantaloupe/ Magnum 45	0.7	434, 436	0.0176 0.0245	0.0049 0.0041	0.0222 0.0284

1. SAI = Sample to Analysis Interval
NOTES: Analytical Method TR 34S-88-10 (MRID# 40803302, LOQ = 0.01 ppm, LOD = 0.003 ppm)
Total ppm parent eq = [RH-3866] + 0.9475[RH-9090]

RAB1's Conclusion: Nine additional trials were submitted: 2 cucumber trials in Regions 1 (1 trial) and 3 (1 trial); 3 muskmelon trials in Regions 5 (1 trial) and 6 (2 trials); and 4 summer squash trials in Regions 1 (1 trial), 3 (1 trial), 6 (1 trial), and 10 (1 trial). The maximum single application rate was 0.1 lb. a.i./A (1.6x). Of the trials previously submitted, only seven were generated at or in excess of the maximum seasonal application rate (0.6 lb. a.i./A). Therefore, 16 field trials have been conducted: 5 cucumber trials in Regions 1 (1 trial), 2 (1 trial), 3 (1 trial), and 5 (2 trials); 5 muskmelon trials in Regions 5 (1 trial), 6 (2 trials) and 10 (2 trials); and 6 summer squash trials in Regions 1 (2 trials), 3 (1 trial), 6 (2 trials), and 10 (1 trial). According to the current guidance (Table 1 of OPPTS 860.1500), for the establishment of a tolerance on the cucurbit crop group, a minimum of 17 trials should be conducted on the following commodities: 6 cucumber trials in Regions 2 (2 trials), 3 (1 trials), 5 (2 trials), and 6 (1 trial); 6 muskmelon trials in Regions 2 (1 trial), 5 (1 trial), 6 (1 trial), and 10 (3 trials); and 5 summer squash trials in Regions 1 (1 trial), 2 (1 trial), 3 (1 trial), 5 (1 trial), and 10 (1 trial). Table 2 lists the submitted and recommended field trial locations for cucumbers, muskmelons, and summer squash.

Table 2. Field Trial Distribution (Actual vs. Suggested).

Commodity	Actual Field Trial Distribution	Suggested Field Trial Distribution
Cucumbers	5 trials Region 1 (1 trial) Region 2 (1 trial) Region 3 (1 trial) Region 5 (2 trials)	6 trials Region 2 (2 trials) Region 3 (1 trial) Region 5 (2 trials) Region 6 (1 trial)
Muskmelon	5 trials Region 5 (1 trial) Region 6 (2 trials) Region 10 (2 trials)	6 trials Region 2 (1 trial) Region 5 (1 trial) Region 6 (1 trial) Region 10 (3 trials)
Squash	6 trials Region 1 (2 trials) Region 3 (1 trial) Region 6 (2 trials) Region 10 (1 trial)	5 trials Region 1 (1 trial) Region 2 (1 trial) Region 3 (1 trial) Region 5 (1 trial) Region 10 (1 trial).

RAB1 has determined that the submitted trial data are adequate to support a permanent registration for the use of myclobutanil on the cucurbit crop group.

The combined residues of myclobutanil and its metabolite RH-9090 in/on the cucurbit crop group treated at application rates of 0.6 - 0.75 lb. a.i./A and harvested at 0-day PHIs ranged from 0.004-0.105 ppm. The available data indicate that the combined residues of myclobutanil and its metabolite RH-9090 will not exceed 0.2 ppm in/on the cucurbit crop group. Therefore, the appropriate tolerance level for the combined residues of myclobutanil and its metabolite RH-9090 is 0.2 ppm. **The petitioner should submit a revised Section F.**

Deficiency - Conclusion 7 (from Memo, D. Davis 2/8/93)

7. The frozen stability of the regulable residues has not been adequately demonstrated. Acceptance of the residue chemistry data reviewed in support of this petition is contingent upon the satisfactory resolution of this deficiency. The petitioner may either conduct a storage stability study on a representative member of the cucurbit crop group or conduct storage stability studies on four diverse crops (see the Storage Stability section of this review for recommended crops) to supplement the apple and grape data in the Agency's files.

Petitioner's Response: Submission of the following storage stability study:

Storage Stability Study: RH-3866 & RH-9090 in Cucurbits. MRID# 446798-05.

In this study, 10g of homogenized cucumber samples were weighed in 4oz. polypropylene containers. The samples were spiked with a solution of RH-3866 and RH-9090, each at a concentration of 0.5ppm, and stored at approximately -10°C. One set (three samples) of spiked

cucumber samples, a control sample, and two fresh fortified samples were analyzed concurrently at the following time intervals: 0, 3, 6, 12, 18, 24, 30, and 36 months. The samples were analyzed with Rohm and Haas Analytical Method TR 34S-88-10 (MRID# 40803302), with minor modifications. The quantification of RH-3866 and RH-9090 residues was completed via gas chromatography using a RTX-35 30 m column and a Capillary Thermionic Specific Detector. For both analytes, the limit of quantification (LOQ) is 0.01 ppm. The storage stability results for RH-3866 and RH-9090 are listed in Tables 3 and 4, respectively.

Table 3. Storage Stability of RH-3866 in Cucurbits.

