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

CONFIDENTIAL

FEB 8 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: New Chemical Review of Myclobutanil (RH-3866).

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

TO: Amy Rispin, Chief
Science Integration Staff
Hazard Evaluation Division (TS-769C)

and

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

Attached is the Product Chemistry and Residue Chemistry review package for myclobutanil (RH-3866; Rally™; Nova™; Systhane™), written in RCB by Dr. Maxie Jo Nelson.

These reviews include data received by RCB through February 5, 1988.

The HED due date for these reviews is February 11, 1988. The RD due date for these reviews is March 3, 1988.

This is a first time, food-use, permanent tolerance request for myclobutanil (PP#7F3476/FAP#7H5524). The reviews of the Product Chemistry and Residue Chemistry data have been formatted to serve as a Myclobutanil Registration Standard.

RCB's Product Chemistry review of myclobutanil is for RH-3866 Technical only. As required by the Registration Standards Policy Group, the product chemistry data for end-use products are not included in this review. Also, as requested by Mr. Herb Harrison of RD, RCB no longer addresses the physical/chemical properties of manufacturing-use products.

In accordance with instructions from Mr. Henry Jacoby, SIPS/HED, Table A's (Generic Data Requirements) for Product Chemistry (RH-3866 Technical) and Residue Chemistry are not being provided at this time. These Tables will be generated by RCB when all the data deficiencies listed in these reviews have been filled.

Attachments #2 and #6 to this memorandum contain Confidential Business Information (CBI), and are to be protected. The cc distribution of the CBI copies is indicated below.

Attachments to this Memorandum:

Attachment #1: New Chemical Residue Chemistry Review, Myclobutanil (Rally™) [93 pp]

Attachment #2: CONFIDENTIAL APPENDIX to the New Chemical Review, Myclobutanil (Rally™) [12 pp]

Attachment #3: International Residue Limit (Codex) Status Sheet [1 p]

Attachment #4: Guidance for Orchard Spray Application [4 pp]

Attachment #5: New Chemical Product Chemistry Review, RH-3866 (Technical) [10 pp]

Attachment #6: CONFIDENTIAL APPENDIXES A thru E to the New Chemical Product Chemistry Review, RH-3866 (Technical) [25 pp]

cc (Cover Memo Only):

A. Barton/HED, J. Heckman/HED, D. Baker/IR-4.

cc (Cover Memo plus the non-CBI Attachments, #1, 3, 4, and 5):

Reading File, Circulation, M. Nelson/RCB, H. Jacoby/HED.

cc (Cover Memo plus ALL Attachments, #1-6):

PP#7F3476/FAP#7H5524, Myclobutanil Registration Standard File, TOX (P. Hurley), ISB/PMSD (E. Eldredge).

TS-769C:RCB:Reviewer(MJN):CM#2:Rm804:557-7324:typist(mjn):1/19/88:edit:1/31/88:finaledit:2/7/88.
ReviewPkgRDI:SectionHead:RSQuick:1/22/88:DeputyChief:RDSchmitt:1/26/88:Chief:CLTrichilo:1/26/88.

ATTACHMENT 1

DATE: February 5, 1988

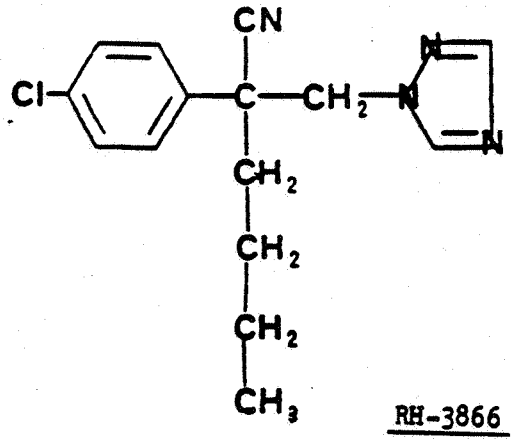
SUBJECT: New Chemical Residue Chemistry Review
MYCLOBUTANIL (RALLY™)

REVIEWER: Maxie Jo Nelson, Ph.D., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

PRODUCT MANAGER: Lois A. Rossi
P. M. #21
Herbicide-Fungicide Branch
Registration Division (TS-767C)

Petition Nos:	7F3476/7H5524.
EPA Reg. Nos:	707-EER, 707-ERE, 707-ERL, 707-ERN, 707-ERR.
MRID/Acces. Nos:	266075; 266105-266117; 143769; 145682; 165036; 403662-00 thru -01; 404092-02 thru -05; 404800-00; 404801-00; 404813 -00 thru -01; 404980-01.
RCB Nos:	2047-2051; 2055-2056; 2090-2094; 2912-2916; 3084-3091; 3238-3246; 3322-3323.
Common Name:	Myclobutanil (ANSI)
Trade Names:	Rally™, Nova™, Systhane™
Company Code Names:	RH-3866, RH-53,866
Chemical Name:	alpha-butyl-alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile. (CAS# 88671-89-0)

Type Product:	Fungicide
Petitioner:	Rohm and Haas Company Philadelphia, PA
Commodities:	Apples; Grapes; Their Processed Commodities; Meat and Milk; Poultry and Eggs.
Chemical Structure:	



RH-3866

TABLE OF CONTENTS FOR RESIDUE CHEMISTRY REVIEW

5

I. SUMMARY OF DEFICIENCIES FOR RESIDUE CHEMISTRY

Proposed Tolerances

A revised Section F is needed. Provided the storage stability issue is satisfactorily resolved (see STORAGE STABILITY and MAGNITUDE OF THE RESIDUE sections of this review) and method trials are successful, it should propose:

For 40 CFR 180.XXX:

a. Tolerances for combined residues of RH-3866 and its metabolite RH-9090 (free and bound) in or on:

Apples.....0.5 ppm
Grapes.....1.0 ppm

b. Tolerances for combined residues of RH-3866 and its RH-9090 (free and bound) and diol metabolites in:

Milk.....0.05 ppm

c. Tolerances for combined residues of RH-3866 and its RH-9090 (free and bound), diol, and hydroxy-lactone metabolites in:

Meat, fat, and meat by-products (except liver) of cattle, goats, hogs, horses, and sheep).....0.05 ppm

Liver of cattle, goats, hogs, horses, and sheep.....0.3 ppm

Meat, fat, and meat byproducts of poultry.....0.02 ppm

Eggs.....0.02 ppm

For 21 CFR 193.XXX:

Tolerances for combined residues of RH-3866 and its metabolite RH-9090 (free and bound) in:

Raisins.....10.0 ppm

For 21 CFR 561.XXX:

Tolerances for combined residues of RH-3866 and its metabolite RH-9090 (free and bound) in:

Apple pomace.....5.0 ppm
Grape pomace.....10.0 ppm
Raisin waste.....25.0 ppm

Directions for Use

The proposed Directions for Use on apples of Rally™ 40W (EPA Reg. No. 707-ERE), Rally™ 60DF (EPA Reg. No. 707-ERR), and Nova™ 40W in Water-Soluble Pouches (EPA Reg. No. 707-EER) need to be revised to:

1. Add information on the use rates in terms of ozs or lbs ai/A.

2. Delete reference to use of a concentrate spray, unless the petitioner can supply data from apple field trials reflecting use of concentrate sprays of these formulations.

3. Express spray volumes in terms of tree row volume rather than tree height. The petitioner is advised to consult the Attachment to this review entitled, "Guidance for Orchard Spray Application", for advice in preparation of revised labels using this procedure.

4. Specify on the labeling that all tank mates must be cleared (i.e., have established tolerances) by EPA for use on apples.

Additionally, the proposed Directions for Use on apples of Nova™ 40W in Water-Soluble Pouches also needs to be revised to limit use to application by ground equipment only.

A revised Section B for this petition incorporating these requested label changes needs to be submitted.

8

The proposed Directions for Use on grapes of Rally™ 40W (EPA Reg. No. 707-ERE), Rally™ 40W in Water-Soluble Pouches (EPA Reg. No. 707-ERL), and Rally™ 60DF (EPA Reg. No. 707-ERR) need to be revised to:

1. Add information on the use rates in terms of ozs or lbs ai/A.

2. Specify on the labeling that all tank mates must be cleared (i.e., have established tolerances) by EPA for use on grapes.

A revised Section B for this petition incorporating these label changes for each of these formulations needs to be submitted.

Residue Analytical Methods

Residue analytical methods have been submitted for the determination of RH-3866, RH-9089, and RH-9090 (free and conjugated) in apples and grapes (TR 310-84-27, with Addendums TR 31H-86-15 and TR 31S-87-46); RH-9090 (free only) in crops and RH-3866 in crops, meat, milk, and eggs (TR 310-84-13, with Addendum TR 310-86-09); RH-9090 (free only) in meat, milk, and eggs (TR 31S-87-09); and, RH-0294 (diol) in milk (TR 31S-87-02).

We withhold judgment on the adequacy of these analytical methods for residue data gathering and/or enforcement purposes pending completion of method trials by COB/BUD chemists, and receipt/review by RCB of the report(s) from COB on the results of these trials.

Residue analytical methods are also needed for the determination of RH-9090 (conjugated) in milk, and RH-9090 (conjugated), RH-0294 and the hydroxy-lactone in eggs and animal tissues. The sensitivity of such method(s) should be $\leq$ 0.01 ppm, if possible.

FDA multiresidue information via protocols I thru IV has been submitted for RH-3866 and RH-9090 (free). Testing through these four protocols is also required of the other components of the regulable residue: RH-9090 (conjugated), RH-0294, and the hydroxy-lactone.

The petitioner is urged to look into the possibility of consolidating proposed enforcement methods for myclobutanil and metabolites into one or two "total residue" methods applicable to determining the regulable residue in crops and animal commodities (meat, milk, and eggs).

4/

Storage Stability

The following additional storage stability data are needed:

- RH-9090 (free and conjugated) in apples and grapes.
- RH-3866 in apple pomace; grape pomace; raisin waste; and raisins. (This requirement only applies if these processing fractions were frozen-stored for longer than two weeks prior to analysis.)
- RH-9090 (free and conjugated) in apple pomace; grape pomace; raisin waste; and raisins. (This requirement only applies if these processing fractions were frozen-stored for longer than two weeks prior to analysis.)

The length of the storage stability studies on these matrices/compounds should be of sufficient duration to validate the crop field trial and processing study data on apples and grapes; i.e., if crop field trial and processed food/feed samples were stored 9 months prior to residue analysis, then a 9-month (minimum) storage stability study to validate the storage of those samples is required.

Magnitude of the Residue

APPLES

Crop Field Trials

The proposed tolerance on apples is 0.5 ppm for combined residues of the parent (RH-3866) and RH-9090 (free and bound). Tentatively, we conclude these field trial data support the proposed tolerance, and that 0.5 ppm is an appropriate level.

Before we can finalize our conclusion about the adequacy of these field trial data to support the proposed tolerance on apples, storage stability data for RH-9090 (free and bound) residues in apples must be submitted and method trials must be successfully completed.

Processed Food and Feed

We withhold judgment on the adequacy of the apple processing studies until storage stability data for residues of RH-9090 (free and bound) in apples are submitted and method trials have been successfully completed.

Also, the date on which processing of apples occurred [TR 31H-86-09; MRID/Acces.# 266031] needs to be provided.

Raw data, processing information, and date of processing, also need to be submitted for the processing of apples from crop field trial 84-0238 [summarized in MRID/Acces.# 266105].

If apple processing fractions were frozen-stored for longer than 2 weeks prior to analysis, storage stability data of appropriate duration for RH-3866 and RH-9090 (free and conjugated) residues in apple processing fractions will also be needed.

Tentatively, we consider a feed additive tolerance proposal based on < 10X concentration factor in apple pomace to be appropriate.

(See PROPOSED TOLERANCES; a revised Section F for "apple pomace" is needed. Tentatively, 5 ppm would appear to be the appropriate tolerance level.)

GRAPES

Crop Field Trials

The proposed tolerance on grapes is 1.0 ppm for combined residues of the parent (RH-3866) and RH-9090 (free and bound). Tentatively, we conclude these field trial data support the proposed tolerance, and that 1.0 ppm is an appropriate level.

Before we can finalize our conclusion about the adequacy of these field trial data to support the proposed tolerance on grapes, storage stability data for RH-9090 (free and bound) residues in grapes must be submitted and method trials must be successfully completed.

Processed Food and Feed

We withhold judgment on the adequacy of the grape processing studies until storage stability data for residues of RH-9090 (free and bound) in grapes are submitted and method trials have been successfully completed.

Also, the dates on which processing of grapes occurred [TR 31H-86-11; MRID/Acces.# 266032] needs to be provided.

If grape processing fractions were frozen-stored for longer than two weeks prior to analysis, storage stability data of appropriate duration for RH-3866 and RH-9090 (free and conjugated) residues in grape processing fractions will also be needed.

Tentatively, we consider food and feed additive tolerance proposals based on < 10X concentration in raisins and grape pomace and ≤ 25X concentration in raisin waste to be appropriate.

A revised Section F for "grape pomace" is needed. (See PROPOSED TOLERANCES section of this review.) Tentatively, it appears 10 ppm would be the appropriate tolerance level.

CATTLE

Adequate feeding study data have been submitted for lactating dairy cattle (ruminant).

At the dietary burden (4.5-5.5 ppm/day to cattle) associated with the proposed use on apples and grapes, appropriate tolerances will be 0.05 ppm for milk and the meat, fat, and meat by-products (except liver) of cattle, goats, hogs, horses, and sheep; and, 0.3 ppm for liver of cattle, goats, hogs, horses, and sheep.

This conclusion is contingent upon successful method trials for the components of the regulable residue being conducted by COB/BUD, and demonstrating an adequate level of recovery and sensitivity at (or below) these suggested tolerance levels.

A revised Section F proposing appropriate tolerances for the regulable residue will need to be submitted.

POULTRY

Adequate feeding study data have been submitted for laying hens (poultry).

At the dietary burden (0.75 ppm/day to poultry) associated with the proposed use on apples and grapes, appropriate tolerances will be 0.02 ppm for eggs and the meat, fat, and meat by-products of poultry.

This conclusion is contingent upon successful method trials for the components of the regulable residue being conducted by COB/BUD, and demonstrating an adequate level of recovery and sensitivity at (or below) these suggested tolerance levels.

A revised Section F proposing appropriate tolerances for the regulable residue will need to be submitted.

II. TOPICAL SUMMARIES FOR RESIDUE CHEMISTRY

A. Background

Temporary tolerances are presently in effect for myclobutanil residues in or on apples and grapes; raisins; raisin waste, grape and apple pomaces; meat, fat, and meat by-products of cattle, goats, hogs, horses, poultry, and sheep; milk; and, eggs. These tolerances are set to expire on February 28, 1988.

B. Proposed Tolerances

[Reserved, pending resolution of data gaps associated with this topic area. See SUMMARY OF DEFICIENCIES section of this review.]

C. Chemical Identity

Discussed in the companion New Chemical Product Chemistry Review of RH-3866 Technical (dated 2/5/88), which see.

D. Directions for Use

[Reserved, pending resolution of data gaps associated with this topic area. See SUMMARY OF DEFICIENCIES section of this review.]

E. Nature of the Residue

1. Plants

a. Apples

The nature of the residues in apples is adequately understood. Myclobutanil [RH-3866] is metabolized by hydroxylation of the #3 carbon on the butyl chain, with subsequent conjugation to form glucoside(s). The residue to be regulated in apples and apple by-products is the combined residue of RH-3866 and its alcohol metabolite RH-9090 (free and conjugated).

b. Grapes

The nature of the residues in grapes is adequately understood. Myclobutanil is metabolized via the same pathway as that demonstrated for apples. The regulable residue for grapes and grape by-products is the same as for apples: combined residues of RH-3866 and its alcohol metabolite RH-9090 (free and conjugated).

2. Livestock

a. Cattle

The nature of the residue in ruminants is adequately understood. RH-3866 is metabolized via butyl side chain reaction to the unstable ketone RH-9089, then reduced to the stable alcohol RH-9090. RH-9090 may be either hydroxylated to form the diol RH-0294, or conjugated. The hydroxy-lactone is also a component of the terminal residue. In liver and kidney, four metabolites were found: the hydroxy-lactone, the diol RH-0294, RH-9090, and RH-9089; no parent RH-3866 was reported. Fat contained insufficient residue for characterization. In milk and urine, diol RH-0294, RH-9090, and RH-9090 conjugates were found.

The residues to be regulated are:

In milk, combined residues of parent RH-3866, its alcohol metabolite RH-9090 (free and conjugated), and the diol metabolite RH-0294.

In tissues (meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep), combined residues of parent RH-3866, the alcohol metabolite RH-9090 (free and conjugated), the diol metabolite RH-0294, and the hydroxy-lactone.

b. Poultry

The nature of the residue in poultry is adequately understood. Myclobutanil is metabolized in a fashion similar to that in ruminants. In eggs, RH-9090 (free and conjugated), the hydroxy-lactone, RH-9089, and RH-0294 were identified. In liver and kidney, RH-0294, RH-9090 (free and, in liver, conjugated), RH-9089, the

hydroxy-lactone, and parent RH-3866 were reported. In fat, RH-9090, hydroxy-lactone, and RH-3866 were found; in breast and thigh, RH-0294, RH-9090 conjugates, RH-9089, and RH-3866 were present.

The residues to be regulated in eggs, and the meat, fat, and meat by-products of poultry are combined residues of parent RH-3866, its alcohol metabolite RH-9090 (free and conjugated), its diol metabolite RH-0294, and the hydroxy-lactone.

F. Residue Analytical Methods

[Reserved, pending resolution of data gaps associated with this topic area. See SUMMARY OF DEFICIENCIES section of this review.]

G. Storage Stability Data

[Reserved, pending resolution of data gaps associated with this topic area. See SUMMARY OF DEFICIENCIES section of this review.]

H. Magnitude of the Residue

1. Apples

a. Crop Field Trials

[Reserved, pending resolution of data gaps associated with this topic area. See SUMMARY OF DEFICIENCIES section of this review.]

b. Processed Food and Feed

[Reserved, pending resolution of data gaps associated with this topic area. See SUMMARY OF DEFICIENCIES section of this review.]

2. Grapes

a. Crop Field Trials

[Reserved, pending resolution of data gaps associated with this topic area. See SUMMARY OF DEFICIENCIES section of this review.]

b. Processed Food and Feed

[Reserved, pending resolution of data gaps associated with this topic area. See SUMMARY OF DEFICIENCIES section of this review.]

3. Cattle

[Reserved, pending resolution of data gaps associated with this topic area. See SUMMARY OF DEFICIENCIES section of this review.]

4. Poultry

[Reserved, pending resolution of data gaps associated with this topic area. See SUMMARY OF DEFICIENCIES section of this review.]

I. Tolerance Assessment

If/when the permanent tolerances of this present petition are favorably recommended for, a request for an updated TAS assessment will be initiated by this reviewer to the TAS Program Staff of RCB. Any TAS review which is then performed will issue as a separate memo, directed to the Product Manager (L. Rossi, PM 21, HFB/RD).

J. International Harmonization

There are no Canadian or Mexican IRLs established for myclobutanil, and no Codex proposal for myclobutanil at Step 6 or above. The question of compatibility/harmonization of the tolerance expression and/or residue level(s) thus does not arise in connection with the review of this petition.

K. Other Considerations

No "Other Considerations" apply in the review of this petition.

III. DETAILED CONSIDERATIONS FOR RESIDUE CHEMISTRY

A. BACKGROUND

- Summary. Temporary tolerances are presently in effect for myclobutanil residues in or on apples and grapes; raisins; raisin waste, grape and apple pomaces; meat, fat, and meat by-products of cattle, goats, hogs, horses, poultry, and sheep; milk; and, eggs. These tolerances are set to expire on February 28, 1988.