Storage Period (months)	Date of Analysis	Fresh Fortified Recovery (%)		Aged Sample Recovery (%)			Average (%) Recovery		Corrected Recovery%
		#1	#2	#1	#2	#3	Fresh	Aged	
0	12/9/91	74.6	82.2	76.8	75.0	87.6	78.4	79.8	102
3	3/13/92	93.0	94.6	97.2	81.0	79.8	93.8	86.0	91.7
6	6/11/92	72.0	80.6	81.8	71.0	68.4	76.3	73.7	96.6
12	12/17/92	111	103	82.2	82.8	74.4	107	79.8	74.6
18	7/8/93	112	116	103	101	109	114	104	91.2
24	12/20/93	81.8	77.6	102	101	92.4	79.7	98.5	123
30	6/13, 14/94	96.6	87.6	80.4	86.8	83.6	92.1	83.6	90.8
36	12/21/94	97.8	101	94.2	97.4	105	99.4	98.9	99.5
						Average	92.6	88.1	
						Standard Deviation	13.9	11.1	

NOTES:
1. Analytical Method TR 34S-88-10, Method LOQ=0.01 ppm, LOD=0.003 ppm.
2. When recovery is >100%, decimals are ignored in reporting data
3. Control sample at 18 month interval contained 0.0221 ppm RH-3866.

Table 4. Storage Stability of RH-9090 in Cucurbits.

Storage Period (months)	Date of Analysis	Fresh Fortified Recovery (%)		Aged Sample Recovery (%)			Average (%) Recovery		Corrected % Recovery
		#1	#2	#1	#2	#3	Fresh	Aged	
0	12/9/91	86.4	96.8	85.4	92.6	109	91.6	95.6	104
3	3/14/92	85.2	87.2	87.0	80.6	85.6	86.2	84.4	97.9
6	6/10/92	77.6	94.0	88.6	92.4	89.4	85.8	90.1	105
12	12/21/92	109	125	97.0	96.6	86.4	117	93.3	79.7
18	7/14/93	86.0	88.6	79.8	87.2	84.8	87.3	83.9	96.1
24	12/22/93	88.6	79.4	101	109	110	84.0	107	127
30	6/15/94	110	114	98.6	108	96.6	112	101	90.2
36	12/21/94	84.6	107	88.2	85.8	94.4	95.8	89.5	93.4
						Average	95.0	93.1	
						Standard Deviation	12.7	7.9	

NOTES:
1. Analytical Method TR 34S-88-10, Method LOQ=0.01 ppm, LOD=0.003 ppm.
2. When recovery is >100%, decimals are ignored in reporting data
3. Control sample at 0,3, 12, & 18 month interval contained 0.0396, 0.0562, 0.0345, & 0.0692 ppm RH-9090.

RAB1's Conclusion: The frozen stability of regulable residues have been adequately demonstrated. Residues of myclobutanil (RH-3866) and its alcohol metabolite (RH-9090) are stable in the cucurbit group for at least 36 months. As all the samples in the submitted crop field trials were stored less than 36 months, storage stability of myclobutanil and its alcohol metabolite in cucurbits has been adequately demonstrated. This deficiency is now resolved.

cc: PP#2F04155, J. Rowell (RAB1)
RDI: M. Morrow (9/17/99), Chemists (9/16/99), G. Kramer (9/2/99).
J. Rowell:806W:CM#2:(703)305-5564:7509C:RAB1

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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FEB 8 1993

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

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#2F04155 Myclobutanil (Nova®/Rally®) Fungicide in or on the Cucurbit Crop Group. Evaluation of analytical method and magnitude of residue data.
MRID Nos: 424766-01
CBTS No: 10707
DP Barcode: D183273

FROM: Donna S. Davis, Chemist
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THROUGH: Debra Edwards, Ph.D., Chief
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TO: J. Fairfax/S. Lewis, PM Team 21
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Registration Division (H7505C)

Rohm and Haas Company requests the establishment of a permanent tolerance for the combined residues of myclobutanil, (α-butyl-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile) and its metabolite, α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile (free and bound) in or on the cucurbit crop group at 0.5 ppm.

Background:

The following terms as defined below are used interchangeably throughout this review.

myclobutanil: RH-3866 (α-butyl-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile)
alcohol metabolite: RH-9090 (α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile)
diol metabolite: RH-0294 (α-(4-chlorophenyl)-α-(3,4-dihydroxybutyl)-1*H*-1,2,4-triazole-1-propanenitrile)

Permanent tolerances are established (40CFR §180.443(a)) for the

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combined residues of the fungicide, myclobutanil and its alcohol metabolite (free and bound) in or on apples at 0.5 ppm, cherries (sweet and sour) at 4.0 (expiration date of 10/1/94), grapes at 1.0 ppm, nectarines at 2.0 ppm (exp. 10/1/94) and peaches at 2.0 (exp. 10/1/94). Tolerances for the combined residues of myclobutanil, its RH-9090 metabolite and its diol metabolite are established (40CFR §180.443(b)) at 0.05 ppm for milk. Tolerances are established (40CFR §180.443(c)) for the combined residues of myclobutanil and its RH-9090 metabolite (free) in or on the following: meat, fat and meat by-products (except liver) of cattle, goats, hogs, horses and sheep at 0.05 ppm, liver of cattle, goats, hogs, horses and sheep at 0.3 ppm, meat, fat and meat by-products of poultry at 0.02 ppm and eggs at 0.02 ppm. Food additive tolerances are established (40CFR §185.4350) for the combined residues of myclobutanil and its RH-9090 metabolite (free and bound) in or on raisins at 10.0 ppm. Feed additive tolerances are established (40CFR §186.4350) for the combined residues of the fungicide, myclobutanil and its alcohol metabolite in or on apple pomace (wet and dry) at 5.0 ppm, grape pomace (wet and dry) at 10.0 ppm and raisin waste at 25.0 ppm.

Permanent tolerances are pending for the pome fruit crop group, plums, dried prunes, bananas, tomatoes and the processed commodities of tomatoes. CBTS has recommended in favor of the establishment of a permanent tolerance for the combined residues of myclobutanil and its alcohol metabolite (free and bound) in or on the pome fruit crop group at 0.5 ppm (PP#9F3812, M. Nelson, 4/10/90), plums at 1.0 ppm (PP#1F3954, R. Lascola, 6/3/92 and dried prunes at 4.0 ppm (FAP#1H5608, R. Lascola, 6/3/92), TOX considerations permitting. CBTS has recommended in favor of a tolerance on apricots at 2.0 ppm with an expiration date of 3/31/94 (PP#1F3954, R. Lascola, 6/3/92), TOX considerations permitting.

A temporary tolerance was established for the combined residues of myclobutanil and its RH-9090 metabolite (free and bound) in or on the cucurbit crop group with an expiration date of 1/31/92 (PP#9G3765). CBTS has recommended in favor of extending until 1/22/93 the EUP/temporary tolerance of 0.5 ppm, TOX considerations permitting.

Conclusions:

1. The manufacturing process of technical myclobutanil, RH-3866 has been adequately discussed in DEBs review of PP#9G3765 (C. Trichilo, 9/19/88). The TGAI is 93.9 % pure and the impurities found are not likely to pose a residue problem at the proposed application rate.

2. CBTS concludes that the proposed use labels for Rally 40W and Nova® 40W are adequate provided additional residue data are generated to reflect application intervals of less than 7 days. If no additional data are generated, the suggestion to

reduce the application interval to less than 7 days should be removed from the label.

3. The nature of the residue in the cucurbit crop group commodities has been adequately defined by translation of data from other crops. The combined residues of the parent compound, (α-butyl-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile) and its metabolite (α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile) (free and bound) are the residues of regulatory concern.

4. Since there are no animal feed items associated with commodities in the cucurbit crop group, a discussion of animal metabolism and secondary residues of myclobutanil in animal commodities is not relevant to this petition.

5a. CBTS concludes that adequate analytical methodologies are available for enforcement of the proposed tolerance in or on the cucurbit crop group. The proposed enforcement method has been forwarded to FDA for inclusion in PAM II.

5b. The fortification data provided adequately validate the data collection methods used to produce residue data considered in support of this petition.

6a. The acceptance of the residue data reviewed in this memorandum is contingent upon the satisfactory resolution of the questions raised in this review (see Magnitude of the Residue - Plants section of this review). If the petitioner is unable to provide the supporting data needed to resolve the issues raised, new field trials will be needed to replace those previously submitted.

6b. A sufficient number of crop field trials have not been submitted to support the establishment of a permanent tolerance for a crop grouping. The petitioner should conduct at least seven new field trials on representative crops to provide sufficient residue data for evaluation of the appropriateness of setting a tolerance for the cucurbit crop group (see Magnitude of the Residue -Plants section of this review for details).

6c. Determination of the adequacy of the geographical representation of the residue data will be withheld until CBTS is in receipt of all the studies required. Further, an evaluation of the appropriateness of 0.5 ppm as the tolerance level for residues of myclobutanil in or on the cucurbit crop group will be made when the petitioner has submitted all the residue data needed to properly evaluate a request for a permanent tolerance.

7. The frozen stability of the regulable residues has not been adequately demonstrated. Acceptance of the residue chemistry data reviewed in support of this petition is contingent upon the satisfactory resolution of this deficiency. The petitioner may either conduct a storage stability study on a representative member of the cucurbit crop group or conduct storage stability studies on four diverse crops (see the Storage Stability section of this review for recommended crops) to supplement the apple and grape data in the Agency's files.

8. Since there are no existing Codex, Canadian or Mexican tolerances for the residues of myclobutanil in or on the cucurbit crop group, establishment of a U.S. tolerance will not cause international harmonization problems.

Recommendations:

CBTS can not, at this time, recommend for the establishment of the proposed tolerance of 0.5 ppm for residues of myclobutanil and its alcohol metabolite (free and bound) in or on the cucurbit crop group for the reasons stated in Conclusions 2, 6a, 6b, 6c and 7.

To resolve the deficiencies noted, CBTS recommends the following:

- Either conduct a frozen storage stability study of appropriate duration on a representative member of the cucurbit crop group or submit data verifying the frozen stability of myclobutanil and its RH-9090 metabolite in or on four diverse crops. If the second option is selected, CBTS requests data demonstrating the frozen stability of the residues of interest in or on an oilseed crop, a non-oily grain, a leafy vegetable and a root crop in addition to the apple and grape (fruit) data in the Agency's files.

- Conduct at least seven new crop field trials. Cucumber sites should include Florida and New York. Melon sites should include Texas, Arizona and Indiana and new field trials on squash should be conducted with summer squash. During the field portion of the studies, pesticide use patterns should closely match the proposed use pattern maximum application rate and minimum reapplication interval. If the petitioner wishes to continue to support use of the fungicide at reapplication intervals of less than seven days, data must be generated to reflect this use. The analytical phase of the study should include quality control measures to insure the integrity of the data. CBTS highly recommends that control samples and fortified samples be extracted and analyzed concurrently with field samples. Information on storage conditions and sampling dates, extraction dates and analysis

dates should be submitted with each field trial. Finally, if samples are stored for longer than 30 days between harvest and analysis, storage stability data will be required to validate the frozen stability of the regulable residues for an appropriate duration.

Note to PM: CBTS requests submission of this entire review to the petitioner.

Detailed Considerations

Manufacture and Formulation:

The process by which technical myclobutanil, RH-3866 is synthesized has been adequately described in the confidential appendix to DEBs review of PP#9G3765 (C. Trichilo, 9/19/88). The TGAI is 93.9% pure. The principle impurities found are not likely to pose a residue problem at the maximum proposed use rate.