* * * * *

Discussion. This petition (PP#7F3476/FAP#7H5524) proposes the first permanent tolerances for myclobutanil.

There have been two previous petitions (PP#4G3149; PP#7G3479/FAP#7H5523) proposing temporary tolerances.

As a result of those previous petitions, temporary tolerances are presently in effect for:

(a) Combined residues of myclobutanil and its metabolites containing both the chlorophenyl and triazole rings in or on apples and grapes at 0.5 ppm; liver of cattle, goats, hogs, horses, and sheep at 0.2 ppm; meat, fat, and meat by-products (except liver) of cattle, goats, hogs, horses, and sheep at 0.04 ppm; meat, fat, and meat by-products of poultry, eggs, and milk at 0.02 ppm;

(b) Residues of myclobutanil per se in apple pomace, grape pomace, and raisins at 5 ppm; and, raisin waste at 12.5 ppm.

These temporary tolerances are set to expire on February 28, 1988.

PP#7F3476/FAP#7H5524 was subjected to a new chemical screen by RCB in December, 1986. The petition failed the screen (see the 12/16/86 review of S. Malak).

On April 7, 1987, RCB was informed that myclobutanil had passed all HED branch scientific screens. The due date for completion of reviews is March 3, 1988.

B. PROPOSED TOLERANCES

- Summary. A revised Section F is needed. Provided the storage stability issue is satisfactorily resolved (see STORAGE STABILITY and MAGNITUDE OF THE RESIDUE sections of this review) and method trials are successful, it should propose:

For 40 CFR 180.XXX:

a. Tolerances for combined residues of RH-3866 and its metabolite RH-9090 (free and bound) in or on:

Apples.....0.5 ppm
Grapes.....1.0 ppm

b. Tolerances for combined residues of RH-3866 and its RH-9090 (free and bound) and diol metabolites in:

Milk.....0.05 ppm

c. Tolerances for combined residues of RH-3866 and its RH-9090 (free and bound), diol, and hydroxy-lactone metabolites in:

Meat, fat, and meat by-products (except liver) of cattle, goats, hogs, horses, and sheep).....0.05 ppm

Liver of cattle, goats, hogs, horses, and sheep.....0.3 ppm

Meat, fat, and meat byproducts of poultry.....0.02 ppm

Eggs.....0.02 ppm

For 21 CFR 193.XXX:

Tolerances for combined residues of RH-3866 and its metabolite RH-9090 (free and bound) in:

Raisins.....10.0 ppm

For 21 CFR 561.XXX:

Tolerances for combined residues of RH-3866 and its metabolite RH-9090 (free and bound) in:

Apple pomace.....5.0 ppm
Grape pomace.....10.0 ppm
Raisin waste.....25.0 ppm

* * * * *

Discussion. The petitioner, Rohm and Haas Company, Philadelphia, PA, proposes [MRID/Acces.# 266075, Section F] permanent tolerances for residues of the fungicide alpha-butyl-alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile [aka myclobutanil (ANSI)] and its metabolites containing both the chlorophenyl and triazole rings in or on the following:

Apples:	Whole Fruit	0.5 ppm
	Wet Pomace	1.0 ppm
	Dry Pomace	5.0 ppm
Grapes:	Whole Fruit	1.0 ppm
	Wet Pomace	2.0 ppm
	Dry Pomace	10.0 ppm
	Raisins	10.0 ppm
	Raisin Waste	25.0 ppm
Meat and Meat By-Products (except liver)		0.04 ppm
Liver (cattle, goats, hogs, horses or sheep)		0.5 ppm
Milk		0.1 ppm
Eggs		0.04 ppm

This proposal is unacceptable for the following reasons:

(1) The tolerance expression should be worded in terms of combined residues of myclobutanil and specific metabolites;

(2) Current RCB policy is to establish only one tolerance level covering both the wet and dry pomaces of a raw agricultural commodity (RAC);

(3) The "meat and meat by-products" tolerance proposal needs to include "fat", and to specify the livestock to be covered;

(4) The "liver" tolerance proposal needs to be reworded to say "and" instead of "or";

(5) Tolerances need to be proposed for the meat, fat, and meat by-products of poultry.

(6) Revised tolerance levels are needed for the animal commodity items.

Additionally, there is a storage stability issue (see STORAGE STABILITY and MAGNITUDE OF THE RESIDUE sections of this review) which needs to be addressed, and various method trials to be successfully conducted, prior to a final determination on RCB's part as to appropriate levels for proposed tolerances.

C. CHEMICAL IDENTITY

- Summary. This topic is the subject of a separate RCB review entitled: "New Chemical Product Chemistry Review, RH-3866 (Technical)". Myclobutanil has four end-use products: Rally™ 40W, Rally™ 40W in Water-Soluble Pouches, Rally™ 60DF, and Nova™ 40W in Water-Soluble Pouches proposed for use on apples and/or grapes.

* * * * *

Discussion. The manufacture, formulation, and all other aspects of the product chemistry of RH-3866 Technical (EPA Reg. No. 707-ERN) are discussed in the separate RCB review (M. Nelson, 2/5/88) on myclobutanil entitled: "New Chemical Product Chemistry Review, RH-3866 (Technical)".

None of the impurities associated with the manufacturing process of RH-3866 Technical are expected to pose a residue problem.

Myclobutanil is formulated into four end-use products: Rally™ 40W Agricultural Fungicide (EPA Reg. No. 707-ERE); Rally™ 40W Agricultural Fungicide in Water-Soluble Pouches (EPA Reg. No. 707-ERL); Rally™ 60DF Agricultural Fungicide (EPA Reg. No. 707-ERR); and, Nova™ 40W Agricultural Fungicide in Water-Soluble Pouches (EPA Reg. No. 707-EER) for the proposed use on apples and grapes. [MRID/Acces.# 266075, Section A; additional information in various applications for Section 3 registration, Nov. 1987, no MRID/Acces. Nos. assigned.]

Rally™ 40W, Rally™ 40W in Water-Soluble Pouches, and Nova™ 40W in Water-Soluble Pouches are wettable powder formulations containing 40% by weight active ingredient (myclobutanil). Rally™ 60DF is a dry flowable formulation containing 60% by weight active ingredient (myclobutanil).

A copy of the Confidential Statement of Formula for each of these end-use products is in the Confidential Appendix to this review.

It is the responsibility of RD to ensure the inert ingredients in each of these formulations are cleared for use under 40 CFR 180.1001 (c) or (d).

D. DIRECTIONS FOR USE

1. APPLES

- Summary. The proposed Directions for Use on apples of Rally™ 40W, Rally™ 60DF, and Nova™ 40W in Water-Soluble Pouches need to be revised to:

  1. Add information on the use rates in terms of ozs or lbs ai/A.

  2. Delete reference to use of a concentrate spray, unless the petitioner can supply data from apple field trials reflecting use of concentrate sprays of these formulations.

  3. Express spray volumes in terms of tree row volume rather than tree height. The petitioner is advised to consult the Attachment to this review entitled, "Guidance for Orchard Spray Application", for advice in preparation of revised labels using this procedure.

  4. Specify on the labeling that all tank mates must be cleared (i.e., have established tolerances) by EPA for use on apples.

  Additionally, the proposed Directions for Use on apples of Nova™ 40W in Water-Soluble Pouches also needs to be revised to limit use to application by ground equipment.

  A revised Section B for this petition incorporating these requested label changes needs to be submitted.

* * * * *

Discussion. Rally™ 40W (EPA Reg. No. 707-ERE), Rally™ 60DF (EPA Reg. No. 707-ERR), and Nova™ 40W in Water-Soluble Pouches (EPA Reg. No. 707-EER) formulations are each proposed for use on apples; the Rally™ 40W in Water-Soluble Pouches (EPA Reg. No. 707-ERL) formulation is not. [MRID/Acces.# 266075, Sec-

The Rally™ 40W, Rally™ 60DF, and Nova™ 40W in Water-Soluble Pouches proposed Directions for Use each call for repetitive foliar sprays to provide thorough coverage.

The Rally™ 40W and Rally™ 60DF proposed Directions for Use specify application by ground equipment. The Nova™ 40W in Water-Soluble Pouches formulation does not indicate the type application equipment permitted for use.

Since there are no field trial data with apples (or grapes) reflecting aerial application of Rally™ or Nova™ formulations, use must be restricted to ground application equipment only.

In all other respects (application rates of ai, timing, PHI, total ai/A/season, label restrictions, etc.) the Nova™ 40W in Water-Soluble Pouches proposed Directions for use are the same as those for Rally™ 40W and Rally™ 60DF.

Applications are to commence early in the season, depending on the nature of the disease to be controlled, and continue at 7- to 10-day intervals.

The diseases to be controlled on apples are scab, powdery mildew, and rusts.

Label use recommendations (ounces product per 100 gallons spray) are based on dilute sprays with a 400 gallon per acre base.

These range from 1.25-2.5 ozs/100 gallons spray for Rally™ 40W and Nova™ 40W in Water-Soluble Pouches and 0.8-1.6 ozs/100 gallons spray for Rally™ 60DF (i.e., in each case, 0.5-1.0 oz ai/ 100 gallons spray), depending on the nature and pressure of the disease to be controlled.

Since orchard tree heights, tree spacing, and pruning practices vary, additional guidance in calculating proper use rates (based on tree height) is also given. In orchards which receive only minimal pruning, the per acre use rate is increased 1.4X.

Directions specify to apply the same rate of product in dilute or concentrate sprays. No information is given as to what is meant by "concentrate spray".

The general directions for use indicate tank mixing with other fungicides, insecticides, growth regulators, micronutrients, and spray adjuvants is permitted.

A tank mixture with Dithane™ M-45 (mancozeb ai) fungicide or another protectant fungicide is specifically recommended for improved fruit scab and summer disease control.

A tolerance is established (40 CFR 180.176) for residues of mancozeb (a fungicide which is a coordination product of zinc ion and maneb) in or on apples.

The following label restrictions are specified in the Rally™ 40W, Rally™ 60DF, and Nova™ 40W in Water-Soluble Pouches proposed Directions for Use:

- Do not apply within 14 days of harvest.
- Do not apply more than 5 lbs of Rally™ 40W or Nova™ 40W in Water-Soluble Pouches or 3.3 lbs of Rally™ 60DF (i.e., in each case, 2 lbs ai) per acre per season.
- Do not graze livestock in treated areas or feed cover crops grown in treated areas to livestock.

We consider the Rally™ 40W, Rally™ 60DF, and Nova™ 40W in Water-Soluble Pouches proposed Directions for Use on apples to be deficient for the following reasons:

1. The use rate in terms of ozs or lbs ai/A is not given.

2. Only one apple field trial [86-0297; MRID/Acces.# 266111; 84 gpa spray volume applied] reflects use of <150 gpa of spray solution per application. (See Table 17.)

   Thus, use of a concentrate spray is not supported. Reference to use of a concentrate spray must therefore be deleted from the proposed Directions for Use of each of these formulations unless the petitioner can supply data from apple field trials reflecting use of concentrate sprays of these formulations.

3. Spray volumes should be expressed in terms of tree row volume rather than tree height. The petitioner is advised to consult the Attachment to this review entitled, "Guidance for Orchard Spray Application", for advice in the preparation of revised labels using this procedure.

4. It needs to be specified on the labeling that all tank mates must be cleared (i.e., have established tolerances) by EPA for use on apples.

Additionally, the proposed Directions for Use on apples of Nova™ 40W in Water-Soluble Pouches also needs to be revised to limit use to application by ground equipment.

A revised Section B for this petition incorporating these label changes needs to be submitted.

Field trial data on apples have been submitted to support use of the Rally™ 40W formulation.

No field trial data on apples (or grapes) have been submitted for either the Rally™ 60DF or Nova™ 40W in Water-Soluble Pouches formulation.

However, we do not consider field trial data on apples reflecting application of the Rally™ 60DF of Nova™ 40W in Water-Soluble Pouches formulations to be needed, for the following reasons:

- the proposed Directions for Use on apples of Rally™ 40W, Rally™ 60DF, and Nova™ 40W in Water-Soluble Pouches are the same;
- all three are dry formulations;
- use will be limited to application as dilute sprays (unless supporting data for use of concentrate sprays can be provided);
- the nature of the inerts [redacted] see the Confidential Appendix to this review) in the Rally™ 60DF formulation would not be expected to affect either the amount or decline of residues in apples vis-a-vis the Rally™ 40W formulation; and,
- [redacted] which would not affect the residue).

2. GRAPES

- Summary. The proposed Directions for Use on grapes of Rally™ 40W, Rally™ 60DF, and Rally™ 40W in Water-Soluble Pouches need to be revised to:

  1. Add information on the use rates in terms of ozs or lbs ai/A.

  2. Specify on the labeling that all tank mates must be cleared (i.e., have established tolerances) by EPA for use on grapes.

  A revised Section B for this petition incorporating these label changes for each of these formulations needs to be submitted.

* * * * *

Discussion. Rally™ 40W (EPA Reg. No. 707-ERE), Rally™ 40W in Water-Soluble Pouches (EPA Reg. No. 707-ERL), and Rally™ 60DF (EPA Reg. No. 707-ERR) formulations are each proposed for use on grapes; the Nova™ 40W in Water-Soluble Pouches (EPA Reg. No. 707-EER) formulation is not. [MRID/Acces.# 266075, Section B, and applications for Section 3 Registration, 11/87.]

In each instance the proposed Directions for Use call for repetitive foliar sprays uniformly applied via ground sprayer using 50 or more gallons per acre to provide thorough coverage.

The spray schedules call for applications to commence early in the season (depending on the disease to be controlled) and to continue at 14- to 21-day intervals.

The diseases to be controlled on grapes are powdery mildew and black rot.

Proposed use rates are 2-3.3 ounces (Rally™ 60DF) or 3-5 ounces (Rally™ 40W or Rally™ 40W in Water-Soluble Pouches) of product per acre per application. This corresponds to 1.2-2 ozs ai/A/ application of each formulation.

The higher rate is to be used on susceptible varieties or under heavy disease pressure.

No specific tank mates are listed. However, the general label directions indicate co-applied fungicides, insecticides, growth regulators, micronutrients, and spray adjuvants may be used.

Tank mixtures with gibberellic acid products are specifically not recommended for use on grapes.

The following label restrictions are specified in the Rally™ 40W, Rally™ 40W in Water-Soluble Pouches, and Rally™ 60DF proposed Directions for Use:

- Do not apply more than 1 lb of 60DF or 1.5 lbs of 40W or 40W in Water-Soluble Pouches (i.e., in each case, 0.6 lb ai) per acre per season.
- Do not apply within 14 days of harvest.

We consider the Rally™ 40W, Rally™ 40W in Water-Soluble Pouches, and Rally™ 60DF proposed Directions for Use on grapes to be deficient for the following reasons:

1. The use rate in terms of oz or lbs ai/A is not given.
2. It needs to be specified on the labeling that all tank mates must be cleared (i.e., have established tolerances) by EPA for use on grapes.

A revised Section B for this petition incorporating these label changes for each of these formulations needs to be submitted.

Field trial data on grapes have been submitted to support use of the Rally™ 40W formulation.

No field trial data on grapes (or apples) have been submitted for either the Rally™ 40W in Water-Soluble Pouches or Rally™ 60DF formulation.

However, we do not consider field trial data on grapes reflecting application of the Rally™ 40W in Water-Soluble Pouches or Rally™ 60DF formulations to be needed, for the following reasons:

- the proposed Directions for Use on grapes of Rally™ 40W, Rally™ 60DF, and Rally™ 40W in Water-Soluble Pouches are the same;
- all three are dry formulations;

- use will be limited to application as dilute sprays;

- the nature of the inerts [redacted] see the Confidential Appendix to this review) in the Rally™ 60DF formulation would not be expected to affect either the amount or decline of residues in apples vis-a-vis the Rally™ 40W formulation; and,

- [redacted] which would not affect the residue).

E. NATURE OF THE RESIDUE

1. PLANTS

a. Apples

- Summary. The nature of the residues in apples is adequately understood. Myclobutanil [RH-3866] is metabolized by hydroxylation of the #3 carbon on the butyl chain, with subsequent conjugation to form glucoside(s). The residue to be regulated in apples and apple by-products is the combined residue of RH-3866 and its alcohol metabolite RH-9090 (free and conjugated).

* * * * *

Discussion. No additional metabolism studies for myclobutanil in/on apples were submitted with the petition under review here (PP#7F3476/FAP#7H5524).

RCB has previously concluded (R. Loranger review of 6/16/87, PP#7G3479/FAP#7H5523, the details of which are incorporated herein by reference) that an adequate study [Technical Report (TR) 310-84-31; MRID/Acces.# 073599] has been conducted to determine the metabolism of myclobutanil in apples.

To summarize, portions of two semi-dwarf McIntosh apple trees were treated with aqueous spray solutions of ^{14}C-labeled RH-3866. One tree was treated with ^{14}C-labeled in the phenyl ring while the other was treated with triazole ring labeled ^{14}C-RH3866.

Ten applications of 0.21 lb ai/A, for a total of 2.1 lb ai/A, were made at 1-2 week intervals, with a treatment-to-sampling interval (TSI) after last application of 14 days.

Apples from both trees were separately harvested and processed into juice and pomace. These apple fractions were then radioassayed using standard combustion and liquid scintillation counting (LSC) techniques.

After radioassay the composition of the residues in each processed fraction was determined by thin-layer chromatographic (TLC) comparison with authentic standards, and quantitated by LSC.

Residue results (total activities) are shown in Table 1:

Table 1

Residues in Apples and Apple Fractions[1]

Fraction	Site of ^{14}C Label	
	Phenyl	Triazole
Juice	0.15[2]	0.12
Wet Pomace	1.00	0.66
Whole Apples[3]	0.48	0.32

[1] Data extracted from Table I, TR 310-84-31.
[2] PPM of residue, calculated as RH-3866.
[3] Calculated from residues in juice and pomace.

Table 2 gives the quantitative composition of each fraction:

Table 2

Overall Distribution of the Residue in Apples[1]

Fraction	Compound[2]	Site of ^{14}C Label	
		Phenyl	Triazole
Juice	RH-3866	22%[3]	24%
	RH-9089	1	1
	RH-9090	26	25
	Conjugated RH-9090	41	30
	Total	90	80
Wet Pomace	RH-3866	55	56
	RH-9089	2	3
	RH-9090	8	8
	Conjugated RH-9090	20	18
	Total	85	85
Whole Fruit[4]	RH-3866	49	49
	RH-9089	2	3
	RH-9090	11	11
	Conjugated RH-9090	24	21
	Total	86	84

[1] Data extracted from Table II, TR 310-84-31.
[2] For chemical names, see Table 3; for chemical structures, see Figure 1.
[3] Percent of the total residue in the processed fraction.
[4] Calculated from juice and pomace data.

Between 80% and 90% of the residue in each fraction is accounted for. The residue which is not accounted for is divided into a number of fractions during metabolite identification, which precludes the possible existence of a major unidentified metabolite.

Table 3

Identification of Compounds

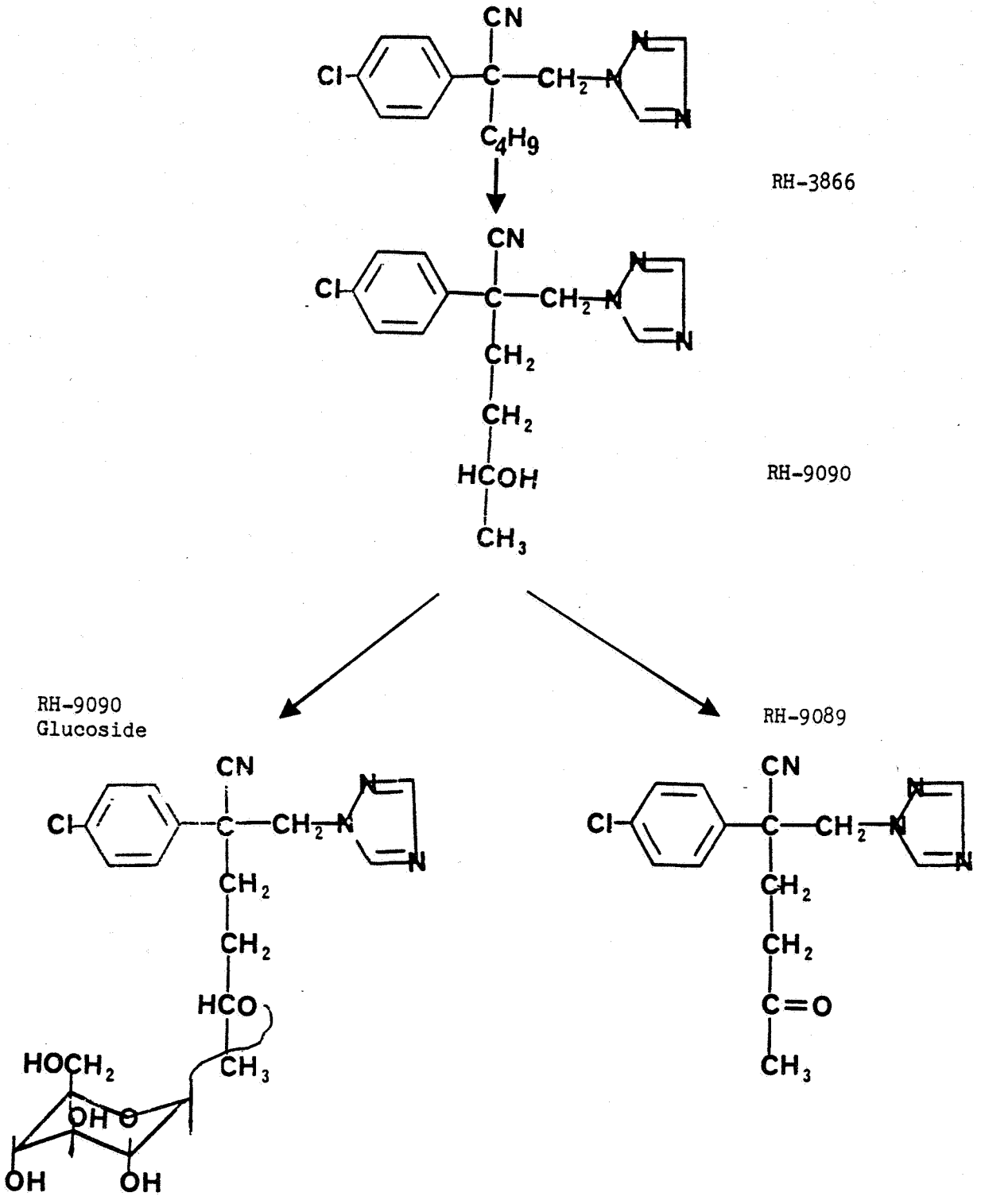
Developmental Code Name	Chemical Name
RH-3866	alpha-butyl-alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile [MYCLOBUTANIL]
RH-9090	alpha-(3-hydroxybutyl)-alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile
RH-9089	alpha-(3-ketobutyl)-alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile

These data support the hypothesis that myclobutanil is metabolized via hydroxylation of the #3 carbon on the butyl chain with subsequent conjugation to form the glucoside.

The proposed metabolic pathway for RH-3866 in apples is shown in Figure 1.

Figure 1

Metabolism of RH-3866 in Apples and Grapes



b. Grapes

° Summary. The nature of the residues in grapes is adequately understood. Myclobutanil is metabolized via the same pathway as that demonstrated for apples. The regulable residue for grapes and grape by-products is the same as for apples: combined residues of RH-3866 and its alcohol metabolite RH-9090 (free and conjugated).

* * * * *

Discussion. No additional metabolism studies for myclobutanil in/on grapes were submitted with the petition under review here (PP#7F3476/FAP#7H5524).

RCB has previously concluded (R. Loranger review of 6/16/87, PP#7G3479/FAP#7H5523, the details of which are incorporated herein by reference) that an adequate study [TR 310-84-30; MRID/Acces.# 073599] has been conducted to determine the metabolism of myclobutanil in grapes.

To summarize, grape vines were treated with aqueous spray solutions of ^{14}C-RH-3866, labeled in either the phenyl (PHE) or triazole (TRI) ring.

The vines were treated five times at 0.045 lb ai/A/application on a weekly interval, and samples of grapes and foliage taken after each treatment.

Harvested grapes were processed into pomace and juice. Portions of each were subjected to combustion analysis for determination of total activity.

Characterization of residues was accomplished by TLC fractionation followed by electron-capture gas-liquid chromatographic (EC-GLC) comparison with authentic standards. Quantification was via LSC of TLC fractions.

The presence of RH-9090 glucoside in grape fractions was confirmed by enzymatic (glucosidase) and TLC/GLC techniques, and comparison with authentic standards.

Residue results indicate total activity in grapes (calculated as RH-3866) increased erratically with the number of applications, ranging from 0.017-0.38 ppm (PHE) and 0.014-0.31 ppm (TRI).

Residue results (total activities) for grape byproducts are shown in Table 4:

Table 4

Residues in Grapes and Grape Fractions[1]

Fraction	Site of ^{14}C Label	
	Phenyl	Triazole
Juice	0.042[2]	0.034
Wet Pomace[3]	0.97	0.91
Dry Pomace	2.81	2.43
Whole Grapes[4]	0.32	0.24

[1] Data extracted from Tables 1 and 2, TR 310-84-30.
[2] PPM of residue calculated as RH-3866
[3] Apparently based on residue values in dry pomace, corrected for moisture content for wet pomace.
[4] Calculated from juice and pomace data; in 6/16/87 review, R. Loranger, PP# 7G3479/FAP#7H5523, we calculated 0.26 and 0.21 ppm, respectively.

Table 5 gives the quantitative composition of each fraction:

Table 5

Overall Distribution of the Residue in Grapes[1]

Fraction	Compound[2]	Site of ^{14}C Label	
		Phenyl	Triazole
Juice	RH-3866	33%[3]	26%
	RH-9089	4	3
	RH-9090	23	14
	Conjugated RH-9090	24	17
	Total	84	60
Dry Pomace	RH-3866	71	72
	RH-9089	1	1
	RH-9090	7	6
	Conjugated RH-9090	3	3
	Total	82	82
Whole Fruit[4]	RH-3866	66	66
	RH-9089	1	1
	RH-9090	9	7
	Conjugated RH-9090	6	5
	Total	82	79

[1] Data extracted from Tables 6 and 8, TR 310-84-30.
[2] For chemical names, see Table 3; for chemical structures, see Figure 1.
[3] Percent of the total residue.
[4] Calculated from juice and pomace data.

The proposed metabolic pathway for RH-3866 in grapes is shown in Figure 1.

2. LIVESTOCK

a. Cattle

- Summary. The nature of the residue in ruminants is adequately understood. RH-3866 is metabolized via butyl side chain reaction to the unstable ketone RH-9089, then reduced to the stable alcohol RH-9090. RH-9090 may be either hydroxylated to form the diol RH-0294, or conjugated. The hydroxy-lactone is also a component of the terminal residue. In liver and kidney, four metabolites were found: the hydroxy-lactone, the diol RH-0294, RH-9090, and RH-9089; no parent RH-3866 was reported. Fat contained insufficient residue for characterization. In milk and urine, diol RH-0294, RH-9090, and RH-9090 conjugates were found.

  The residues to be regulated are:

  In milk, combined residues of parent RH-3866, its alcohol metabolite RH-9090 (free and conjugated), and the diol metabolite RH-0294.

  In tissues (meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep), combined residues of parent RH-3866, the alcohol metabolite RH-9090 (free and conjugated), the diol metabolite RH-0294, and the hydroxy-lactone.

* * * * *

Discussion. To support the request for permanent tolerances, the petitioner has provided information on the distribution and characterization of residues in tissues, organs, milk, and excreta from dairy cows fed a ^{14}C mixture of parent and two of its metabolites (RH-9090 and RH-9089).

That report [TR 31H-86-18; MRID/Acces.# 266106] comprises the metabolism portion of a combination feeding/metabolism study conducted with lactating dairy cattle using a radioactive mixture for dosing purposes, and has not been submitted prior to this petition.

The feeding study portion [TR 31H-86-13; MRID/Acces.# 266028] has previously been submitted (PP#7G3479/FAP#7H5523) and reviewed (6/16/87 memo of R. Loranger, the details of which are incorporated herein by reference).

Information on that feeding study is summarized below. It is relevant to do so here since cow(s) fed at the highest level (38.3 ppm) were the source of the tissue, organ, milk, and excreta samples used for metabolite characterization.

Following a 2-week acclimation period, 4 groups of 2 lactating dairy cows each received a ^{14}C mixture of RH-3866/RH-9090/RH-9089 (32:58:10) at dose concentrations actually equivalent to 1.18, 2.83, 11.8, and 38.3 ppm (based upon their observed average feed consumption of 14.6 kg/day) for 10 consecutive days. One additional cow was maintained as a control and fed a placebo.

The doses were in gelatin capsules containing the ^{14}C material incorporated into a ground wheat carrier, and were orally administered once daily by balling gun.

The ^{14}C RH-3866 was uniformly labeled in the phenyl ring. The ^{14}C RH-9090 and ^{14}C RH-9089 were labeled on carbons 3 and 5 of the triazole ring.

Milk and excreta samples were collected daily and frozen, and tissue and organ samples were collected at sacrifice (on day 11, 24-hours after termination of feeding) and frozen.

The in-life portion of the feeding study was conducted for Rohm and Haas by Analytical Bio-Chemistry Laboratories (ABC Labs), Columbia, MO; metabolite characterization was done by Rohm and Haas.

Total ^{14}C activity was determined by standard combustion and LSC techniques.

Table 21, located in the MAGNITUDE OF THE RESIDUE - CATTLE section of this review, provides summary information on the level of ^{14}C residues (in ppm, expressed as RH-3866 equivalents) in milk and tissues. That information is germane to considerations of appropriate tolerance levels for meat and milk, and is discussed there.

Table 6, below, summarizes information on the distribution of ^{14}C activity as percentages of total dose and recovered dose.

Table 6

Distribution of ^{14}C Activity (%) in Dairy Cattle[1]

Sample	Distribution of ^{14}C Activity[2] as a Percentage of: Total Dose — Treatment Level (ppm) 1.18	2.83	11.8	38.3	Recovered Activity — Treatment Level (ppm) 1.18	2.83	11.8	38.3
Urine	39	32	36	32	47.35	52.77	53.95	50.28
Feces	43	28	30	31	52.20	47.35	44.96	48.71
Milk	0.06	0.44	0.46	0.34	0.07	0.73	0.69	0.53
Tissues	0.31	0.20	0.27	0.30	0.38	0.33	0.40	0.48
Liver	0.23	0.16	0.14	0.12	0.28	0.26	0.21	0.19
Muscle	NDR[3]	NDR	NDR	0.096	NDR	NDR	NDR	0.15
Fat	NDR	NDR	NDR	0.015	NDR	NDR	NDR	0.02
Kidney	NDR	NDR	0.01	0.004	NDR	NDR	NDR	0.01
Blood	NDR	NDR	0.06	0.04	NDR	NDR	0.10	0.06
Gall Bladder	0.08	0.04	0.06	0.029	0.10	0.07	0.09	0.05
TOTAL %:	82	61	67	64			N/A	

1 Data extracted from Tables I and II, TR 31H-86-18.
2 Average of 2 cows/treatment level. Feeding was with a mixture of ^{14}C RH-3866/RH9090/RH9089 (32:58:10).
3 NDR = No detectable activity.

As shown, recovery of the total administered dose from urine, feces, milk, and tissue (includes organs and blood) samples ranged from 61-82% (average 68%) for the 4 dosing levels.

Over 98% of the recovered ^{14}C activity was in the excreta, with the urine generally containing slightly more than the feces. Total residues in tissues and organs ranged from 0.33-0.48% of the recovered radioactivity; most was in the liver (0.19-0.28%).

Residues in milk ranged from 0.07-0.73% of the recovered ^{14}C activity, and were distributed (average value) as follows: milk solids (37%), fat pad (2%), lactose (1%), acetonitrile precipitated proteins (2%), and whey solubles (58%).

Characterization and quantitation of residues were accomplished by TLC/radioautography, GLC, mass spectrometry (MS), high performance liquid chromatography (HPLC) and/or nuclear magnetic resonance (NMR) techniques, with comparisons to authentic ^{14}C standard solutions of RH-3866, RH-9090, RH-9089, RH-0294, and hydroxy-lactone.

In urine, RH-9090 (free) accounted for <3% of the recovered ^{14}C activity in urine, and RH-0294 for 13-15%. The remainder of the radioactivity (>80%) was associated with $\geq$ 4 polar metabolites, shown by MS to be conjugates of RH-9090. [Note: RH-9089 has no site for conjugation.] RH-3866, RH-9089, and the hydroxy-lactone were not reported as present.

In milk, residue characterization was performed on both the soluble whey and milk solids fractions. These constitute 95% of the ^{14}C activity recovered in milk.

In the soluble whey fraction, RH-0294 comprised 27-33% of the ^{14}C activity and RH-9090 5-21%. The remainder of the radioactivity was spread over 4 polar peaks. These polar metabolites co-chromatographed with the urinary polar metabolites, and were thus thought to be conjugates of RH-9090. A similar qualitative residue picture emerged from the milk solids fraction. Quantitation was not possible there, owing to the low activity in the water-soluble and methanol-extractable fractions. RH-3866, RH-9089, and the hydroxy-lactone were not found.

In liver, 4 metabolites were identified: the hydroxy-lactone (46.4%), RH-9090 (42.5%), RH-0294 (6.7%), and RH-9089 (3.8%). No RH-3866 was detected.

In kidney, the same 4 metabolites as in liver were identified: RH-0294 (41.4%), RH-9090 (23.4%), the hydroxy-lactone (22.1%), and RH-9089 (13.1%). No RH-3866 was detected.

In conclusion, Table 6 shows the distribution of ^{14}C activity in urine, milk, and tissues of dairy cattle from the feeding/metabolism study conducted at 1.18-38.3 ppm (actual dose) with a radioactive mixture of RH-3866/RH-9090/RH-9089 (32:58:10).

Characterization and quantitation of residues revealed that no RH-3866 was detected in dairy cattle, and only a small amount of RH-9089 was observed.

This suggests that RH-3866 was rapidly oxidized to RH-9089 and then reduced to the stable metabolite RH-9090. RH-9090 could be either hydroxylated to form RH-0294 or conjugated. RH-0294 appears to be a very stable compound as it was present in the urine, milk, liver, and kidney. The hydroxy-lactone was also a significant component of the residue in liver and kidney.

Polar metabolites ($\geq$4) were detected in urine and milk fractions. These co-chromatographed together; MS analysis demonstrated they were conjugates of RH-9090.

We note that a second cow feeding/metabolism study has been conducted. The feeding study portion [TR 810-84-12; MRID/Acces.# 00145682/072905] of it was submitted with PP#4G3149, and is discussed in our (R. Loranger) 1/9/85 review of that petition. The metabolism portion [TR 31H-86-19; MRID/Acces.# 266027] of it was submitted with PP#7G3479/FAP#7H5523, and is discussed in our (R. Loranger) review of 6/16/87. Both those reviews are incorporated herein by reference.

The study involved feeding at 10 ppm for 5 days. Only two cows were used. Each received ^{14}C RH-3866, either phenyl or triazole ring labeled. One additional cow was maintained as a control. Sacrifice was within 24 hours after the last dose. Residues in milk and tissues were determined by radioanalysis. Characterization of milk identified RH-0294 and RH-9090; there were also several unidentified, polar metabolites. The urine contained RH-0294, RH-9090, the hydroxy-lactone, and several unidentified polar metabolites. Residues in tissues were not characterized.

In poultry, these same metabolites were identified; the conjugate, RH-9090-sulfate, was also specifically identified in poultry liver and eggs.

An overall summary of the components of the residue found in both dairy cattle and laying hens is given in Table 7.

The chemical structures of RH-3866 metabolites found in dairy cattle and laying hens are depicted in Figure 2.

We consider the nature of the residue in ruminants to be adequately understood. The residues to be regulated are:

A. In milk, combined residues of parent RH-3866, its alcohol metabolite RH-9090 (free and conjugated), and the diol metabolite RH-0294.

B. In tissues (meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep), combined residues of parent RH-3866, its alcohol metabolite RH-9090 (free and conjugated), the diol metabolite RH-0294, and the hydroxy-lactone.

Table 7

Summary of Residue[1] Components in Dairy Cattle and Laying Hens[2]

Matrix	Components of the Residue						
	RH-3866	RH-9089	RH-9090	RH-0294	Hydroxy Lactone	RH-9090 Conjugates	Other
Dairy Cattle							
Urine	-	-	+	++	-	+++	-
Milk	-	-	+	++	-	+++	-
Liver	-	+	+++	+	+++	- [3]	-
Kidney	-	+	++	+++	++	- [3]	-
Laying Hens							
Eggs	-	++	+++	++	++	+ [3]	+
Liver	++ [4]	++	++	+	++	++	-
Kidney	++ [4]	++	++	+	++	-	-
Fat	+++ [4]	-	++	-	++	-	+
Breast	+ [4]	++	-	++	-	++	-
Thigh	+ [4]	++	-	++	-	++	-

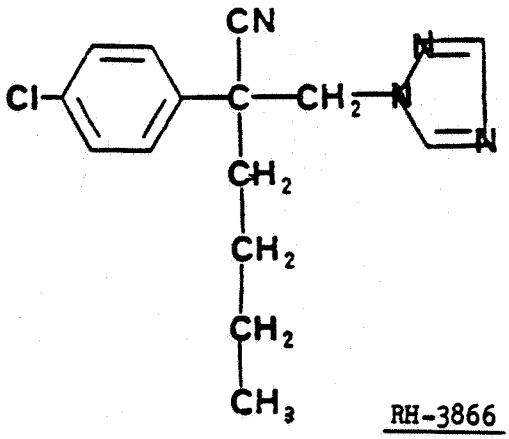
1 + = present; - = absent. Multiple +'s indicate relative % of residue.

2 Data extracted from information in TR 31H-86-18 (dairy cattle) TR-31H-86-17 (laying hens).

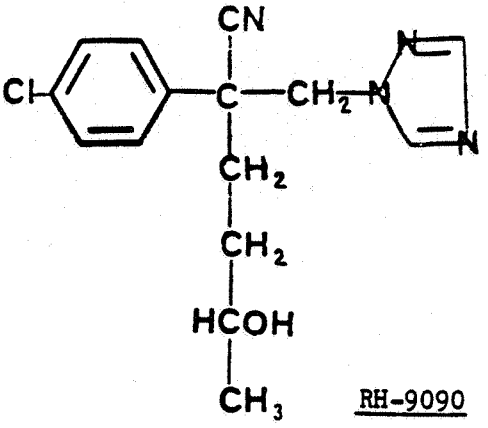
3 Not specified whether the RH-9090 reported was free, conjugated, or total.