The formulated product contains 40 % ai by weight and 60 % inerts. It is in the purview of RD to clear the inerts in the formulated product under 40CFR §180.1001. The formulated product is a wettable powder, manufactured by Rohm and Haas, Philadelphia, PA. Two formulations are marketed for myclobutanil; both packaged as water-soluble pouches:

Rally® 40W Agricultural Fungicide (EPA Reg No. 707-215)
Nova® 40W Agricultural Fungicide (EPA Reg No. 707-221)

Proposed Use:

Rally® 40W/Nova® 40W is to be applied via ground or aerial application, foliarly, at a rate of 2.0 - 2.5 **oz.**/A (0.051 - 0.0625 lb ai/A) at the first sign of disease development. Initial treatment is followed by repeat applications at seven to ten day intervals, however, if conditions favor heavy disease, a reduction in the application interval is suggested. The following restrictions apply

- Do not apply this product through any type of irrigation system.
- For aerial applications, apply in a minimum of 10 gallons of water per acre.
- Do not apply more than 1.5 lbs/A (0.6 lbs ai/A) per crop.
- Do not plant a crop not specifically mentioned on this label within 18 months of using Rally® 40W/Nova® 40W fungicide.

There are no PHI restrictions on the label.

CBTS concludes that the proposed use directions are adequate with the following stipulation. The proposed label allows for repeat applications at frequencies of less than 7 day intervals, however, very limited residue data has been submitted to support a reapplication interval of less than 7 days. If the petitioner wishes to retain the option of a shorter application interval on the label, CBTS requires that residue data be generated to clearly define the level of residue in the RAC at the time of harvest as a consequence of this use pattern. If no additional data are generated reflecting a shorter application interval, the statement "*If environmental conditions favor heavy disease development, reduce application interval*" should be removed from the label.

Nature of the Residue - Plants:

No plant metabolism data was submitted with this petition. Plant metabolism data on wheat, grapes and apples have been reviewed with past petitions. A brief summary of that metabolism data is provided to elucidate the regulable residues in or on members of the cucurbit crop group.

A translocation study was conducted in connection with PP#4G3149. A methanol solution of ^{14}C-labeled RH-3866 was applied to a single wheat blade and a single leaf of grape and apple seedlings. Plants were taken at various intervals, lyophilized and autoradiographed. For wheat, the treated blade, roots and remaining foliage were separately combusted to quantitate the extent of translocation. In a second study, seedlings were grown in nutrient solutions of ^{14}C-labeled RH-3866. These plants were also lyophilized and autoradiographed with some combustion to measure the extent of absorption and translocation. The studies were reviewed (R. Loranger, 1/9/85) and it was concluded that very little RH-3866 translocates beyond treated leaves following foliar application; however, when absorbed by roots, the fungicide translocates readily throughout the entire plant.

Additional plant metabolism data was generated in support of PP#4G3149. Wheat plants grown under field conditions were treated with the fungicide myclobutanil, RH-3866, and the resulting metabolic pathway was proposed. RH-3866 is oxidized on the butyl chain to yield the alcohol RH-9090 (free and bound) as a major metabolite. The alcohol is further oxidized to the ketone (2-6% of final residue). The data was reviewed (R. Loranger, 1/9/85) and found to be adequate. As a result, the regulable residues were defined as the parent fungicide, RH-3866 and its alcohol metabolite, RH-9090 (free and bound).

Apple and grape metabolism data were reported in PP#7G3479. It was

concluded that the nature of the residue in apples and apple by-products was adequately understood (R. Loranger, 6/16/87). RH-3866 is metabolized by hydroxylation of the number three carbon on the butyl chain, with subsequent conjugation to form glucoside(s). Small amounts (1-3% of whole fruit) of the ketone are also present. The results of the grape metabolism study showed that grape metabolism proceeds via the same pathway as apples, and as a result for both apple and grape commodities (and their by-products) the regulable residues were determined to be RH-3866 and RH-9090 (free and bound).

Based on the fact that the fruit metabolic pathway is the same as that of wheat metabolism, and given the limited translocation observed from foliar application, the metabolism data are adequate to translate to the cucurbit crop group. CBTS therefore concludes that the nature of the residue in the cucurbit crop group is adequately delineated based on data from other crops, and we further conclude that the combined residues of the parent herbicide, myclobutanil, (α-butyl-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile) and its metabolite (α-(3-hydroxybutyl)-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile) (free and bound) are the residues of regulatory concern.

Nature of the Residue - Animals:

Animal metabolism data were not submitted with this petition. Since there are no animal feed items associated with commodities in the cucurbit crop group, a discussion of animal metabolism and secondary residues of myclobutanil in animal commodities is not relevant to this petition.

Analytical Methods - Enforcement:

The Pestrak data base (11/6/90) indicates that the parent compound, myclobutanil, is not recovered via multiresidue method protocol E (PAM I 211.1 and 212.1), is completely recovered via protocol D (PAM I 232.4) and has a variable recovery via protocol A under special instrument conditions (PAM I 242.2). The metabolite, RH-9090 is similarly not recovered via protocol E, and has a variable recovery via protocol A under special instrument conditions. Recovery of RH-9090 via protocol D is only partial.

An analytical method (34S-88-10) entitled "RH-3866 Total Residue Analytical Method for Apple and Grape" has undergone successful method validation by the agency (PP#7F3476/FAP#7H5524, M. Nelson, 4/14/88) and has been submitted for publication in PAM II as Method I, §180.443 (letter from M. Nelson to A. Marcotte, 7/18/89).

CBTS concludes that adequate methodologies are available for enforcement of the proposed tolerance on members of the cucurbit

crop group.

Analytical Methods - Data Collection Methods:

The residue data submitted by the petitioner was generated either by method 310-84-27; method 310-84-27, addendum 31H-86-15; or by 34S-88-10 (310-84-27 as amended by 31H-86-15 and 31S-87-67).