4 In Group 6 hens (i.e., those in which ^{14}C RH-3866 was fed).

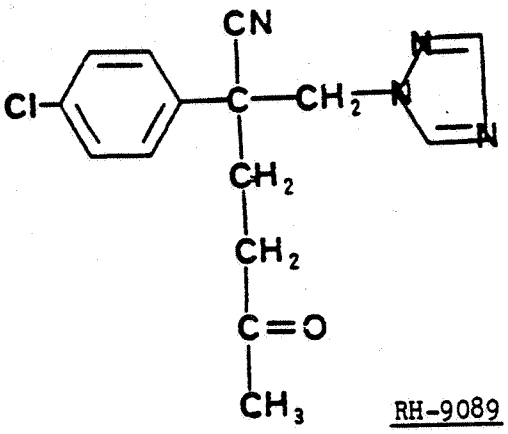
FIGURE 2: RESIDUES IN CATTLE AND POULTRY



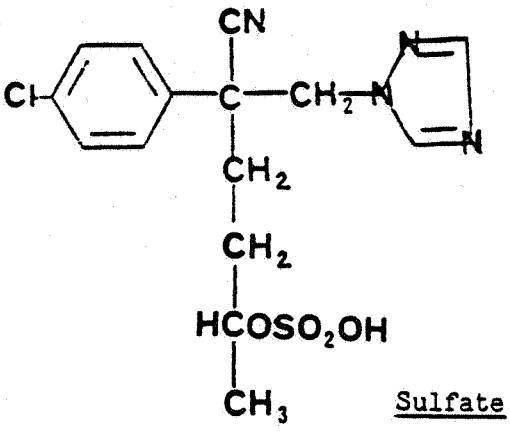
RH-3866



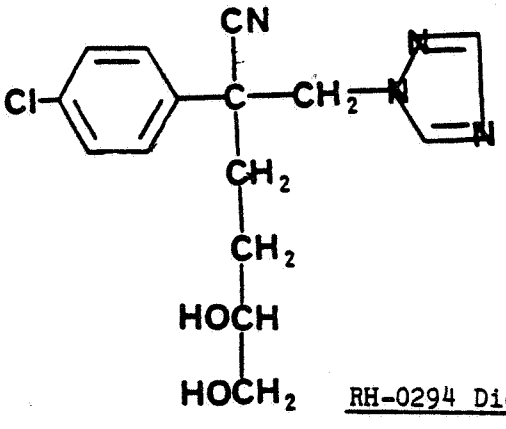
RH-9090 (free and conjugated)



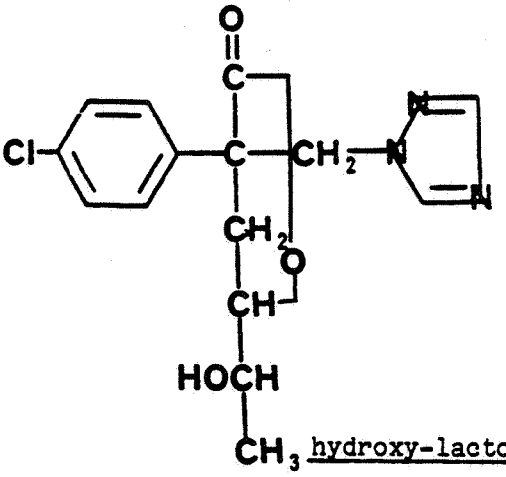
RH-9089



Sulfate



RH-0294 Diol



hydroxy-lactone

b. Poultry

- Summary. The nature of the residue in poultry is adequately understood. Myclobutanil is metabolized in a fashion similar to that in ruminants. In eggs, RH-9090 (free and conjugated), the hydroxy-lactone, RH-9089, and RH-0294 were identified. In liver and kidney, RH-0294, RH-9090 (free and, in liver, conjugated), RH-9089, the hydroxy-lactone, and parent RH-3866 were reported. In fat, RH-9090, hydroxy-lactone, and RH-3866 were found; in breast and thigh, RH-0294, RH-9090 conjugates, RH-9089, and RH-3866 were present.

  The residues to be regulated in eggs, and the meat, fat, and meat by-products of poultry are combined residues of parent RH-3866, its alcohol metabolite RH-9090 (free and conjugated), its diol metabolite RH-0294, and the hydroxy-lactone.

* * * * *

Discussion. The petitioner conducted a combination feeding/metabolism study using radioactive materials fed to poultry.

The feeding study aspect [TR 31H-86-16, MRID/Acces.# 266029] has previously been submitted (PP#7G3479/FAP#7H5523) and reviewed (6/16/87 memo of R. Loranger, the details of which are incorporated herein by reference). For convenience, it is summarized in the MAGNITUDE OF THE RESIDUE - POULTRY section of this present review, which see.

The metabolism study aspect, which addresses the disposition and metabolism of RH-3866 and metabolites in laying hens, is contained in a report [TR 31H-86-17, MRID/Acces.# 266107], not submitted prior to this petition, PP#7F3476/FAP#7H5524.

In brief, following a 1-week acclimation period, 2 groups (called Groups 6 and 7, respectively) of 3 white leghorn laying hens (individually caged) received oral doses (via gelatin capsules, force-fed) for 7 consecutive days of either ^{14}C RH-3866 or ^{14}C RH-9090/RH-9089 (82:18) at levels of 110 ppm to permit metabolite identification. Hens also received 110 g. of layer mash/24-hour period, and water ad libitum.

As in the feeding study, the ^{14}C RH-3866 was uniformly phenyl ring labeled, while the ^{14}C RH-9090 and ^{14}C RH-90899 were labeled at carbons 3 and 5 of the triazole ring.

Egg and excreta samples were collected daily and frozen. Hens were sacrificed 24 hours after the final dose, and tissues and whole organs were collected and frozen.

The in-life portion of the study was conducted for Rohm and Haas by Agrisearch, Inc., Mt. Airy, MD; collected samples were shipped frozen to Rohm and Haas for storage and analysis.

Total ^{14}C activity was determined by standard combustion and LSC techniques. The results are shown in Table 8:

Table 8

Summary of ^{14}C Residues[1] in Poultry

Matrix	Group 6[2]	Group 7[3]
Fat	0.017[4]	0.010[4]
Liver	0.55	0.31
Kidney	0.33	0.17
Breast	0.061	0.083
Thigh	0.060	0.071
Excreta[5]	--	--
Eggs[6]	--	--

1 Maximum value, in ppm, calculated as RH-3866. Data are extracted from Appendix A and Table I, TR 31H-86-17.
2 Fed ^{14}C phenyl ring labeled RH-3866 at 110 ppm dosing level for 7 consecutive days.
3 Fed triazole ring labeled ^{14}C RH-9090 and ^{14}C RH-9089 (82:18) at 110 ppm dosing level for 7 consecutive days.
4 Residue values from Appendix A, p. 27, TR 31H-86-17, are 0.31 ppm (Group 6) and 0.37 ppm (Group 7) for fat tissue.
5 No information provided.
6 Not reported in any of the Tables; p. 10 of TR 31H-86-17 states a maximum residue of 0.55 ppm for whole egg; but, raw data in Appendix A (pp. 24-25) seem to indicate a residue range of 0.07-2.00 ppm in whole egg.

Characterization and quantitation of residues were accomplished by TLC/radioautography, HPLC, and/or EC-GLC techniques, with comparisons to authentic ^{14}C standard solutions of RH-3866, RH-9090, RH-9089, RH-9090-sulfate, RH-0294, and the hydroxy-lactone.

In eggs, RH-9090 was found to be the major metabolite (47-67%); the hydroxy-lactone (14-19%), RH-9089 (up to 21%), RH-0294 (up to 15%), and RH-9090-sulfate (up to 8%) were also identified; Unknown(s) accounted for up to 8% of the ^{14}C activity and metabolite(s) described as "less polar than RH-3866" accounted for up to 11%. Parent RH-3866 was not present.

In liver and kidney, extracts were resolved by HPLC into fractions with retention times matching the ^{14}C standards of RH-3866 (30-43% in Group 6 hens); RH-0294 (up to 14%); RH-9090, RH-9089, and hydroxy-lactone metabolites (35 to 85%); and, in liver, RH-9090-sulfate (or polar) metabolite (up to 20%).

Fat tissue from Group 6 hens contained RH-3866 (85%); hydroxy-lactone (12%); and Other (3%). In fat from Group 7 hens, metabolite(s) "less polar than RH-3866" were the predominant residue (35%); also present were hydroxy-lactone (27%); RH-9090 (23%); and Polar (16%).

In breast and thigh, RH-9089, RH-0294, and RH-9090-sulfate (or polar) metabolites all comprised an appreciable portion of the residue. The distribution of residue varied widely with the extract fraction being analyzed. RH-3866 was a minor portion of the residue in thigh (3%) and breast (8%) tissues from Group 6 hens.

In conclusion, the data indicate that RH-3866 is extensively metabolized in poultry. The very low residue levels found (see Table 8) and the high dose level (110 ppm) demonstrate RH-3866 and its metabolites do not accumulate in organs, tissues, or eggs of hens. Over 95% of the administered dose was found in the excreta.

The residue in poultry tissue and eggs is comprised of RH-3866 and its metabolites RH-9090 (free and conjugated), RH-9089, RH-0294 (diol), and the hydroxy-lactone.

As shown in Table 7, these same residues are also present in dairy cattle.

We consider the nature of the residue in poultry to be adequately understood. The residues to be regulated in eggs, and the meat, fat, and meat by-products of poultry are combined residues of parent RH-3866, its alcohol metabolite RH-9090 (free and conjugated), its diol metabolite RH-0294, and the hydroxy-lactone.

F. RESIDUE ANALYTICAL METHODS

- Summary. Residue analytical methods have been submitted for the determination of RH-3866, RH-9089, and RH-9090 (free and conjugated) in apples and grapes (TR 310-84-27, with Addendums TR 31H-86-15 and TR 31S-87-46); RH-9090 (free only) in crops and RH-3866 in crops, meat, milk, and eggs (TR 310-84-13, with Addendum TR 310-86-09); RH-9090 (free only) in meat, milk, and eggs (TR 31S-87-09); and, RH-0294 (diol) in milk (TR 31S-87-02).

  We withhold judgment on the adequacy of these analytical methods for residue data gathering and/or enforcement purposes pending completion of method trials by COB/BUD chemists, and receipt/review by RCB of the report(s) from COB on the results of these trials.

  Residue analytical methods are also needed for the determination of RH-9090 (conjugated) in milk, and RH-9090 (conjugated), RH-0294 and the hydroxy-lactone in eggs and animal tissues. The sensitivity of such method(s) should be $\leq$ 0.01 ppm, if possible.

  FDA multiresidue information via protocols I thru IV has been submitted for RH-3866 and RH-9090 (free). Testing through these four protocols is also required of the other components of the regulable residue: RH-9090 (conjugated), RH-0294, and the hydroxy-lactone.

  The petitioner is urged to look into the possibility of consolidating proposed enforcement methods for myclobutanil and metabolites into one or two "total residue" methods applicable to determining the regulable residue in crops and animal commodities (meat, milk, and eggs).

* * * * *

Discussion. A number of residue analytical methods and addendums thereto have been developed for myclobutanil and/or its metabolites, depending on the particular application. The methods relevant to supporting this petition are discussed below.

1. "RH-3866 Total Residue Analytical Method for Apple and Grape", TR 310-84-27 [MRID/Acces.# 143769, 073600].

This method was originally submitted with PP#4G3149, but was not reviewed until our (R. Loranger) memo of 6/16/87, PP# 7G3479/FAP#7H5523, the details of which are incorporated herein by reference.

The Total Residue analytical method is applicable to residues of parent RH-3866, the alcohol RH-9090, RH-9090 conjugates (glucosides), and the ketone RH-9089 in apples and grapes.

Samples of apples (quartered) or grapes (whole) are chopped in a food processor with dry ice, which is removed by sublimation, and 10 gram portions soxhlet-extracted overnight (16-hour reflux) with 0.5N hydrochloric acid/methanol. The extraction converts RH-9090 conjugates to free RH-9090.

After cooling and basification, sodium borohydride is added to reduce the ketone RH-9089 to the alcohol RH-9090.

The extract is cleaned-up by petroleum ether partitioning, two methylene chloride partitionings, Chelex 100-Fe^{+++} activated affinity column chromatography, and Florisil column chromatography.

RH-3866 and RH-9090 quantitation is performed by gas-liquid chromatography (GLC) using a 100/120 mesh 2% OV-101 ultrabond packed column, with nitrogen/phosphorus (N/P) and electron capture (EC) detectors, respectively.

RH-3866 and RH-9090 are separately determined. The limit of quantitation of each is 0.01 ppm, and fortification data at this level are provided along with representative chromatograms of RH-3866 and RH-9090 residue determinations from control, treated, and fortified apple and grape samples.

Peak areas on the chromatograms are compared to standard curves of RH-3866 and RH-9090, with residues reported as the sum of RH-3866 and "total RH-9090". The latter refers to the fact that the RH-9090 peak represents free RH-9090; conjugated RH-9090, which was hydrolyzed to free RH-9090 during extraction; and RH-9089, which was reduced to free RH-9090 by a sodium borohydride step.

Fortification recoveries via this Total Residue method are summarized in Table 9 for actual field trials and processing studies on apples and grapes.

Table 9

Recovery Values by the RH-3866 Total Residue Method[1]

A. RH-3866[2]

Matrix	Spike (ppm)	n[3]	Recovery (%) Range	Recovery (%) Average	Control (ppm)
Grapes	0.025-1.0	19	50-119	88.2	<0.01
Apples	0.05-0.80	18	53-119	90.6	<0.01
Grape Fractions	0.05-0.50	13	46-110	79.8	≤0.018
Apple Fractions	0.04-0.10	3	67-138	100.0	<0.10
TOTAL:	0.025-1.0	53	46-138	87.6	<0.10

B. RH-9090 (free)[2]

Matrix	Spike (ppm)	n[3]	Recovery (%) Range	Recovery (%) Average	Control (ppm)
Grapes	0.025-0.35	18	44-109	67.3	<0.01
Apples	0.01-0.38	20	43-118	77.6	≤0.014
Grape Fractions	0.05-0.38	13	54-91	76.3	≤0.016
Apple Fractions	0.25-1.0	3	42-46	43.7	<0.01
TOTAL:	0.025-1.0	54	42-118	72.0	≤0.016

B. RH-9090 (glycoside)[4]

Matrix	Spike (ppm)	n[3]	Recovery (%) Range	Recovery (%) Average	Control (ppm)
Grapes	0.02-0.08	5	49-91	77.4	<0.01
Apples	0.02-0.38	11	56-98	81.7	<0.01
TOTAL:	0.02-0.38	16	49-98	80.4	<0.01

1 TR 310-84-27 [MRID/Acces.# 143769, 073600], usually with its Addendum TR 31H-86-15 [MRID/Acces.# 165036, 266030].
2 Raw recovery data are in the MRID/Acces.#s listed in Tables 17, 18, 19, and 20.
3 n = number of fortified samples.
4 Raw recovery data are in MRID/Acces.# 404092-03.

The efficiency of extraction was determined using grapes and apples field-treated with ^{14}C RH-3866. Samples were combusted and radioassayed as a measure of total ^{14}C activity. They were then soxhlet-extracted and the extract radioassayed. The extraction efficiency was 95% for grapes and 96% for apples.

Confirmatory analysis is achieved by two means: (a) use of an alternate column, 2% OV-17 + 1% OV-210 on 100/120 mesh Supelcoport; or, (b) using the EC detector to measure RH-3866 residues and the N/P detector to measure RH-9090 residues.

A non-CBI copy of this report (TR 310-84-27) has been submitted, and assigned MRID/Acces.# 143769.

We withhold judgment on the adequacy of this residue analytical method for either residue data gathering or enforcement purposes pending completion of a method trial by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of such a trial.

A method trial of this method, TR 310-84-27, to be conducted on apples (or grapes) was requested by RCB (R. Loranger, memo of 7/1/87) in conjunction with PP#7G3479/FAP#7H5523. That trial has not yet been completed.

2. "Addendum to RH-3866 Total Residue Analytical Method for Grape and Apple (TR 310-84-27)", TR 31H-86-15 [MRID/ Acces.# 165036, 266030].

This Addendum was submitted with PP#7G3479/FAP#7H5523, and is discussed in our (R. Loranger) review of 6/16/87, the details of which are incorporated herein by reference.

This Addendum consists of modifications to the Total Residue method, TR 310-84-27, which have been made to improve sample clean-up and RH-9090 quantitation.

These improvements are also said to allow the Total Residue method to be applied to a wider range of substrates, including apple and grape processed fractions.

The modifications to the Total Residue method deal with preparation of the Chelex 100-Fe^{+++} resin (Section 5.5); additional washing in the second methylene chloride partitioning (Section 5.6); substitution of a Bio-Sil A column for the Florisil column, and use of eluants keyed to the Bio-Sil A column (Section 5.7); and, changes in the EC-GLC conditions (flow rate, temperatures, etc.) for RH-9090 quantitation, including a change from a packed to a capillary column, Megabore DB-17 (Section 5.8).

Limited validation data and representative chromatograms are submitted. For RH-3866, 88% was recovered from a 0.1 ppm fortification to grapes, and 80%, from a 0.8 ppm spike to apples. For RH-9090, 74% was recovered from a 0.05 ppm fortification to grapes, and 69% from a 0.17 ppm spike to apples.

NDR of either RH-3866 or RH-9090 were observed in control apple and grape samples.

The limit of quantitation appears to be in the 0.01-0.02 ppm range, based on the limited recovery data. No validation data below 0.05 ppm were submitted with this Addendum report.

In Table 9, a summary of recovery values for actual field trials and processing studies with apples and grapes based on analysis by the Total Residue method are tabulated. The recovery data from grapes and grape fractions all reflect use of this Addendum to the Total Residue method. The recovery data for apples and apple fractions are a mix of the original Total Residue method 1984 trials) and incorporation of the Addendum (1985 and 1986 trials).

A non-CBI copy of this report (TR 31H-86-15) has been submitted, and assigned MRID/Acces.# 165036.

We withhold comment on this Addendum (TR 31H-86-15) pending completion of the method trial on TR 310-84-27 being conducted by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of that trial.

The method trial request on TR 310-84-27 (R. Loranger, memo of 7/1/87, PP# 7G3479/FAP#7H5523) specified that Addendum TR 31H-86-15 be included in the trial. The MTO has not yet been completed.

3. "Addendum 2 to RH-3866 Total Residue Analytical Method for Grape and Apple (TR 310-84-27)", TR 31S-87-46 [MRID/Acces.# 404092-02 and 404980-01].

Addendum 2 was submitted as an amendment (received by the Agency 11/13/87) to PP#7F3476/FAP#7H5524, and has not heretofore been reviewed.

A duplicate copy (non-CBI) was also submitted [12/30/87; same MRID/Acces.#] and, subsequently, a version (also non-CBI) revised [2/1/88; assigned MRID/Acces.# 404980-01] at our request (telecon, M. Nelson to M. Morelli, Rohm and Haas, 1/29/88) to clarify that the GLC conditions in Section 5.8 of Addendum 2 (TR 31S-87-46) apply to quantitation of RH-9090 only.

Addendum 2 consists of modifications to the Total Residue method, TR 310-84-27, which have been made to improve sample clean-up, the quality of chromatograms, and the recovery of RH-9090.

The modifications in Addendum 2 consist of:

(a) Section 5.5 - Details for a methanol pre-wash of the Chelex-100 (prior to preparation of the Chelex 100-Fe^{+++} resin) to reduce reagent artifacts on GLC;

(b) Section 5.5 - Changes in the elution solutions used with the Chelex 100-Fe^{+++} column (use 25 ml of 1:4 methanol-water as a rinse instead of 50 ml; use 200 ml of 1:1 methanol-water as a wash instead of 170 ml of 0.5N triazole in 1:1 methanol-water. Use of triazole has been eliminated.);

(c) Section 5.6 - Elimination of the water wash of methylene chloride in the second partitioning process; and,

(d) Section 5.7 - The RH-3866 fraction is now to be eluted from the Bio-Sil A column with 100 ml (instead of 75 ml) of 25% acetone/toluene, and the RH-9090 fraction with 100 ml (instead of 75 ml) of 50% acetone/toluene.

Where overlap occurs, modifications made by Addendum 2 (TR 31S-87-46) supersede those made by the first Addendum (TR 31H-86-15) to TR 310-84-27.

Validation data were submitted with the Addendum 2 report. The results are tabulated in Table 10.

Table 10

Recoveries Using Addendum 2 of TR 310-84-27[1,2]

	RH-3866			RH-9090		
Matrix	Spike (ppm)	Recovery	n[3]	Spike (ppm)	Recovery	n
Apples	0.48	91-99%	4	0.10	77-80%	4
Grapes	0.48	88%	1	0.10	88%	1
AVERAGE		94%	5		80%	5

1 NDR (<0.01 ppm) were in control samples. The limit of quantitation was estimated by comparing chromatograms from controls and reference standard solutions.
2 Data extracted from chromatograms, TR 31S-87-46.
3 n = number of samples fortified.

We note that Sections 5.8 of Addendum 2 (TR 31S-87-46) and Addendum 1 (TR 31H-86-15) to TR 310-84-27 list revised GLC quantitation conditions for RH-9090.

Those conditions, as specified in these two Addendums are identical, and call for continued use of an EC detector, but a switch to a capillary column (Megabore DB-17, 30m) to quantitate RH-9090.

The conditions for quantitation of RH-3866 remain as originally given in TR 310-84-27: N/P detector and a 6' packed column (2% OV101-ultrabond, 100/120 mesh).

Thus, RH-3866 and RH-9090 are quantitated by different columns, (packed vs capillary), column materials (2% OV101-ultrabond vs DB-17), GLC detectors (N/P vs EC) and instrument conditions.

We withhold comment on this Addendum (TR 31S-87-46) pending completion of the method trial on TR 310-84-27 being conducted by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of that trial.

In its request for additional method trials on myclobutanil (M. Nelson, memo of 1/11/88, PP#7F3476/FAP#7H5524), RCB asked that Addendum 2, TR 31-H-87-46, be incorporated into the method trial being run on TR 310-84-27, if it were feasible for COB/BUD to do so at this time. It is our understanding that COB/BUD does intend to incorporate this Addendum 2 into its method trial. (Meeting of 1/29/88 between RCB and COB/BUD personnel.)

4. "Supplemental Data for the RH-3866 Total Residue Method (TR 310-84-27)", TR 31S-87-37 [MRID/Acces.# 404092-03].

This report was submitted as an amendment (received by the Agency 11/13/87) to PP#7F3476/FAP#7H5524, and has not heretofore been reviewed.

This report was generated as a result of a comment in the RCB review (R. Loranger) of 6/16/87, PP#7G3479/FAP#7H5523, that one of the additional requirements for permanent tolerances for myclobutanil on apples and grapes would be "Recovery data [via the Total Residue Analytical Method, TR 310-84-27] for RH-9090 glucoside in apples and grapes at levels down to at least 0.05 ppm. Several other fortifications in the range of 0.1 to 1.0 ppm should also be tested."

RH-9090 ^{14}C glycoside was purified and characterized from wheat straw. No details of this were provided.

Control grapes and apples were fortified with this RH-9090 ^{14}C glycoside standard, and residues analyzed by the Total Residue Analytical Method (TR 310-84-27).

Apparently only at the highest fortification level were any modifications to the Total Residue Analytical Method used. The report specifically states the representative chromatograms of those particular samples reflect use of Addendum 2 improvements.

RH-9090 Glycoside recovery data from apples and grapes are summarized in Table 11.

Table 11

RH-9090 Glycoside Recoveries from Apples and Grapes Using Total Residue Analytical Method TR 310-84-27[1]

Fortification Level (ppm)	Recovery (%)[2] Grapes	Apples
0.02	91	77
0.04	80	70
0.075	90,77	82,88
0.08	49	56
0.38[3]	--	84,88,83, 85,88,98

1 Data extracted from page 3, TR 31S-87-37.
2 Average is: grapes, 77%; apples, 82%; overall, 80%.
3 Addendum 2 (TR 31S-87-46) to TR 310-84-27 used.

Chromatograms of a control grape and apple sample indicated NDR, which we estimate to be <0.01 ppm based on comparison with the reference standard solutions of RH-9090 glycoside.

RCB has not requested a method trial be run on RH-9090 glycoside. We reserve the option to do so at a future date, if we consider it advisable. For now, we conclude that validation of RH-9090 glycoside in apples and grapes is adequate, based on the petitioner's data.

A non-CBI copy of this report (TR 31S-87-37) has also been received [12/30/87; no separate MRID/Acces.# was assigned].

5. "Analytical Method for the Measure of RH-3866 Residues in Various Crops, Soil, Meat, Milk, and Eggs and RH-9090 Residues in Various Crops and Soil", TR 310-84-13 [MRID/Acces.# 145682, 072905].

This method was originally submitted with PP#4G3149, and reviewed in our (R. Loranger) memo of 1/9/85, the details of which are incorporated herein by reference.

This method is applicable to RH-3866 and RH-9090 (free only) residues in crops, and parent RH-3866 in meat, milk, and eggs.

There is an initial sample preparation step. Crop samples are chopped in a food processor; animal tissues are minced in a grinder; eggs are homogenized in a blender; raisins and milk are not pre-processed.

Residues are extracted from 10 gram sample portions with methanol (grapes, raisins, milk, eggs, kidney, liver, muscle); 0.1N sodium hydroxide-in-methanol (apples); or, n-heptane (fat).

This is followed by an additional extraction step with hexane, and methylene chloride partitioning (2X).

After evaporation and reconstitution with toluene, the sample is quantitatively transferred to an activated Florisil (60-100 mesh) column. RH-3866 is eluted from the column with a 1% methanol-toluene solution; RH-9090 is eluted off the column with 7.5% methanol-toluene.

Samples are evaporated to dryness, the residue redissolved in 5-10 ml of toluene, and RH-3866 and RH-9090 residues separately quantitated by EC-GLC using columns (6 ft. coiled glass, 2 mm I.D.) packed with 2% OV-17/1% OV-210 on 100/120 mesh Supelcoport and 2% OV-101 on 100-120 mesh Ultrabond, respectively.

Table 12 summarizes information on levels of fortification, recoveries, and limits of sensitivity via this analytical method (TR 310-84-13) in various substrates.

Numerous representative chromatograms were provided. For parent RH-3866, controls are on the order of <0.001-0.006 ppm in the various matrices, which agrees with the petitioner's claim of 0.005 ppm. For RH-9090, controls are estimated at 0.002-0.005 ppm for apples, grapes, and raisins.

Confirmatory analysis is achieved via use of a N-P detector; column packings are the same as with the EC detector.

Extraction efficiency for the various substrates was determined by adding a known amount of RH-3866 or RH-9090 before extraction/clean-up/analysis. Approximately 95% of those fortifications were reportedly recovered.

A non-CBI copy of this report (TR 310-84-13) has been submitted, and assigned MRID/Acces.# 145682.

Table 12

Summary of Validation Data for RH-3866 and RH-9090 in Various Substrates via Method TR 310-84-13.[1]

	RH-3866[2]			RH-9090[2]		
Matrix	Spike (ppm)	n	% Recov/Avg	Spike (ppm)	n	% Recov/Avg
Apples	0.01-0.1	8	74-100 (89)	0.02	2	85-92 (89)
Grapes	0.01-0.1	6	70-94 (87)	0.02	2	98-109 (103)
Raisins	0.04-0.05	2	65-88 (77)	0.04-0.05	2	65-88 (77)
Beef						
Liver	0.01	2	83-87 (85)			
Kidney	0.01-0.05	2	82-91 (87)			
Fat	0.01-0.05	3	76-88 (82)	No Data		
Muscle	0.01-0.1	2	73-83 (78)			
Milk	0.01	3	68-85 (79)			
Eggs	0.01-0.05	4	85-103 (91)			
TOTAL:	0.01-0.1	32	65-103 (87)	0.02-0.05	6	65-109 (90)

1 Data extracted from Tables II, III, IV, and V, TR 310-84-13.
2 The limit of detection is 0.005 ppm, except for RH-9090 in raisins (L.D. 0.01 ppm).

We withhold judgment on the adequacy of this residue analytical method for either residue data gathering or enforcement purposes pending completion of a method trial by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of such a trial.

A method trial of this method, TR 310-84-13, to be conducted with milk and beef liver was requested by RCB (R. Loranger, memo of 7/1/87) in conjunction with PP#7G3479/FAP#7H5523. That trial has not yet been completed.

6. "Addendum to TR 310-84-13, Analytical Method for RH-3866 and RH-9090", TR 310-86-09 [MRID/Acces.# 165036, 266030].

This Addendum was submitted with PP#7G3479/FAP#7H5523, and is discussed in our (R. Loranger) review of 6/16/87, the details of which are incorporated herein by reference.

This Addendum consists of two modifications for TR 310-84-13:

(a) Section III, E - After evaporation of eluant fractions, the residue is to be dissolved in 3% methanol-toluene (rather than toluene) for GLC analysis; and,

(b) Section III, F, 4 - Standard solutions are to be prepared in 3% methanol-toluene (instead of toluene). The addition of methanol prevents adsorption of RH-3866 and RH-9090 onto glass surfaces.

No validation data for these changes were included in the Addendum.

A non-CBI copy of this report (TR 310-86-09) has been submitted, and assigned MRID/Acces.# 165036.

We withhold comment on this Addendum (TR 310-86-09) pending completion of the method trial on TR 310-84-13 being conducted by CDB/BUD chemists, and receipt/review by RCB of the report from CDB on the results of that trial.

The method trial request on TR 310-84-13 (R. Loranger, memo of 7/1/87, PP# 7G3479/FAP#7H5523) specified that Addendum TR 310-86-09 be included in the trial. The MTO has not yet been completed.

7. "RH-9090 Residue Analytical Method and Validation Data for Meat, Milk, and Eggs", TR 31S-87-09 [MRID/Acces.# 404092-04].

This report was submitted as an amendment (received by the Agency 11/13/87) to PP#7F3476/FAP#7H5524, and has not heretofore been reviewed.

This report was generated as a result of a comment in the RCB review (R. Loranger) of 6/16/87, PP#7G3479/FAP#7H5523, that requirements for permanent tolerances for myclobutanil on apples and grapes would probably include "...validated analytical methods for the metabolites RH-9090, RH-0294, and the hydroxy-lactone in animal tissues, milk, and eggs. A method for RH-9089 may also be required."

This report details an analytical method applicable to the determination of RH-9090 residues in meat, milk, and eggs. The method determines residues of free RH-9090 only. (Telecon of M. Nelson, RCB, to M. Morelli, 215-592-3581, Rohm and Haas, 1/7/88.)

The principle of the analytical procedure is as follows:

There is an initial sample preparation step. Eggs are homogenized in a blender; tissue samples are chopped and blended to a powder in the presence of dry ice, which is then sublimed off in a freezer; milk samples are not pre-processed.

RH-9090 residues are extracted from 20 gram sample portions of milk, egg, and tissue samples with methanol in the presence of Celite-545. Vacuum filter, with washing, and collect all supernatants in a separatory funnel.

Partition the extract with hexane to remove interferences, and then with methylene chloride (2X). Evaporate to dryness and re-dissolve using toluene-acetone 100/20.

Quantitatively transfer the solution to an activated Bio-Sil A column. RH-9090 is eluted from the column with toluene/acetone 100/100, concentrated to dryness, and (for all samples except liver) made to volume with with isooctane/isopropyl alcohol 100/30 for quantitation by GLC.

Liver samples require a further clean-up via reversed phase LC-18 SPE disposable cartridge, eluting with Milli-Q water/methanol 100/100. Concentrate to dryness and bring to an appropriate volume for GLC analysis using isooctane/isopropyl alcohol 100/30.

RH-9090 is determined by GLC using a 0.53 mm ID x 15 m capillary column coated with SPB-608, and a capillary thermionic specific detector optimized for nitrogen selectivity.

Confirmatory analysis is performed via EC-GLC using a 0.53 mm ID x 30 m capillary column coated with DB-17.

Based on examination of the representative chromatograms submitted, the sensitivity of the method is 0.01 ppm for all substrates.

A summary of recovery data for RH-9090 from animal commodity substrates via this analytical procedure (TR 31S-87-09) is presented in Table 13.

Table 13

Summary of Recovery Data for RH-9090 via TR 31S-87-09[1]

Spike (ppm)	Recovery of RH-9090 (%)					
	Eggs	Liver	Beef	Chicken	Kidney	Milk
0.00[2]						
0.01	81-94	69-88	75-104	87-161	88-130	83-87
0.05	88-97	76-114	81-148	88-114	90-94	91-102
0.20	94-100	80-115	91-94	93-99	86-101	92-98
AVG:	91	86	97	107	98	91
n :	12	12	9	10	12	11

1 Data extracted from Tables III-VIII, TR 31S-87-09.
2 Residues in controls were <0.005 ppm.

A non-CBI copy of this report (TR 31S-87-09) has also been received [12/30/87; no separate MRID/Acces.# was assigned].

We withhold judgment on the adequacy of this residue analytical method for either residue data gathering or enforcement purposes pending completion of a method trial by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of such a trial.

A method trial of this method, TR 31S-87-09, to be conducted with milk and beef liver was requested by RCB (M. Nelson, memo of 1/11/88, PP#7F3476/FAP#7H5524). That trial has not yet been completed.

8. "RH-0294 Residue Analytical Method in Milk", TR 31S-87-02, [MRID/Acces.# 403662-01 and 404813-01].

This report was submitted as an amendment (received by the Agency 10/7/87) to PP#7F3476/FAP#7H5524, and has not heretofore been reviewed.

This report was generated as a result of a comment in the RCB review (R. Loranger) of 6/16/87, PP#7G3479/FAP#7H5523, that requirements for permanent tolerances for myclobutanil on apples and grapes would probably include "...validated analytical methods for the metabolites RH-9090, RH-0294, and the hydroxy-lactone in animal tissues, milk, and eggs. A method for RH-9089 may also be required."

This report details an RH-0294 residue analytical method in milk. The diol, RH-0294, is a major milk metabolite of RH-3866.

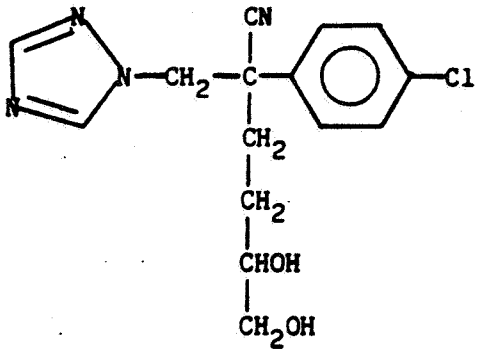
The principle of this method is as follows:

Potassium periodate is added to whole milk (10 g. sample) to oxidatively cleave RH-0294 to alpha-(4-chlorophenyl)-alpha-(2-formylethyl)-1H-1,2,4-triazole-1-propane nitrile.

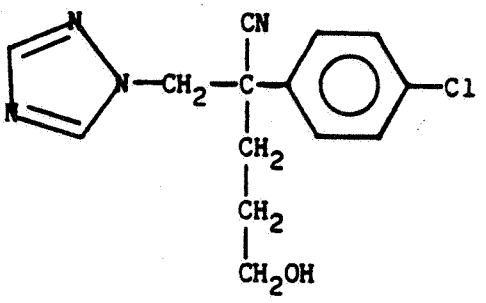
Ethyl alcohol is then added, and the milk centrifuged and the supernatant collected. The precipitate is washed with water and the supernatants combined.

Ethyl acetate is added to the supernatant. Partition and collect the ethyl acetate layer and evaporate to dryness.

Redissolve the residue from the ethyl acetate partition with 10:1 water:methanol and add sodium borohydride to reduce the aldehyde to alpha-(4-chlorophenyl)-alpha-(3-hydroxypropyl)-1H-1,2,4-triazole-1-propane nitrile (RH 66,647).



RH-0294



RH-66,647

Partition into ethyl acetate (3X) and evaporate to dryness. Redissolve the residue with 5% acetone/toluene, and quantitatively transfer to an activated Bio-Sil (100-200 mesh) column.

Wash the column with 5% acetone/toluene, then 50% acetone/toluene; discard these washes. Elute the residue from the column with 90% acetone/toluene, collect and evaporate to dryness.

The sample is now said to be ready for GLC analysis. (No information is given on the volume and solvent used to redissolve the sample residue. We surmise dilute acetone/toluene was used for this purpose, and sample solutions brought to 10 ml.)

Quantitation is performed by GLC on a Megabore DB-17 capillary column (30 m x 0.53 mm) with EC detection.

Table 14 contains a summary of recovery data from milk fortified with known amounts of RH-0294 and analyzed by this procedure (TR 31S-87-02). A representative chromatogram indicates NDR in milk control at a limit of quantitation of 0.01 ppm.

Standard curves were prepared using solutions of known concentrations of RH-66,647. The structure of this compound (and RH-0294) was confirmed by direct exposure probe (DEP) MS.

Table 14

Recoveries[1] of RH-0294 From Milk Using Residue Analytical Method TR 31S-87-02.

PPM Added	% Recovery
0.013	78,95,97,103
0.021	87
0.026	100,104,79,110
0.041	72,71,100
0.052	97,64,96,89
0.062	88
0.077	72,95,115
0.082	115
0.130	93,91,88,80
0.515	108
AVERAGE:	92% (n=26)

[1] Data extracted from Table 2, TR 31S-87-02.

Information is provided in Appendix 2 of TR 31S-87-02 (the non-CBI copy, MRID/Acces.# 404813-01) on the procedures for synthesis of the reference standard RH-6647 (aka RH-66,647). Spectral data (IR and NMR) and elemental analysis information to verify the structure of RH-(6)6,647 were also included.

We withhold judgment on the adequacy of this residue analytical method for either residue data gathering or enforcement purposes pending completion of a method trial by COB/BUD chemists, and receipt/review by RCB of the report from COB on the results of such a trial.

A method trial of this method, TR 31S-87-02, to be conducted with milk was requested by RCB (M. Nelson, memo of 1/11/88, PP#7F3476/FAP#7H5524). That trial has not yet been completed.

The original submission of this method (MRID/Acces.# 403662-01) contained a CBI claim and disclaimer; a clean copy of the method was subsequently submitted (1/20/88; MRID/Acces.# 404813-01) which made no claims of data confidentiality.

8. FDA Multiresidue Procedures

The petitioner has submitted as an amendment (received by the Agency 11/13/87) to PP#7F3476/FAP#7H5524 a report entitled, "FDA Multiresidue Screen Results for RH-3866 and RH-9090", Analytical Report No. 31A-87-58 [MRID/Acces.# 404092-05]. This report has not heretofore been reviewed.

A non-CBI copy of this report (TR 31A-87-58) has also been received [12/30/87; no separate MRID/Acces.# was assigned.]

This report was generated as a result of a comment in the RCB review (R. Loranger) of 6/16/87, PP#7G3479/FAP#7H5523, that requirements for permanent tolerances for myclobutanil on apples and grapes would include "data to show the behavior or recovery of RH-3866 through the multiresidue procedures employed by the Food and Drug Administration."

The objective of the study was to determine the analytical suitability and stability of RH-3866 and RH-9090 by testing them through procedures found in FDA Pesticide Analytical Manual (PAM) Volume I, Protocols I through IV.

This information is not subject to review by RCB/EPA, but will be forwarded to FDA for inclusion in PAM I.

Summary findings are that RH-3866 and RH-9090 will not elute from Florisil under the conditions in PAM I methods 211.14d and 252.12b. Therefore, Protocol I is of limited use for these compounds. Protocols II and III offer only a moderate means of recovering RH-3866 and RH-9090 from foodstuffs. Protocol IV offers from a moderate to a good means for recovering RH-3866 and RH-9090 from foodstuffs.