In brief, method 310-84-27 involves soxhlet extraction of samples with 0.5N HCl/MeOH. RH-9090 conjugates are hydrolyzed during extraction to RH-9090. RH-9089 (ketone) residues are converted to RH-9090 by sodium borohydride reduction. The reaction mixture is washed with petroleum ether and partitioned into methylene chloride. The sample is then cleaned up by Chelex 100-Fe^{+++} affinity chromatography, followed by a second methylene chloride partitioning. Additional sample clean up is facilitated by florisil chromatography. RH-3866 is determined by a gas chromatographic separation with nitrogen phosphorus detection. RH-9090 residues are analyzed by gas chromatography and electron capture detection.

Addendum 31H-86-15 (addendum #1) consists of modifications to 310-84-27 aimed at improving sample clean up and RH-9090 quantitation. The modifications involve changes in the procedure for the preparation of the Chelex 100-Fe^{+++} resin; additional washing in the second methylene chloride partitioning; substitution of a Bio-Sil A column for the florisil column and use of eluants compatible with the Bio-Sil A column; and modifications to the GC/ECD conditions (flow rate, temperature) for RH-9090 quantitation, including a change from packed to capillary column.

Addendum 31S-87-67 (addendum #2) consists of the addition of a methanol pre-wash of the Chelex-100 (prior to the preparation of the Chelex 100-Fe^{+++} resin) to reduce reagent artifacts appearing on the chromatograms. In addition, modifications are made to the elution solutions used with the Chelex 100-Fe^{+++} column; elimination of the water wash of methylene chloride in the second partitioning process; and changes in volume of elution solutions used with the Bio-Sil A column to further change the original method.

Review of the residue data, fortification and control data, and chromatograms submitted shows the method to have a sensitivity of 0.01 ppm. A summary table of the recovery data reported is provided below.

Table 1. Fortification Results for **RH-3866**
Method 310-84-27 and Method 310-84-27 as amended by 31H-86-15

Method	MRID No.	Crop	Fortification Range (ppm)	Recovery Range (%)	Average Recovery (number)
310-84-27	410855 -01	Cantaloupe	0.02 - 0.2	88 - 129	103 (n=3)
	410855 -03	Squash	0.02 - 0.66	75 - 83	78 (n=3)
310-84-27, ad #1	410855 -06	Cucumber	0.02 - 0.1	77 - 84	80 (n=3)

Table 2. Fortification Results for **RH-9090**
Method 310-84-27 and Method 310-84-27 as amended by 31H-86-15

Method	MRID No.	Crop	Fortification Range (ppm)	Recovery Range (ppm)	Average Recovery (number)
310-84-27	410855 -01	Cantaloupe	0.02 - 0.46	55 -93	72 (n=3)
	410855 -03	Squash	0.05 - 0.36	71 - 93	78 (n=3)
310-84-27, ad #1	410855 -06	Cucumber	0.02 - 0.1	54 - 99	81 n=3)

Table 3. Fortification Results for **RH-3866**
Method 34S-88-10

Method	RAR #	Crop	Fort. Level (ppm)	Recovery (%)	Avg Rec ± Std Dev
34S-88-10	90-0089	Cucumber	0.1	102	102 ± 9 (n=11)
	90-0163	Cucumber	0.01	108	
		Cucumber	0.05	111	
	90-0115	Cucumber	0.05	82	
	90-0127	Squash	0.02	94	
	90-0134	Squash	-	-	
	90-0128	Cantaloupe	0.2	101	
	90-0133	Cantaloupe	0.05	107	
	92-0001	Squash	0.05	116	
		Squash	0.05	104	
	91-0072	Squash	0.1	97	
		Squash	0.05	99	

Table 4. Fortification Results for **RH-9090**
Method 34S-88-10

Method	RAR #	Crop	Fort. Level (ppm)	Recovery (%)	Avg. Rec. ± Std. Dev
34S-88-10	90-0089	Cucumber	0.1	107	93 ± 14 (n=13)
	90-0163	Cucumber	0.02	94	
		Cucumber	0.05	92	
	90-0115	Cucumber	0.05	98	
	90-0127	Squash	0.02	81	
	90-0134	Squash	0.01	89	
	90-0128	Cantaloupe	0.02	86	
		Cantaloupe	0.2	68	
	90-0133	Cantaloupe	0.05	97	
	92-0001	Squash	0.1	71	
		Squash	0.1	105	
	91-0001	Squash	0.05	120	
		Squash	0.5	100	

The fortification data above adequately validate the data collection methods used to produce residue data in support of this petition for a permanent tolerance for the combined residues of RH-3866 and RH-9090 (free and bound) in or on members of the cucurbit crop group.

Magnitude of the Residue - Plants:

An aerial vs. ground bridging study was submitted with this petition. In addition, the petitioner has referenced crop field trials previously submitted to the agency in support of a temporary tolerance on the cucurbit crop group (PP#9G3765). Eight of the field trials referenced contain reanalysis of samples originally analyzed by Craven Laboratory. The following field trials with SAIs (sampling to analysis interval) ≥ 1489 days will not be considered in support of this petition. Unacceptable field trials include those with RAR Numbers 86-0220, 86-0240, 86-0239, 86-0270, 88-0147, 86-0271, 87-0356 and 88-0148. The petitioner was notified of the SAI problem and the rationale behind the decision not to review this data in a previous CBTS memo (PP#9G3765, M. Nelson, 5/29/92).