The other components (metabolites) of the regulable residue are also subject to test via the four FDA Multiresidue Protocols.

Thus, information on the recoverability/behavior of bound RH-9090, RH-0294, and the hydroxy-lactone metabolite via the four FDA Multiresidue Protocols also needs to be submitted.

9. Other Residue Analytical Methods Needed to Enforce the Proposed Tolerances

A. RH-9090 (bound) in Milk, Eggs, and Animal Tissues

No residue analytical method has been submitted for a determination of RH-9090 (bound) residues in animal commodities. (TR 31S-87-09 measures free RH-9090 only.)

This metabolite is to be regulated in milk, eggs, and the meat, fat, and meat by-products of cattle, goats, hogs, horses, poultry, and sheep.

A residue analytical method capable of enforcing tolerances of RH-9090 (conjugated) in all these commodities is therefore needed. Method sensitivity should be $\leq$ 0.01 ppm, if possible.

The method, as submitted to the Agency, should be non-CBI.

Once received, the method will be subjected to method trial by COB/BUD to assess its suitability for enforcing proposed tolerances in animal commodities (meat, milk, and eggs).

B. RH-0294 (diol) in Eggs and Animal Tissues

No residue analytical method has been submitted for a determination of RH-0294 (diol) residues in commodities other than milk.

This metabolite is also to be regulated in eggs and the meat, fat, and meat by-products of cattle, goats, hogs, horses, poultry, and sheep.

A residue analytical method capable of enforcing tolerances of RH-0294 in all these commodities is therefore needed. Method sensitivity should be $\leq$ 0.01 ppm, if possible.

The method, as submitted to the Agency, should be non-CBI.

Once received, the method will be subjected to method trial by COB/BUD to assess its suitability for enforcing proposed tolerances in animal commodities (meat, milk, and eggs).

C. Hydroxy-lactone Metabolite in Animal Commodities

No residue analytical method has been submitted for a determination of hydroxy-lactone residues in any commodity.

This metabolite is to be regulated in eggs and the meat, fat, and meat by-products of cattle, goats, hogs, horses, poultry, and sheep.

A residue analytical method capable of enforcing tolerances of the hydroxy-lactone in all these commodities is therefore needed. Method sensitivity should be $\leq$ 0.01 ppm, if possible.

The method, as submitted to the Agency, should be non-CBI.

Once received, the method will be subjected to method trial by COB/BUD to assess its suitability for enforcing proposed tolerances in animal commodities (meat, milk, and eggs).

General Comment on Residue Analytical Methods for Enforcement of Tolerances for Myclobutanil and its Regulable Metabolites.

We urge the petitioner to look into the possibility of consolidating these several analytical methods for determination of residues of myclobutanil and its metabolites into just one or two "total residue" methods applicable to determining the regulable residue in crops and animal commodities (meat, milk, and eggs).

"Total residue" method(s) would facilitate enforcement activities and, in future, any additional residue data gathering on myclobutanil and its metabolites the petitioner may need/intend to undertake.

G. STORAGE STABILITY DATA

- Summary. Residues of RH-3866 per se remain stable in apples and grapes during 2 years of frozen storage.

  Storage stability data (of appropriate length) are needed for RH-9090 (free and conjugated) in apples and grapes.

  Also, if processing fractions were frozen-stored for longer than 2 weeks prior to analysis, appropriate storage stability data are needed for RH-3866 and RH-9090 (free and conjugated) in apple and grape pomaces, raisins, and raisin waste to validate the residue data of these compounds in these matrices.

* * * * *

Discussion. The petitioner has now provided final reports of studies on the effect of long-term frozen storage on RH-3866 parent compound residues in apples [TR 31H-86-04; MRID/Acces.# 266109] and grapes [TR 31H-86-06; MRID/Acces.# 266115].

The interim reports [TR 310-85-03, apples; TR 310-85-02, grapes] have previously been submitted [MRID/Acces.# 073600] and reviewed (R. Loranger, 6/16/87, PP#7G3479/FAP#7H5523).

Control apple or grape samples were chopped in a Hobart food chopper with dry ice, which was removed by sublimation in a freezer. Four 10-gram sample portions of each crop were weighed into separate vials for use at each time interval as a control; a control which would be fortified at the time of analysis; and fortified (on 0-day) duplicates.

Fortification with RH-3866 was at the 0.1 ppm level. One each of the duplicates of apples and grapes to be analyzed at 0-day, 1-year, and 2-years was fortified on 0-day with 0.1 ppm ^{14}C RH-3866. Frozen storage was at -15°C.

At the specified time intervals, crop samples were analyzed by the residue analytical method [TR 310-84-13; MRID/Acces.# 072905] which measures parent RH-3866 only. A fresh fortification was concurrently run at each time interval.

The stability of RH-3866 residues during the course of these studies is summarized in Table 15:

Table 15

Stability of RH-3866 Residues† in Stored Apples and Grapes[1,2]

Length of Storage	% Recovery - APPLES[3]		% Recovery - GRAPES[4]	
	Fresh[5]	Aged[6]	Fresh[5]	Aged[6]
Day 0	89[7]	100,98	99[7]	102,98
Day 7	99	103,99	100	96,96
Day 14	97	89,92	100	101,108
Day 28	103	100,106	106	93,96
3 Months	104	104,107	100	97,102
6 Months	94	92,103	92	93,102
1 Year	95	82,89;86[7]	105	103;105[7]
2 Year	105	93;85[7]	98	90;84[7]
Range:	89-105	85-104	92-106	84-108
AVERAGE:	98 ± 5	95 ± 8	100 ± 4	98 ± 6

† Analyses via Parent Residue Method, TR 310-84-13.
1 Controls contained NDR (<0.01 ppm).
2 Fortified with 0.1 ppm RH-3866.
3 Data extracted from Table I, TR 31H-86-04.
4 Data extracted from Table I, TR 31H-86-06.
5 Fortified at time of analysis.
6 Fortified on Day Zero.
7 Fortified with ^{14}C-RH-3866.

Extraction efficiency was determined in 0-day, 1-year, and 2-year ^{14}C-fortified apple and grape samples by subjecting aliquots of the methanolic extract to radioassay (LSC) and the dried filter cake to combustion and radioassay (LSC).

Extraction efficiencies are shown in Table 16:

Table 16

Extraction Efficiency of RH-3866 From Stored Apples[1] and Grapes[2] via the Parent Residue Analytical Method[3]

Length of Storage	Extraction Efficiency (%) from the: Filter Cake		^{14}C GLC Solution	
	Apples	Grapes	Apples	Grapes
0-Day	99	100	99	--
1-Year	98	98	87	96
2-Year	99	97	90	89

1 Data extracted from Table II, TR 31H-86-04.
2 Data extracted from Tables I and II, TR 31H-86-06.
3 Parent Residue Analytical Method is TR 310-84-13.

No data were presented for the storage stability of RH-9090 (free or conjugated) in apples or grapes, or for RH-3866 or RH-9090 (free or conjugated) in apple or grape processing fractions.

The following additional storage stability data are needed:

- RH-9090 (free and conjugated) in apples and grapes.
- RH-3866 in apple pomace; grape pomace; raisin waste; and raisins. (This requirement only applies if these processing fractions were frozen-stored for longer than two weeks prior to analysis.)
- RH-9090 (free and conjugated) in apple pomace; grape pomace; raisin waste; and raisins. (This requirement only applies if these processing fractions were frozen-stored for longer than two weeks prior to analysis.)

The length of the storage stability studies on these matrices/compounds should be of sufficient duration to validate the crop field trial and processing study data on apples and grapes; i.e., if crop field trial and processed food/feed samples were stored 9 months prior to residue analysis, then a 9-month (minimum) storage stability study to validate the storage of those samples is required.

(Note: For this petition, storage stability data are not being requested in connection with animal commodity items since the metabolism/feeding studies of dairy cattle and laying hens were conducted with radiolabeled compounds.)

H. MAGNITUDE OF THE RESIDUE

1. APPLES

a. Crop Field Trials

- Summary. Supporting residue data are available from 15 field trials with apples.

  Tentatively, we conclude these field trial data support the proposed tolerance of 0.5 ppm for combined residues of RH-3866 and RH-9090 (free and bound) in or on apples.

  A final determination awaits the submission/evaluation of storage stability data for RH-9090 (free and bound) in apples and the completion of successful method trials.

* * * * *

Discussion. The data from the supporting crop field trials for apples are located in MRID/Acces.# 073600, PP#4G3149; MRID/Acces.# 266031, PP#7G3479/FAP#7H5523; and, MRID/Acces.# 266108, 266110, and 266111, PP#7F3476/FAP#7H5524.

The relevant information is summarized in Table 17.

As can be seen, data from 15 crop field trials with apples are listed. These represent crop years 1984-1986. All field trials were conducted using the Rally™ 40W formulation.

Field trial sites were located in SC (1), VA (2), PA (4), OH (2), MI (1), WI (2), OR (2), and WA (1). These represent the major growing regions in the USA, and provide adequate geographical representation for apples.

The field trials involved 8 varieties of apples and 4 soil types. Applications were all by ground spray equipment, and all but one study (@ 84 gpa) entailed dilute sprays of 150-600 gpa/application.

Use of concentrate sprays, as proposed in the Directions for Use of Rally™ 40W, Rally™ 60DF, and Nova™ 40W in Water-Soluble Pouches, is thus not supported by these field trials. (See DIRECTIONS FOR USE section of this review.)

Apple field trials reflect 1-15 applications and an application rate of 0.09-0.5 lb ai/A (versus 0.25 lb ai/A proposed). Total dosage ranged from 0.90-5.17 lbs ai/A/season. (Proposed use permits 2 lbs ai/A/season.)

The proposed PHI is 14 days. For those trials which provided residue decline data, the 14-day PHI value is the one usually reported in Table 17.

Apples were analyzed by the RH-3866 Total Residue analytical method (TR 310-84-27), with Addendum (31H-86-15) incorporated.

The Total Residue method measures RH-3866 parent compound and "total RH-9090" residues. Total RH-9090 residues consist of RH-9090, RH-9090 released from conjugates, and RH-9089 (which has been reduced to RH-9090).

The proposed tolerance on apples is 0.5 ppm for combined residues of the parent (RH-3866) and RH-9090 (free and bound). Tentatively, we conclude that these field trial data support the proposed tolerance, and that 0.5 ppm is an appropriate level.

Before we can finalize our conclusion about the adequacy of these field trial data to support the proposed tolerance on apples, storage stability data for RH-9090 (free and bound) residues in apples must be submitted and method trials must be successfully completed.

Based on the raw data, apple samples were stored 5 weeks to 9^{+} months prior to residue analysis.

See discussion in the STORAGE STABILITY section of this review.

Table 17

Summary of Apple Field Trial Data[a,b]

Trial	MRID/Acces.	Site	Variety	Soil Type	gpa[1]	Storage[2]
84-0212	073600	SC	Winesap	sandy clay	---	3+ mos
84-0238[3]	073600	VA	Rome	----	400	3+ mos
84-0241	073600	PA	Multi	silty loam	400	8 wks
84-0274	073600	WI	McIntosh	silty loam	300	8 wks
84-0300	073600	WI	McIntosh	silty loam	300	5 wks
84-0384	073600	PA	Rome	sandy loam	300	2 mos
85-0320	266108	PA	G. Delic.	silty loam	400	9+ mos
85-0334	266108	VA	Rome	clay loam	150	9+ mos
85-0422	266108	OR	Newton	silty loam	250	8+ mos
85-0490[4]	266110	MI	R. Delic.	clay loam	300	9 mos
85-0542[3,4]	266031	OH	G. Delic.	silty loam	400	9 mos
85-0543	266108	OH	R. Delic.	silty loam	400	9+ mos
85-0551	266108	WA	Rome	silty loam	600	8+ mos
86-0260[4]	266111	PA	McIntosh	silty loam	400	5-7 wks
86-0297[4]	266111	OR	Granny Sm.	silty loam	84	5-7 wks

Trial	Dosage (lbs ai/A)[5]			#Reps	PHI	MAXIMUM Residue (ppm)[6]		
	#Appl.	rate	Total			RH-3866	RH-9090[7]	Total
84-0212	14	0.14	1.96	3	6	0.332	0.150	0.482
84-0238[3]	6	0.25	1.50	3	23	0.010[8]	0.040[8]	0.050
" " "	"	0.50	3.00	"	"	0.071[8]	0.036[8]	0.107
84-0241	15	0.24	3.60	3	14	0.490	0.111	0.601[9]
84-0274	9	0.38	3.42	3	14	0.227	0.053	0.280
84-0300	10	0.09	0.90	3	12	0.036	0.024	0.060
84-0384	11	0.47	5.17	4	13	0.142	0.028	0.170
85-0320	13	0.24	3.12	2	14	0.152	0.063	0.215
85-0334	11	0.36	3.96	2	13	0.091	0.077	0.168
85-0422	9	0.25	2.25	2	14	0.213	0.053	0.266
85-0490[4]	10	0.25	2.50	2	7	0.157	0.014	0.171
85-0542[3,4]	14	0.25	3.50	2	14	0.204	0.061	0.265
85-0543	14	0.25	3.50	2	14	0.305	0.017	0.322
85-0551	8	0.375	3.00	2	14	0.091	0.027	0.118
86-0260[4]	1	0.24	0.24	2	14	0.027	<0.010	0.027
86-0297[4]	5	0.21	1.05	2	14	0.071	<0.010	0.071

a Summary data compiled by this reviewer.
b Residue analyses via TR 310-84-27 with Addendum TR 31H-86-15.
1 Spray volume per acre.
2 Length of frozen storage prior to analysis.
3 Apples used in processing studies.
4 Residue decline studies in apples.
5 Rally™ 40W formulation used in all trials.
6 Corrected for overall average recovery of 90% for RH-3866 and 70% for RH-9090.
7 Free and Conjugated.
8 Average of all (3) replicates.
9 Average of all (3) replicates: 0.239 ppm RH-3866 + 0.092 ppm RH-9090 = 0.331 ppm.

b. Processed Food and Feed

- Summary. We withhold judgment on the adequacy of these apple processing studies until storage stability data for residues of RH-9090 (free and bound) in apples are submitted and method trials have been successfully completed.

  Also, the date on which processing of apples occurred [TR 31H-86-09; MRID/Acces.# 266031] needs to be provided.

  Raw data, processing information, and date of processing, also need to be submitted for the processing of apples from crop field trial 84-0238 [summarized in MRID/Acces.# 266105].

  If apple processing fractions were frozen-stored for longer than 2 weeks prior to analysis, storage stability data of appropriate duration for RH-3866 and RH-9090 (free and bound) residues in apple processing fractions will also be needed.

  Tentatively, we consider a feed additive tolerance proposal based on < 10X concentration factor in apple pomace to be appropriate.

  A revised Section F for "apple pomace" is needed. (See PROPOSED TOLERANCES section of this review.) Tentatively, it appears 5 ppm would be the appropriate tolerance level.

* * * * *

Discussion. An apple processing study was conducted for PP#7G3479/FAP#7H5523, and the data submitted in TR 31H-86-09 [MRID/Acces.# 266031]. Those data and details of the processing procedure were discussed in the RCB (R. Loranger) review of 6/16/87, aforecited petition, the details of which are incorporated herein by reference.

To summarize, samples of treated apples (from the 21-day PHI) from crop field trial 85-0542 (see Table 17 for details of the field trial) were processed at Rohm and Haas Laboratories (Spring House, PA) to yield cider, wet pomace, and dry pomace.

Fruit and processed fractions were analyzed by the RH-3866 total residue analytical method [TR 310-84-27, MRID/Acces.# 073600, 143769], as amended by TR 31H-86-15 [MRID/Acces.# 266030, 165036].

Residues were corrected for an overall average recovery of 90% for RH-3866 and 70% for RH-9090. Sensitivity is 0.01 ppm for both RH-3866 and RH-9090 residues in all processed fractions.

The results are summarized in Table 18.

Table 18

Summary of Results of Apple Processing Studies[1]

Trial	MRID/Acces.	Sample	AVERAGE Residue (ppm)[2,3] RH-3866	RH-9090[4]	Total	Conc. Factor[5]
85-0542[6]	266031	Fruit	0.150	0.083	0.233	1.00
		Cider	0.016	0.022	0.038	0.16
		Wet Pomace	0.451	0.027	0.478	2.05
		Dry Pomace	1.465	0.113	1.578	6.77
84-0238[7]	266105	Fruit	0.010	0.040	0.050	1.00
		Cider	0.019	<0.010	0.019	0.38
		Wet Pomace	0.083	0.009	0.092	1.84
		Dry Pomace	0.274	0.032	0.306	6.12

1 Data extracted from Table 10, Section D, MRID/Acces.# 266105.
2 Average of 2-3 replicates of each sample.
3 Corrected for average overall recovery of 90% for RH-3866 and 70% for RH-9090.
4 Free and bound.
5 Calculated by this reviewer.
6 Analyses via TR 310-84-27 with Addendum TR 31H-86-15.
7 Analyses via TR 310-84-27.

A second apple processing study is also discussed in the RCB review (R. Loranger) of 6/16/87, PP#7G3479/FAP#7H5523. The details and raw data of that processing study have not been submitted, but the results are included in the Summary and Discussion Volume [MRID/Acces.# 266105] of PP#7F3476/FAP#7H5524.

Therein we are told that samples of treated apples from crop field trial 84-0238 (see Table 17 for details of the crop field trial; partial raw data for 84-0238, limited to apples per se,

were submitted in MRID/Acces.# 073600) were processed into cider, wet pomace, and dry pomace.

It is stated that fruit and processed fractions were analyzed by the RH-3866 total residue method (no mention of its Addendum), and presumably residue values were corrected for recovery (the overall average which is used on all data of these petitions is 90% for RH-3866 and 70% for RH-9090). Sensitivity is indicated to be 0.01 ppm for both RH-3866 and RH-9090.

The results from this processing study are also summarized in Table 18.

As can be seen, there is a close similarity in the concentration factors from both processing studies. No concentration of residues is shown to occur in cider; concentration in wet apple pomace was 2X and in dry apple pomace, 6-7X.

No information is available on the length of storage prior to analysis of apple processed fractions from field trial 84-0238. The partial raw data available (on apples per se from that field trial; MRID/Acces.# 073600) indicate storage of the fruit for 3^+ months prior to analysis.

We would like to have all the raw data from crop field trial 84-0238, including all information on the processing of apples (with date of processing), if the petitioner has the data available. If not, we can still consider the study as supplemental, and base our conclusions primarily on apple processing data in TR 31H-86-09 [MRID/Acces.# 266031], which is from crop field trial 85-0542, and for which complete residue data are available.

Based on the raw data in TR 31H-86-09, fruit and processed fractions from apple field trial 85-0542 were not analyzed for 9-10 months following harvest. During the interim they were presumably maintained in frozen storage.

No date for the processing of apples from this field trial is provided. Thus, we do not know if processed fractions were subjected to frozen storage prior to analysis. The petitioner will need to clarify this point (i.e., provide the date when processing was performed).

If processed apple fractions were subjected to frozen storage for longer than a two-week period prior to analysis, then storage stability validation data will be needed for RH-3866 and RH-9090 (free and bound) residues in apple processing fractions.

Storage stability data are also needed for RH-9090 residues in apples.

(Also see discussion in the STORAGE STABILITY section of this review.)

Subject to the storage stability validation of RH-9090 (free and bound) residues in apples per se and (if apple processing fractions were frozen-stored longer than two weeks prior to analysis) RH-3866 and RH-9090 (free and bound) residues in apple processing fractions, we tentatively conclude that adequate studies have been conducted and submitted for the processing of apples. Method trials on apples (or grapes) must also be successfully completed.

Tentatively, we consider a feed additive tolerance proposal based on < 10X concentration factor in apple pomace to be appropriate.

As discussed in the PROPOSED TOLERANCES section, the petitioner needs to submit a revised Section F. Among the revisions needed, the tolerance should be proposed in terms of "apple pomace" (i.e., delete reference to "wet" and "dry"); tentatively, it appears 5 ppm would be the appropriate tolerance level.

2. GRAPES

a. Crop Field Trials

- Summary. Supporting residue data are available from 14 field trials with grapes.

  Tentatively, we conclude these field trial data support the proposed tolerance of 1.0 ppm for combined residues of RH-3866 and RH-9090 (free and bound) in or on grapes.

  A final determination awaits the submission/evaluation of storage stability data for RH-9090 (free and bound) in grapes and the completion of successful method trials.

* * * * *

Discussion. The data from the supporting crop field trials for grapes are located in MRID/Acces.# 266032, PP#7G3479/FAP#7H5523, and MRID/Acces.# 266112, 266113, 266114, 266116, and 266117, PP#7F3476/FAP#7H5524.

The relevant information is summarized in Table 19.

As can be seen, data from 14 crop field trials with grapes are listed. These represent crop years 1985 and 1986. All field trials were conducted using the Rally™ 40W formulation.

Field trial sites were located in CA (9), NY (1), and PA (4). These represent the major growing regions in the USA, and are considered to provide adequate geographical representation for grapes.

The field trials involved 10 varieties of grapes and 5 soil types. Applications were by ground rig or hand-held equipment. Highest residues were reported in the grape field trials in which hand sprayers were used to apply the pesticide. As the petitioner explains, use of hand sprayers "can result in direct deposition of a larger percentage of the spray formulation directly onto the fruit causing higher residues than mist blower application."

Grape field trials reflect 1-8 applications and an application rate of 0.073-0.15 lb ai/A (versus 0.125 lb ai/A proposed). The total dosage ranged from 0.125-0.80 lb ai/A/season. (Proposed use permits 0.6 lb ai/A/season.)

The proposed PHI is 14 days. For those trials which provided residue decline data, the 14-day PHI value is the one reported in Table 19.

Grapes were analyzed by the RH-3866 Total Residue analytical method (TR 310-84-27), with Addendum (31H-86-15) incorporated.

The Total Residue method measures RH-3866 parent compound and "total RH-9090" residues. Total RH-9090 residues consist of RH-9090, RH-9090 released from conjugates, and RH-9089 (which has been reduced to RH-9090).

The proposed tolerance on grapes is 1.0 ppm for combined residues of the parent (RH-3866) and RH-9090 (free and bound). Tentatively, we conclude these field trial data support the proposed tolerance, and that 1.0 ppm is an appropriate level.

Before we can finalize our conclusion about the adequacy of these field trial data to support the proposed tolerance on grapes, storage stability data for RH-9090 (free and bound) residues in grapes must be submitted and method trials must be successfully completed.

Based on the raw data, grape samples were stored 1 week to 10 months prior to residue analysis.

See discussion in the STORAGE STABILITY section of this review.

Table 19

Summary of Grape Field Trial Data[a,b]

Trial	MRID/Acces.	Site	Variety	Soil Type	gpa[1]	Storage[2]
85-0323[3,4]	266032	CA	Thompson	loam	100	10 mos
85-0360[4]	266116	PA	Concord	silty loam	100	9 mos
85-0372[5]	266112	CA	Savignon	clay loam	100	9 mos
85-0373[5]	266112	CA	Riesling	sandy loam	100	9-10 mos
85-0374	266112	CA	Muscatcan	clay loam	100	9+ mos
85-0419[3,5]	266032	CA	Pinot Noir	silty clay	100	9-10 mos
85-0637[4,5]	266116	NY	Rosette	loam	200	9 mos
86-0175	266113	CA	Flame	loam	---	1 week
86-0195	266113	CA	Thompson	----	---	1-2 wks
86-0231	266114	CA	Muscat	clay loam	100	7 wks
86-0233	266114	CA	Riesling	clay loam	100	7 wks
86-0262[4,5]	266117	PA	Niagara	silty loam	10	3-6 wks
86-0263[4,5]	266117	PA	Concord	silty loam	10	3-5 wks
86-0264[4,5]	266117	PA	Catawba	silty loam	10	4-6 wks

	Dosage (lbs ai/A)[6]					MAXIMUM Residue (ppm)[7]		
Trial	#Appl.	rate	Total	#Reps	PHI	RH-3866	RH-9090[8]	Total
85-0323[3,4]	5	0.10	0.50	3	14	0.210	0.061	0.271
85-0360[4]	8	0.10	0.80	2	14	1.370	0.172	1.542[9]
85-0372[5]	5	0.10	0.50	2	14	0.385	0.034	0.419
85-0373[5]	5	0.10	0.50	3	14	0.665	0.124	0.789
85-0374	5	0.10	0.50	2	13	0.375	0.041[10]	0.416
85-0419[3,5]	5	0.10	0.50	1	14	0.525	0.087	0.612
85-0637[4,5]	5	0.15	0.75	2	14	0.335	0.079	0.414
86-0175	4	0.10	0.40	3	14	0.105	0.032	0.137
86-0195	5	0.073	0.365	2	14	0.258	0.013	0.271
86-0231	4	0.075	0.30	3	14	0.101	0.084	0.185
86-0233	4	0.075	0.30	3	14	0.194	0.052	0.246
86-0262[4,5]	1	0.125	0.125	2	14	0.610	0.034	0.644
86-0263[4,5]	1	0.125	0.125	2	14	0.367	<0.010	0.367
86-0264[4,5]	1	0.125	0.125	2	14	0.591	0.053	0.644

a Summary data compiled by this reviewer.
b Residue analyses via TR 310-84-27 with Addendum TR 31H-86-15.
1 Spray volume per acre.
2 Length of frozen storage prior to analysis.
3 Grapes used in processing studies.
4 Residue decline studies in grapes.
5 Applications by hand-sprayer.
6 Rally™ 40W formulation used in all trials.
7 Corrected for overall average recovery of 70% for RH-3866 and 70% for RH-9090.
8 Free and Conjugated.
9 Replicate contained 0.786 ppm RH-3866 + 0.166 RH-9090 = total residue of 0.952 ppm; average total, both reps = 1.247 ppm.
10 The average of the two replicates; maximum not available.

b. Processed Food and Feed

- Summary. We withhold judgment on the adequacy of these grape processing studies until storage stability data for residues of RH-9090 (free and bound) in grapes are submitted and method trials have been successfully completed.

  Also, the dates on which processing of grapes occurred [TR 31H-86-11; MRID/Acces.# 266032] needs to be provided.

  If grape processing fractions were frozen-stored for longer than two weeks prior to analysis, storage stability data for RH-3866 and RH-9090 (free and bound) residues in grape processing fractions will also be needed.

  Tentatively, we consider food and feed additive tolerance proposals based on < 10X concentration in raisins and grape pomace and ≤ 25X concentration in raisin waste to be appropriate.

  A revised Section F for "grape pomace" is needed. (See PROPOSED TOLERANCES section of this review.) Tentatively, it appears 10 ppm would be the appropriate tolerance level.

* * * * *

Discussion. Two grape processing studies were conducted for PP#7G3479/FAP#7H5523, and the data submitted in TR 31H-86-11 [MRID/Acces.# 266032]. Those data were discussed in the RCB (R. Loranger) review of 6/16/87, aforecited petition, the details of which are incorporated herein by reference. No additional grape processing data were submitted with the permanent petition (PP#7F3476/FAP#7H5524), under review here.

To summarize, samples of treated grapes from crop field trials 85-0323 and 85-0419 (see Table 19 for details of the field trials) were processed at the California State University, Fresno, by conventional grape processing techniques to yield juice, pomaces, wine, stems, and (for 85-0323) raisins.

Fruit and processed fractions were analyzed by the RH-3866 total residue analytical method [TR 310-84-27, MRID/Acces.# 073600, 143769], as amended by TR 31H-86-15 [MRID/Acces.# 266030, 165036].

Residues were corrected for an overall average recovery of 90% for RH-3866 and 70% for RH-9090. Sensitivity is 0.01 ppm for both RH-3866 and RH-9090 residues in all processed fractions.

The results are summarized in Table 20.

Table 20

Summary of Results† of Grape Processing Studies[1]

Trial	MRID/Acces.	Sample	AVERAGE Residue (ppm)[2,3] RH-3866	RH-9090[4]	Total	Conc. Factor[5]
85-0419	266032	Fruit	0.525	0.073	0.598	1.00
		Juice	0.061	0.011	0.072	0.12
		Wet Pomace	0.666	0.141	0.807	1.35
		Dry Pomace	1.160	0.101	1.261	2.11
		Wine	0.072	0.060	0.132	0.22
		Stem	1.250	0.273	1.523	2.55
85-0323	266032	Fruit	0.129	0.042	0.171	1.00
		Juice	0.043	0.016	0.059	0.35
		Wet Pomace	0.073	0.018	0.091	0.53
		Dry Pomace	0.740	0.257	0.997	5.83
		Wine	0.039	0.022	0.061	0.36
		Filtered Wine	0.042	<0.010	0.042	0.25
		Wine Lees	0.219	0.016	0.235	1.37
		Stem	<0.010	<0.010	<0.010	--
		A+B Raisins	0.776	0.164	0.940	5.50
		C Raisin	0.820	0.250	1.07	6.26
		Midget Raisin	0.668	0.244	0.932	5.45
		Raisin Waste	3.43	0.797	4.23	24.7

† Residues analyses via TR 310-84-27 with Addendum TR 31H-86-15.
1 Data extracted from Table 11, Section D, MRID/Acces.# 266105.
2 Average of 1-3 replicates per sample.
3 Corrected for overall average recovery of 90% for RH-3866 and 70% for RH-9090.
4 Free and bound.
5 Calculated by this reviewer.

As can be seen, no concentration of residues occurred in juice or wine. Concentration factors of 6-7X for raisins, 25X for raisin waste, and up to 6X for grape pomace (wet and dry) were reported.

Based on the raw data, the grapes from crop field trials 85-0323 and 85-0419 were not analyzed for 9-10 months following harvest. During the interim they were presumably maintained in frozen storage.

No dates for the processing of grapes from these field trials are provided. Thus, we do not know if processed fractions were subjected to frozen storage prior to analysis. The petitioner will need to clarify this point (i.e., provide the dates when processing was performed).

If processed grape fractions were subjected to frozen storage for longer than a two-week period prior to analysis, then storage stability validation data will be needed for RH-3866 and RH-9090 (free and bound) residues in grape processing fractions.

Storage stability data are also needed for RH-9090 residues in grapes.

(Also see discussion in the STORAGE STABILITY section of this review.)

Subject to the storage stability validation of RH-9090 (free and bound) residues in grapes per se and (if grape processing fractions were frozen-stored longer than two weeks prior to analysis) RH-3866 and RH-9090 (free and bound) residues in grape processing fractions, we tentatively conclude that adequate studies have been conducted and submitted for the processing of grapes. Method trials on grapes (or apples) must also be successfully completed.

Tentatively, we consider food and feed additive tolerance proposals based on < 10X concentration factor in grape pomace, < 10X concentration factor in raisins, and $\leq$ 25X concentration factor in raisin waste to be appropriate.

As discussed in the PROPOSED TOLERANCES section, the petitioner needs to submit a revised Section F. Among the revisions needed, the tolerance should be proposed in terms of "grape pomace" (i.e., delete reference to "wet" and "dry"); tentatively, it appears 10 ppm would be the appropriate tolerance level.

3. CATTLE

- Summary. Adequate feeding study data have been submitted for lactating dairy cattle (ruminant).

  At the dietary burden (4.5-5.5 ppm/day to cattle) associated with the proposed use on apples and grapes, appropriate tolerances will be 0.05 ppm for milk and the meat, fat, and meat by-products (except liver) of cattle, goats, hogs, horses, and sheep; and, 0.3 ppm for liver of cattle, goats, hogs, horses, and sheep.

  This conclusion is contingent upon successful method trials for the components of the regulable residue and adequate recovery/sensitivity at (or below) these suggested tolerance levels.

  A revised Section F proposing appropriate tolerances for the regulable residue will need to be submitted.

* * * * *

Discussion. No new dairy cattle feeding study for myclobutanil (or its metabolites) was submitted with this present petition.

A multilevel dairy cattle feeding/metabolism study has been conducted, and the feeding study portion [TR 31H-86-13; MRID/Acces.# 266028] of it submitted and reviewed (R. Loranger memo of 6/16/87, the details of which are incorporated herein by reference) in conjunction with PP#7G3479/FAP#7H5523.

A summary of the experimental design of that feeding study is presented in the NATURE OF THE RESIDUE - LIVESTOCK - CATTLE section of this review. It will not be reiterated here.

Table 21 provides summary information on the level of ^{14}C residues occurring in milk and tissues as a result of that feeding study.

A second cow feeding/metabolism study exists. The feeding study portion [TR 810-84-12; MRID/Acces.# 00145682/072905] of it was submitted with PP#4G3149, and is discussed in our memo (R. Loranger) of 1/9/85 (the details of which are incorporated herein by reference) of that petition.

A summary of the experimental design of that feeding study is presented in the NATURE OF THE RESIDUE - LIVESTOCK - CATTLE section of this review. It will not be reiterated here.

Total residues (maximum value, in ppm, calculated as RH-3866) from that feeding (10 ppm of ^{14}C RH-3866, phenyl or triazole ring labeled for 5 days; 1 cow each) study were: milk, 0.043 ppm; liver, 0.42 ppm; kidney, 0.11 ppm; fat, 0.036 ppm; and, muscle, 0.014 ppm.

Table 21

Summary of ^{14}C Residues[1] in Dairy Cattle from 10-Day Feeding

Matrix	Actual Feeding Level (ppm)[2,3]			
	1.18 ppm	2.83 ppm	11.8 ppm	38.3 ppm
Milk	0.008	0.030	0.095	0.258
Liver	0.047	0.108	0.321	0.965
Kidney	<0.02[4]	<0.02	0.060	0.182
Fat	<0.02	<0.02	<0.02	0.073
Muscle	<0.02	<0.02	<0.02	0.098

1 Maximum values, in ppm, calculated as RH-3866.
2 Data extracted from Summary Table II, TR 31H-86-13.
3 A ^{14}C mixture of RH-3866/RH-9090/RH-9089 (32:58:10) was fed for 10 days.
4 The minimum quantifiable limit is 0.02 ppm in tissues and 0.005 ppm in milk.

Residue levels in milk and tissues of dairy cattle from the two studies (TR 31H-86-13 vs TR 810-84-12) are in general agreement.

The cattle feed items in this petition are listed in Table 22:

Table 22

Apple and Grape Feed Items in Cattle Diet

Feed Item	% of Cattle Diet[1]	
	Beef	Dairy
Apple pomace	50	25
Grape pomace	30	20
Raisin waste	10	10

1 Information from Table II, Pesticide Assessment Guidelines, Subdivision O - Residue Chemistry, 10/82.

and meat by-products of cattle, goats, hogs, horses, and sheep to cover the dietary burdens calculated above would be:

Milk.....	0.05 ppm
Meat, fat, and meat by-products (except liver) of cattle, goats, hogs, horses, and sheep.....	0.05 ppm
Liver of cattle, goats, hogs, horse, and sheep	0.3 ppm

These suggestions are contingent upon the method trials to be conducted by COB/BUD on the components of the regulable residue (see RESIDUE ANALYTICAL METHODS section of this review) being satisfactory, and demonstrating an adequate level of recovery/sensitivity at (or below) these levels.

A revised Section F proposing appropriate tolerances for the regulable residue will be needed.

NOTE: Generally, we prefer that feeding studies involve measurement of residues with the "cold" analytical method(s) that will be used for enforcement purposes. However, in the present cases for cattle and poultry (study details on the latter are in the MAGNITUDE OF THE RESIDUE - POULTRY section), total residues based on radioactivity are so low that we will accept these ^{14}C studies as the "conventional" feeding studies. If these studies were to be repeated using cold material, detectable residues are likely to be found only in beef liver and perhaps kidney at the dietary burdens anticipated from the grape and apple uses. The petitioner should be alerted, however, to the fact that future uses of myclobutanil which significantly increase the dietary burden for livestock (including poultry) may trigger the need for conventional feeding studies.

4. POULTRY

- Summary. Adequate feeding study data have been submitted for laying hens (poultry).

  At the dietary burden (0.75 ppm/day to poultry) associated with the proposed use on apples and grapes, appropriate tolerances will be 0.02 ppm for eggs and the meat, fat, and meat by-products of poultry.

  This conclusion is contingent upon successful method trials for the components of the regulable residue and adequate recovery/sensitivity at (or below) these suggested tolerance levels.

  A revised Section F proposing appropriate tolerances for the regulable residue will need to be submitted.

* * * * *

Discussion. No poultry feeding study for myclobutanil (or its metabolites) was submitted with this present petition.

However, a poultry feeding study [TR 31H-86-16; MRID/Acces.# 266029] was submitted and reviewed (R. Loranger memo of 6/16/87, the details of which are incorporated herein by reference) in conjunction with PP#7G3479/FAP#7H5523.

Based on that study, temporary tolerances are currently in effect for myclobutanil (and metabolites) residues in poultry tissues and eggs at 0.02 ppm.

To summarize, after a 1-week acclimation period, 5 groups of 10 white leghorn hens (individually caged) were force-fed (daily, for 28 consecutive days) a gelatin capsule containing a dose level of 0, 1, 3, 10 or 30 ppm of a ^{14}C RH-3866/RH-9090/RH-9089 mixture (45:45:10) on layer mash. (Actual dose levels, based on radioassay, were 1.05, 3.57, 10.2, and 28.3 ppm.) Hens also received 110 g of layer mash (as daily feed) and water ad libitum.

Two additional groups of 3 hens each (Groups 6 and 7) received oral doses of ^{14}C RH-3866 or ^{14}C RH-9090/RH9089 (82:18) at a 110 ppm level for 7 consecutive days to provide tissue, organ, and egg samples for metabolite identification and quantitation. The characterization of those residues is the subject of TR 31H-86-17 [MRID/Acces.# 266107], which is discussed in the NATURE OF THE RESIDUE - POULTRY section of this review.

^{14}C RH-3866 was uniformly phenyl ring labeled; ^{14}C RH-9090 and ^{14}C-9089 were labeled on carbons 3 and 5 of the triazole ring.

Egg and excreta samples were collected daily. After a <24-hour, 7- or 14-day withdrawal period from dosing, hens of Groups 1-5 were sacrificed, and samples of fat, liver, kidney, breast, thigh, gizzard, and heart were collected, frozen, pooled, and radioassayed (combustion or LSC).

Table 24 summarizes the total activity in poultry tissue, organ, and egg samples for all dosages.

Table 24

Summary of ^{14}C Residues[1,2] in Poultry from 28-Day Feeding[3]

Matrix	Actual Feeding Level (ppm)			
	1.05	3.57	10.2	28.3
Eggs	0.005	0.013	0.034	0.129
Fat	<0.005	<0.005	<0.015	<0.045
Liver	0.003	0.006	0.018	0.047
Kidney	<0.002	0.003	<0.006	0.021
Breast	<0.002	0.004	0.008	0.027
Thigh	<0.002	0.003	0.006	0.019

1 Maximum values, in ppm, calculated as RH-3866. Data extracted from Table 5 (eggs) and Table 8 (tissues), TR 31H-86-16.

2 The limit of quantitation varied from 0.002 to 0.045 ppm depending upon the substrate and feeding level.

3 Data in Table reflect sacrifice at < 24 hours after withdrawal of dose; NDR were found in any samples from the 7- or 14-day withdrawal intervals.