1986 Crop Field Trials

Three crop field trials were conducted in 1986 to obtain residue levels resulting from the use of myclobutanil on cantaloupes, squash and cucumbers. The cantaloupe field trial (MRID No. 410855-01/RAR No. 86-0369) was carried out in Maryland; the squash field trial (MRID No. 410855-03/RAR No. 86-0219) was conducted in Florida and the cucumber field trial (MRID No. 410855-06/RAR No. 86-0226) was carried out in California. Each trial involved multiple applications of the fungicide, myclobutanil (40W formulation) to a single site. Cantaloupe received seven applications of fungicide at a rate of 0.063 lb ai/A for a total crop exposure of 0.441 lb ai/A. Squash received eight applications of myclobutanil at a rate of 0.063 lb ai/A for a total crop exposure of 0.504 lb ai/A. Cucumbers received three applications of fungicide at a rate of 0.125 lb ai/A (twice the proposed label use) for a total crop exposure of 0.375 lb ai/A. No information is provided on the retreatment intervals for the cantaloupe and squash trials. The fungicide was reapplied at 6 - 7 day intervals during the cucumber field trial. The fungicide was applied foliarly in solution at a rate of 30 - 50 gal/A. Cantaloupe and squash samples were harvested at 0, 3, 5 and 10 days TSI (treatment to sampling interval). Cucumber samples were harvested at 0,4,6 and 11 days TSI. Data is reported for three samples at each harvesting interval, however, it is unclear if three separate plots were sprayed and sampled, or if one plot was treated and three samples were taken. The analytical data for the three trials was generated by Rohm and Haas Company, Spring House, PA and is summarized in tabular form at the end of this section.

Discussion

Additional information on the field portion of the three field trials is needed to adequately evaluate the applicability of the results to the establishment of a permanent tolerance. The petitioner is requested to supply the following supporting data. Information on retreatment intervals should be provided for the cantaloupe and squash trials. Additionally, clarification is requested as to the number of plots involved in each of the trials. For each trial, residue levels are reported for three samples at each harvesting interval. Were three plots treated at each site and sampled, or was a single plot treated and three samples taken? Following harvest, how were cantaloupe and cucumber samples treated/stored? The petitioner is requested to supply information on sample processing and sample storage.

Additional supporting data is requested from the petitioner on the analytical portion of these field trials. Dates of extraction and conditions of extract storage should be elucidated. The petitioner should explain why the RH-3866 and RH-9090 residues found in all three trials were corrected for 90% and 70% average recovery, respectively, when the fortification data provided do not support these averages. From the residue data reported, it is apparent that fortified samples were not injected with each set of field samples injected. Were field samples extracted with fortified samples and controls as a quality assurance measure, if not, what quality control mechanism was in place to insure the analytical integrity of the field residues reported? The petitioner is asked to comment on the following analytical concern in the squash field trial results. Chromatograms of samples injected on 02/20/87 and 02/19/87 show a large "interference" peak at a retention time close to RH-3866. Later samples do not show the same peak. Was the peak due to contamination picked up during the extraction process or was it a column or detector contamination problem? Was a confirmatory technique run on a representative sample to be sure that the peak was not a residue of interest? What impact did the interference have on quantitation of RH-3866 or the method sensitivity?

The fungicide use pattern employed to generate the residue data in these studies did not emulate the proposed use pattern in this petition. In the cantaloupe and squash trials, the fungicide was applied at the maximum label rate, but the maximum seasonal maximum rate was not applied to the crop. Myclobutanil was applied at twice the proposed use rate in the cucumber trial, but again, the maximum seasonal rate was not applied to the crop. Given the fact that the data must be extrapolated to estimate residues which would be present on the RAC at the time of harvest as a result of the proposed use; this data will be considered as supporting data only, and will not be considered as stand alone data on which to base the establishment of a permanent tolerance.

1990 Crop field Trials

MRID No. 421890-01
Seven sites (CA(2), OH, MI, NC, TX, and PA) were chosen for crop field trials on the 40 W formulated product of RH-3866 on the representative members of the cucurbit crop group (40CFR §180.34), cucumbers, squash and cantaloupe. At each site, three plots were designated, one to serve as an untreated control source, and two plots for fungicide treatment. One treated plot received five applications of RH-3866 at a rate of 0.125 lb ai/A (twice the proposed use rate) for a total of 0.626 lb ai/A with the exception of the cantaloupe trials. In the cantaloupe trials an additional application was made for a total seasonal application of 0.75 lb ai/A. The second treated plot received five applications of RH-3866 at a rate of 0.063 lb ai/A for a total crop exposure of 0.315 lb ai/A for cucumbers and squash and six applications for cantaloupe for a total exposure of 0.378 lb ai/A. Both plots were treated on the same days at retreatment intervals which ranged from 6 to 12 days. The fungicide was applied foliarly by hand equipment in a water solution at a rate of 20 - 50 gal/A. After the final treatment, the crops were harvested at 0, 3 and 7 days TSI with the exception of the MI cucumber trial which had TSIs of 0, 2 and 6 days. Samples were shipped fresh to Rohm and Haas where they were stored frozen until analysis. All sample processing was done at Rohm and Haas and subsamples were shipped to Centre Analytical Laboratory, Spring House, PA for extraction and analysis. Residue data is summarized in table form at the end of this section.

Discussion
Sufficient raw data has been supplied to verify the field portion of the 1990 crop field trials, however additional information needs to be supplied for the analytical phase of the study. Information to be supplied by the petitioner includes sample extraction dates and extract storage conditions. The petitioner is asked to explain why residues of RH-3866 and RH-9090 were corrected for an average recovery of 90% and 85%, respectively, when the results of actual fortifications do not support these averages. Additionally, the petitioner is asked to explain why the detector response as indicated by several "curved" standard curves was not linear for all runs. The method clearly states that given the concentrations injected and the injection volume, the detector response should be linear over the range of standard concentrations.

Only residue levels generated from the 2X application will be considered as stand alone data on which to base the establishment of a permanent tolerance level since the maximum seasonal rate was reached. Data from plots treated at the lower rate (1X) will only be considered as supporting data which can be extrapolated to estimate the residue levels expected in the RAC at the time of harvest based on the proposed use contained in this petition.

Aerial vs. Ground Bridging Study

Crop Field Trial - MRID No. 424766-01

Two sites (CA and FL) were chosen to conduct crop field trials on two varieties of squash. The study was designed to be an aerial vs ground application bridging study. Two plots were selected for treatment. Each plot received three foliar treatments of myclobutanil (40W formulation) at a rate of 0.125 lb ai/A for a total of 0.375 lb ai/A. One plot was treated with ground equipment and the fungicide was applied in a water solution at a rate of 41 - 43 gal/A. The second plot was treated with aerial equipment and the pesticide was applied in solution at a rate of 5 gal/A. A third plot was untreated and served as a control source. Squash was harvested at 0, 3 and 7 days TSI (treatment to sampling interval) at the Florida site and at 0 days at the California site. Samples from California were shipped fresh and stored frozen at Rohm and Haas until analysis. Samples from Florida were frozen after harvest and shipped frozen to Rohm and Haas. All sample processing was done at Rohm and Haas. Sample analysis was performed at Centre Analytical Laboratory, State College, PA. The results are summarized in tabular format at the end of this section.

Discussion

Adequate information has been supplied by the petitioner to confirm all aspects of the field portion of this trial. The analytical portion has been adequately supported by the raw data submitted, however, the petitioner is asked to explain why average recoveries of 90% for RH-3866 and 85% for RH-9090 were used to correct residues found. Results should have been corrected using the results of the fortifications run concurrently with the field samples. The petitioner should explain why the detector response for RH-9090 was not linear during several runs.

Table 5. Summary Table
Residue Chemistry Data

Site/ RAR #	Crop	lb ai/ A	Total lb ai/A	TSI[1]	RH-3866 Residue (ppm)[2,3]	RH-9090 Residue (ppm)[2,3]	Total Residue (ppm)[4]
MD 86-0369	Cantaloupe	0.063	0.441	0	0.06	0.13	0.19
FL 86-0219	Squash	0.063	0.504	0	0.01	<0.01	0.02
CA 86-0226	Cucumbers	0.125	0.375	0	0.03	<0.01	0.04
OH 90-0089	Cucumber	**0.125**	**0.625**	**0**	**0.04**	**<0.01**	**0.05**
		0.063	0.315	0	0.05	0.01	0.06
MI 90-0115	Cucumber	**0.125**	**0.625**	**0**	**0.07**	**<0.01**	**0.08**
		0.063	0.315	0	0.02	<0.01	0.03
NC 90-0163	Cucumber	**0.125**	**0.625**	**0**	**0.02**	**<0.01**	**0.03**
		0.063	0.315	0	<0.01	<0.01	0.02
TX 90-0127	Squash	**0.125**	**0.625**	**0**	**0.04**	**<0.01**	**0.05**
		0.063	0.315	0	0.02	<0.01	0.03
PA 90-0134	Squash	**0.125**	**0.625**	**0**	**0.01**	**<0.01**	**0.02**
		0.063	0.315	0	0.01	<0.01	0.02
CA 90-0128	Cantaloupe	**0.125**	**0.750**	**0**	**0.08**	**<0.01**	**0.09**
		0.063	0.378	0	0.03	<0.01	0.04
CA 90-0133	Cantaloupe	**0.125**	**0.750**	**0**	**0.07**	**<0.01**	**0.08**
		0.063	0.378	0	0.05	<0.01	0.06
FL 92-0001	Squash	0.125[G]	0.375	0	0.06[5]	<0.01[5]	0.07
		0.125[A]	0.375	0	0.10[5]	<0.01[5]	0.11
CA 91-0072	Squash	0.125[G]	0.375	0	0.04[5]	<0.01[5]	0.05
		0.125[A]	0.375	0	0.12[5]	<0.01[5]	0.13

[1] TSI is treatment to sampling interval.
[2] RH-3866 residues corrected for 90% average recovery and RH-9090 residues corrected for 70% average recovery unless otherwise noted.
[3] Where duplicate analyses were performed, the highest residues are reported.
[4] Values reported as <0.01 are assigned a value of 0.01 ppm for the total residue calculation.
[5] RH-3866 and RH-9090 residues corrected for an average recovery of 90% and 85% respectively.
[G] Ground application.
[A] Air application.

Note: Those trial results indicated in **bold** meet or exceed the maximum seasonal

rate applied and are considered stand alone data on which to base a decision on the appropriateness of a permanent tolerance. The remaining data should serve as "supporting" data which must be extrapolated to estimate residues of myclobutanil in the RAC at the time of harvest.

A sufficient number of crop field trials have not been submitted to support the establishment of a permanent tolerance for an entire crop group. The petitioner has been advised that additional trials would be required (PP#9G3765, M. Nelson, 5/29/92) in support of a permanent tolerance. Of the trials summarized above, only seven were generated at or in excess of the maximum seasonal application rate, the remainder of the data must be extrapolated to estimate the residues expected in the RAC at the time of harvest from the proposed use; and therefore can only be considered in a supporting light.

The petitioner should conduct at least three additional trials on melons and two additional field trials each on cucumbers and squash for a total of seven new trials needed. Additionally, the petitioner must adequately address the issues raised in this memorandum concerning the field trials submitted thus far. Should the petitioner be unable to satisfactorily resolve the issues raised, additional field trials should be generated to replace those found unacceptable.

CBTS recommends that the field portion of any new studies generated closely match the proposed use pattern. Maximum label application rate and maximum seasonal application should be taken into consideration when designing additional trials. Residue data generated thus far were either conducted at twice the maximum label rate and at the seasonal application rate specified or were conducted at the maximum label rate, but at only a fraction of the seasonal rate. Attention should be given to generating data to support reduced reapplication intervals of less than 7 days if the petitioner wishes to retain this use on the label.

CBTS suggests that sites in Florida and New York be included in the new cucumber trials, and that sites in Texas, Arizona and Indiana be included in the new melon trials. In addition, all new squash residue data should be generated on summer squash. These recommendations are aimed at expanding the geographical representation of the residue data and targeting climatic conditions under which residues may be elevated.

The analytical portion of any new study should contain adequate quality assurance measures to assure the integrity of the residue data generated. Field samples should be extracted and injected with control and fortified samples. Recovery corrections should be made for the efficiency of the method based on concurrently run fortified samples. Fortification levels should be chosen at the method sensitivity level and at levels which bracket actual field

residues. In addition all storage and handling conditions should be included, as well as dates of extraction and analysis.

Determination of the adequacy of the geographical representation of the residue data will be withheld until CBTS is in receipt of all studies necessary for establishment of a permanent tolerance. Additionally, an evaluation of the appropriateness of 0.5 ppm as the tolerance level for myclobutanil and its alcohol metabolite in or on the cucurbit crop group will be made when the petitioner has submitted all the residue data needed to properly evaluate a request for a permanent tolerance on a crop grouping.

Magnitude of the Residue - Animals:

There are no animal feed items associated with the cucurbit crop group, therefore a discussion of the secondary residues of myclobutanil in animal commodities is not relevant to this petition.

Storage Stability:

No new storage stability studies were submitted with this petition. Further, no storage stability data has been submitted to the Agency on a representative commodity in the cucurbit crop group. Previous reviews of myclobutanil tolerance petitions have referenced stability studies on apples and grapes. No other storage stability studies were found in CBTS' files. It should be noted that acceptance of the residue data reviewed in support of this petition is contingent upon the receipt of data confirming the frozen stability of the regulable residues for an appropriate duration in cucurbits. The lack of translatable storage stability data is cited as a deficiency which must be resolved prior to the favorable review of this petition.

For the purposes of granting a temporary tolerance on the cucurbit crop group <u>only</u> CBTS has previously translated storage stability data from apples and grapes (PP#9G3765, J. Smith 8/16/89 and M. Nelson 5/29/92). CBTS informed the petitioner of the need for a storage stability study on a representative commodity in the cucurbit group in order to support a permanent crop group tolerance.

In the recent guidance document entitled "Guidance on Generating Storage Stability Data in Support of Pesticide Residue Chemistry Studies" (January, 1993), the Agency stated its position on storage stability requirements. If residues are shown to be stable in a given commodity, the residues in other crops of the same group (as listed in 40 CFR §180.34(f)) would be assumed to be stable for the

same time period under the same experimental conditions. However, lacking a representative commodity within the same crop grouping, stability data can be translated from one similar commodity to another provided the frozen stability of the residues of interest have been demonstrated in at least five diverse crops (an oilseed, a non-oily grain, a leafy vegetable, a root crop and a fruit or fruiting vegetable are suggested).

In light of the Agency's position, the petitioner has two options with respect to the storage stability deficiency noted. The petitioner may conduct a storage stability study on a representative member of the cucurbit crop group demonstrating the frozen stability of myclobutanil and its RH-9090 metabolite for an appropriate duration. In place of a study on a member of the cucurbit crop group, the petitioner may submit data on four diverse crops (apples and grape data serve to fulfill the stability in a fruit or fruiting vegetable requirement) demonstrating the frozen stability of the regulable residues. Once the frozen stability of the residues of interest have been demonstrated in five diverse crops, data may be translated for future uses of this fungicide.

Other Considerations:

The International Residue Limit Status sheet is attached. Currently there are no Codex, Canadian or Mexican tolerances established for residues of myclobutanil and its RH-9090 metabolite in or on the cucurbit crop group; therefore, the establishment of a U.S. tolerance for this chemical on the cucurbit crop group should cause no international harmonization problems.

cc: RF, SF, Myclobutanil Reg. Std., circ, DDavis, PP#2F04155, TOX(F/H Support)
H-7509C:CBTS:DSD:CM#2:Rm804:305-7085:dd:2/3/93
RDI:Sec Hd:RQuick:2/4/93:BrSrSc:RLoranger:2/4/93:BrChief:DEdwards:2/5/93
Disk:DSD-1 File:MYCL4162.CUC

F. Kuer
2/3/93

Attachment: Page 1 of 1

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL ~~Myclobutanil~~ anil DEB 2-3-93

CODEX NO. _____

CODEX STATUS:

[✓] No Codex Proposal Step 6 or Above

Residue (if Step 8): _____

Crop(s)	Limit (mg/kg)

PROPOSED U.S. TOLERANCES:

Petition No. 2F04155

DEB Reviewer D. Davis

Residue: parent and its α-(3-hydroxybutyl)-α-(4-chlorophe -1H-1,2,4-triazole-1-propanenitrile metab

Crop(s)	Limit (mg/kg)
Cucurbit Crop Grop	0.5 ppm
- Balsam pear	
- Chinese waxgourd	
- citron melon	
- cucumber	
- gherkin	
- gourds	
- muskmelons	
- pumpkin	
- squash	
- watermelon	

CANADIAN LIMITS:

[✓] No Canadian Limit

Residue: _____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

[✓] No Mexican Limit

Residue: _____

Crop(s)	Limit (mg/kg)

NOTES

Form Revised 1989

END OF DOCUMENT