The poultry feed components in this petition are grape pomace and apple pomace. Each may comprise a maximum of 5% of the poultry diet.

Assuming the worst case, that both might be present in the same poultry diet, the dietary burden to poultry from ingesting tolerance level residues of these feed components is:

5% x 10.0 ppm proposed grape pomace tolerance = 0.50 ppm
5% x 5.0 ppm proposed apple pomace tolerance = 0.25 ppm

for a total dietary burden to poultry from these two feed items of 0.75 ppm.

Based on the feeding study data, summarized in Table 24 above, tolerance levels for poultry (meat, fat, and meat by-products) and eggs to cover the dietary burden from feeding of apple and grape pomaces could be established as low as 0.01 ppm.

We note the temporary tolerances for myclobutanil residues (established in conjunction with PP#7G3479/FAP#7H5523) on eggs and the meat, fat, and meat by-products of poultry are set at 0.02 ppm.

The petitioner requested the 0.02 ppm level (which represents 2X the limit of detection for parent compound (RH-3866) or RH-9090) in order to avoid a situation where a minor interferent might be misinterpreted as a violative residue.

Contingent upon the completion of satisfactory method trials by COB/BUD on the components of the regulable residue (see RESIDUE ANALYTICAL METHODS section of this review), and on such trials demonstrating adequate recoveries and sensitivities, we suggest 0.02 ppm as the appropriate level to establish tolerances for eggs and the meat, fat, and meat by-products of poultry.

A revised Section F reflecting appropriate tolerance proposals for the regulable residue will be needed.

I. TOLERANCE ASSESSMENT

- Summary. If/when the permanent tolerances of this present petition are favorably recommended for, a request for an updated TAS assessment will be initiated by this reviewer to the TAS Program Staff of RCB. Any TAS review which is then performed will issue as a separate memo, directed to the Product Manager (L. Rossi, PM 21, HFB/RD).

* * * * *

Discussion. A Tolerance Assessment System (TAS) analysis was performed on myclobutanil (Rally™) in conjunction with the establishment of temporary tolerances. See 9/10/87 review of C. Frick, PP#7G3479/FAP#7H5523.

If/when the permanent tolerances of this present petition are favorably recommended for, a request for an updated TAS assessment will be initiated by this reviewer to the TAS Program Staff of RCB.

Any such TAS review which is then performed will issue as a separate memo, directed to the Product Manager (L. Rossi, PM 21, HFB/RD).

No TAS analysis will be conducted as part of this present review document; TAS considerations are the purview of the TAS Program Staff of RCB.

J. INTERNATIONAL HARMONIZATION

- Summary. There are no Canadian or Mexican IRLs established for myclobutanil, and no Codex proposal for myclobutanil at Step 6 or above. The question of compatibility/ harmonization of the tolerance expression and/or residue level(s) thus does not arise in connection with the review of this petition.

* * * * *

Discussion. There are no Canadian or Mexican international residue limits (IRLs) established for myclobutanil; neither is there any Codex proposal for myclobutanil at Step 6 or above. (See International Residue Limit Status sheet, appended to this review as an Attachment.)

Since there are no established IRLs for myclobutanil, the question of compatibility/harmonization of the tolerance expression and/or residue level(s) does not arise in connection with the review of this petition.

K. OTHER CONSIDERATIONS

- Summary. No "Other Considerations" apply in the review of this petition.

* * * * *

Discussion. All the relevant issues have been addressed under specific topic headings in the body of this review. No "Other Considerations" apply in the review of this petition.

IV. BIBLIOGRAPHY

Technical Report No.	References Used	Accession/ MRID No.
N/A	Summary and Discussion: RH-3866 Residue Chemistry. Rohm and Haas Co. (PP#7F3476, Sec. D, Vol. 31, 10/31/86)	266105
N/A	Reasonable Grounds in Support of the Petition. Rohm and Haas Co. (PP#7F3476, Sec. G, Vol. 1, 10/31/86; and, Amendment of 11/25/87)	266075
	PROPOSED PERMANENT TOLERANCES	
N/A	PP#7F3476/FAP#7H5524, Sec. F, Vol. 1. Rohm and Haas Co., 10/31/86.	266075
	CHEMICAL IDENTITY	
N/A	PP#7F3476/FAP#7H5524, Sec. A, Vol. 1. Rohm and Haas Co., 10/31/86; and, Amendment of 12/24/86.	266075
N/A	Rally™ 60DF Fungicide (EPA Reg. No. 707-ERR), PP# 7F3476/FAP#7H5524, Submission of Revised CSF and Supplemental Product Chemistry Information, Rohm and Haas Co., 1/15/88.	404800-00
N/A	Rally™ 40W Fungicide (EPA Reg. No. 707-ERE), PP# 7F3476/FAP#7H5524, Submission of Revised CSF and Supplemental Product Chemistry Information, Rohm and Haas Co., 1/15/88.	404801-00
N/A	Rally™ 40W Fungicide (in 4 oz. Water-Soluble Pouches), EPA File Symbol 707-ERL, Revised CSF. Rohm and Haas Co., 1/15/88 submission.	None
N/A	Nova™ 40W Fungicide (in 5 oz. Water-Soluble Pouches), EPA File Symbol 707-EER, Revised CSF. Rohm and Haas Co., 1/18/88 submission.	None

Technical Report No.	References Used	Accession/ MRID No.
	DIRECTIONS FOR USE	
N/A	PP#7F3476/FAP#7H5524, Sec. B, Vol. 1. Rohm and Haas Co., as amended 11/87.	266075
N/A	Applications for Section 3 Registration, Rohm and Haas Co., 11/87.	None
	NATURE OF THE RESIDUE - APPLE AND GRAPE	
310-84-31	Nelson, S., and D. Streelman, The Metabolism of RH-3866 in Apples. Rohm and Haas Co., 12/18/84. (PP# 4G3149, Vol. 3, Sec. D1, Tab 4, 5/23/85)	073599
310-84-30	Nelson, S., Metabolism of ^{14}C-RH-3866 in Field-Treated Grapes. Rohm and Haas Co., 12/18/84. (PP# 4G3149, Vol. 3, Sec. D1, Tab 5, 5/23/85)	073599
	NATURE OF THE RESIDUE - COW AND CHICKEN	
31H-86-18	Jacobson, A., Characterization and Identification of Metabolites in Cows Fed a ^{14}C Mixture of RH-3866/RH-9090/RH-9089. Rohm and Haas Co., 10/17/86. (PP#7F3476, Sec. D, Vol. 32, 10/31/86)	266106
31H-86-19	Jacobson, A., Addendum to TR 310-84-12: Characterization of Metabolites in Urine and Milk from Cows fed ^{14}C RH-3866. Rohm and Haas Co., 10/17/86. (PP#7G3479, Sec. D, Vol. 2, 10/31/86)	266027
31H-86-17	Martin, J., Disposition and Metabolism of RH-3866 and Metabolites in Laying Hens. Rohm and Haas Co., 10/15/86. (PP#7F3476, Sec. D, Vol. 33, 10/31/86)	266107

Technical Report No.	References Used	Accession/ MRID No.
	RESIDUE ANALYTICAL METHODS	
310-84-13	Brackett, C., Analytical Method for the Measure of RH-3866 Residues in Various Crops, Soil, Meat, Milk and Eggs and RH-9090 Residues in Various Crops and Soil. Rohm and Haas Co., 6/18/84. (PP#4G3149, Sec. D1, Vol. 11, Tab 9, 9/18/84; non-CBI copy in PP#7F3476, Amendment of 2/17/87)	145682/ 072905
310-86-09	Brackett, C., et al., Addendum to TR 310-84-13, Analytical Method for RH-3866 and RH-9090. Rohm and Haas Co., 2/12/86. (PP#7G3479, Sec. D, Vol. 5, 10/31/86; non-CBI copy in PP#7F3476, Amendment of 2/17/87)	165036/ 266030
31S-87-09	Martin, J., RH-9090 Residue Analytical Method and Validation Data for Meat, Milk, and Eggs. Rohm and Haas Co., 10/30/87. (PP#7F3476, Amendment of 11/13/87; non-CBI copy in Amendment of 12/30/87)	404092-04
310-84-27	Brackett, C., et al., RH-3866 Total Residue Analytical Method for Apple and Grape. Rohm and Haas, 11/16/84. (PP#4G3149, Vol. 4, Sec. D1, Tab 10, 5/23/85; non-CBI copy in PP#7F3476, Amendment of 2/17/87)	143769/ 073600
31H-86-15	Stavinski, S., et al., Addendum to RH-3866 Total Residue Analytical Method for Grape and Apple (TR 310-84-27). Rohm and Haas Co., 7/8/86. (PP#7G3479, Sec. D, Vol. 5, 10/31/86; non-CBI copy in PP#7F3476, Amendment of 2/17/87)	165036/ 266030
31S-87-46	Deakyne, R., et al., Addendum 2 to RH-3866 Total Residue Analytical Method for Grape and Apple (TR 310-84-27). Rohm and Haas Co., 8/3/87. (PP#7F3476, Amendment of 11/13/87; non-CBI copy in Amendment of 12/30/87; slightly revised by Amendment of 2/1/88)	404092-02 and (slightly revised in 404980-01)

Technical Report No.	References Used	Accession/ MRID No.
31S-87-37	Stavinski, S., Reply to the EPA's Request for RH-9090 Glycoside Recovery Data. Supplemental Data for the RH-3866 Total Residue Method (TR 310-84-27). Rohm and Haas Co., 3/87. (PP#7F3476, Amendment of 11/13/87; non-CBI copy in Amendment of 12/30/87)	404092-03
31S-87-02	Mamo, N., RH-0294 Residue Analytical Method in Milk. Rohm and Haas Co., 3/30/87. (PP#7F3476, Amendment of 10/7/87; non-CBI copy in Amendment of 1/18/88)	403662-01 and 404813-01
31A-87-58	Deakyne, R., et al., FDA Multiresidue Screen Results for RH-3866 and RH-9090. Rohm and Haas Co., 10/87. (PP#7F3476, Amendment of 11/13/87; non-CBI copy in Amendment of 12/30/87)	404092-05
	STORAGE STABILITY	
31H-86-04	Deakyne, R., et al., RH-3866 Storage Stability Study in Apples. Rohm and Haas Co., 6/24/86. (PP#7F3476, Sec. D, Vol. 35, 10/31/86)	266109
31H-86-06	Deakyne, R., et al., RH-3866 Storage Stability Study in Grapes. Rohm and Haas Co., 6/30/86. (PP#7F3476, Sec. D, Vol. 41, 10/31/86)	266115
	MAGNITUDE OF THE RESIDUE - APPLES	
-	Analytical Reports for Residues due to RH-3866 in Apples. Rohm and Haas Co., 1984. (PP#4G3149, Sec. D1, Vol. 4, Tab 12, 5/23/85)	073600
31A-86-44	Brackett, C., et al., Analytical Reports for Residues Due to RH-3866 in Apples. Rohm and Haas, 7/17/86. (PP#7F3476, Sec. D, Vol. 34, 10/31/86)	266108

Technical Report No.	References Used	Accession/ MRID No.
31A-86-51	Brackett, C., et al., RH-3866 Residue Decline Studies in Apples. Rohm and Haas Co., 8/7/86. (PP#7F3476, Sec. D, Vol. 36, 10/31/86)	266110
31A-86-70	Deakyne, R., et al., RH-3866 Residue Decline Studies in Apples. Rohm and Haas Co., 10/17/86. (PP#7F3476, Sec. D, Vol. 37, 10/31/86)	266111
31H-86-09	Deakyne, R., et al., RH-3866 Apple Processed Fraction Study. Rohm and Haas Co., 8/14/86. (PP#7G3479, Sec. D, Vol. 6, 10/31/86)	266031
	MAGNITUDE OF THE RESIDUE - GRAPES	
31A-86-42	Brackett, C., et al., Analytical Reports for Residues Due to RH-3866 in Grapes. Rohm and Haas Co., 7/28/86. (PP#7F3476, Sec. D, Vol. 38, 10/31/86)	266112
31A-86-56	Brackett, C., et al., Analytical Reports (for Residues) Due to RH-3866 in Grapes. Rohm and Haas Co., 8/19/86. (PP#7F3476, Sec. D, Vol. 39, 10/31/86)	266113
31A-86-63	Deakyne, R., et al., Analytical Reports for Residues Due to RH-3866 in California Grapes. Rohm and Haas Co., 9/29/86. (PP#7F3476, Sec. D, Vol. 40, 10/31/86)	266114
31A-86-50	Brackett, C., et al., RH-3866 Residue Decline Study in Grapes. Rohm and Haas Co., 8/5/86. (PP#7F3476, Sec. D, Vol. 42, 10/31/86)	266116
31A-86-65	Deakyne, R., et al., RH-3866 Residue Decline Studies in Grapes. Rohm and Haas Co., 10/13/86. (PP#7F3476, Sec. D, Vol. 43, 10/31/86)	266117
31H-86-11	Brackett, C., et al., RH-3866 Grape Processed Fraction Study. Rohm and Haas Co., 8/20/86. (PP#7G3479, Sec. D, Vol. 7, 10/31/86)	266032

Technical Report No.	References Used	Accession/ MRID No.
	FEEDING STUDIES	
31H-86-13	Jacobson, A., ^{14}C RH-3866 Feeding Study in Cows. Rohm and Haas Co., 9/16/86. (PP# 7G3479, Sec. D, Vol. 3, 10/31/86)	266028
310-84-12	Butterworth, D., RH-3866 ^{14}C Cow Metabolism Study - Residue Levels in Milk, Tissue and Excreta and Metabolites in Excreta. Rohm and Haas Co., 6/8/84. (PP#4G3149, Sec. D1, Vol. 11, Tab 8, 9/18/84)	145682/ 072905
31H-86-16	Jacobson, A., ^{14}C RH-3866 Feeding Study in Poultry. Rohm and Haas Co., 9/30/86. (PP#7G3479, Sec. D, Vol. 4, 10/31/86)	266029

V. CONFIDENTIAL APPENDIX

(To RCB Residue Chemistry Review of PP#7F3476/FAP#7H5524)

CONFIDENTIAL STATEMENTS OF FORMULA FOR MYCLOBUTANIL END-USE PRODUCTS PROPOSED FOR USE ON APPLES AND GRAPES.

1. Rally™ 40W (EPA Reg. No. 707-ERE) ..... 2 pages
   (Basic and Alternate Formulations)
2. Rally™ 40W in Water-Soluble Pouches ..... 4 pages
   (EPA Reg. No. 707--ERL)
   (Basic and Alternate Formulations)
3. Rally™ 60DF (EPA Reg. No. 707-ERR) ..... 1 page
   (Basic Formulation)
4. Nova™ 40W in Water-Soluble Pouches ..... 4 pages
   (EPA Reg. No. 707-EER)
   (Basic and Alternate Formulations)

Myclobutanil residue chemistry review

Page _____ is not included in this copy.

Pages 95 through 105 are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

___ A draft product label

X The product confidential statement of formula

___ Information about a pending registration action

___ FIFRA registration data

___ The document is a duplicate of page(s) _____

___ The document is not responsive to the request

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

Attachment 3

3/26

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL myclobutanil

Fred Ives 3/26/87

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. 7F3476/7H5524

RCB Reviewer Nelson

Residue: parent* and metabolites containing both the chlorophenoxy and triazole rings.

Crop(s)	Limit (mg/kg)
apples	0.5
" , wet pomace	1.0
" , dry "	5.0
grapes	1.0
" , wet pomace	2.0
" dry "	10.0
raisins	10.0
" waste	25.0
eggs; meat; meat b-p (except liver)	0.04
milk	0.1
liver (c, g, h, h, s)	0.5

CANADIAN LIMITS:

/√/ No Canadian limit

Residue: _____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

/√/ No Mexican limit

Residue: _____

Crop(s)	Limit (mg/kg)

NOTES:

* α-butyl-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile

"NEW" Chemical

Attachment

Attachment 4

Page 1 of 4

Guidance for Orchard Spray Application

As a guidance to any future orchard spray applications, the petitioner should incorporate one or more of the following concepts in their submissions as the means of instructing the users on how to vary the quantity of a.i./acre that is needed for different tree sizes.

Procedure 1. For High Volume (HV) Spray Applications to Orchards

Determine volume/A to spray orchard to run-off. Use so much active ingredient/ 100 gal and multiply this number by the volume/A to spray your orchard to runoff to determine the amount of active ingredient/A.

For Example:

Step 1: Use rate (determined by petitioner).....0.5 lb act/100 gal.

Step 2: To spray one acre of your orchard to run-off...300 gal/A.

Step 3: The amount of lb a.i./acre in 300 gal of water is 1.5 lb (0.5 lb act/100 gal x 300 gal/A).

Procedure 2. Estimation of Tree Row Volume (TRV) to Calculate the Gallons/A Needed to Spray to Run-off

Step 1: 43,560/between-row spacing (ft) = feet of row/acre.

Step 2: Feet of row/acre x tree height (ft) x cross-row limb spread (ft) = cu ft of TRV/acre.

Step 3: Select one of the following numbers that best indicate the canopy density of each separate orchard or block:

0.70 gal/1,000 cu ft: Trees extremely open, light visible through entire tree, less than 15 scaffold limbs/tree or young tree.

0.75 gal/1,000 cu ft: Trees very open, 18 - 21 scaffold limbs/tree, light penetration throughout tree, healthy spurs within tree canopy.

0.80 gal/1,000 cu ft:	Trees well pruned, adequate light in trees for healthy spurs throughout trunk and scaffold limbs, many holes in foliage where light can be seen through tree.
0.85 gal/1,000 cu ft:	Trees moderately well pruned, reasonable spur population within canopy, tree thick enough that light cannot be seen through bottom two-thirds of tree.
0.90 gal/1,000 cu ft:	Trees pruned minimally, spurs inside canopy are weak due to limited light, very few holes where light can be seen through the tree.
0.95 gal/1,000 cu ft:	Little or no pruning, spurs dead or very weak in canopy, very little light visible through tree.
1.00 gal/1,000 cu ft:	Tree totally unpruned, extremely thick, no light visible anywhere through tree canopy, trees more than 20 ft high.

Step 4: $$\frac{\text{cu ft of TRV/acre (from Step 2)} \times \text{density (from Step 3)}}{1{,}000}$$

= gal of dilute solution to be applied/A.

Step 5: Using the volume of spray to run-off calculated in Step 4 above, calculate the lb a.i./acre using the formula of Procedure 1 (Step 3).

For Example: An orchard has rows spaced 25 ft apart, tree height is 20 ft, and cross row limb spread is 17 ft. The tree density is 0.85.

Step 1: 43,560 ft^2/25 ft = 1,742.4 ft

Step 2: 1,724.4 ft x 20 ft x 17 ft = 592.416 cu ft

Step 3: Density has been given as 0.85

scaffold limbs/tree or young tree.

Step 4: (592.416 x 0.85)/1,000 = 503.5 gal/acre

Step 5: Using the volume of spray to run-off calculated in Step 4 above, calculate the lb a.i./acre using the formula of Procedure 1 (Step 3).

Procedure 3. Estimation of Gallons of Pesticide Spray Solution per acre to Spray to Run-off or LV Application at the Full Leaf Stage of Canopy Using the following Table

Approximate number of gallons of pesticide spray liquid needed per acre for coverage at the full leaf stage of canopy development in tree fruit orchards using high volume (HV) dilute sprays and low volume (LV) concentrate sprays applied with airblast sprayers

Tree height (ft) X Tree width (ft)[b]	Spray Type	Gallons Per Acre[a] distance between tree rows (ft)												
		16	18	20	22	24	26	28	30	32	34	36	38	40
80	HV	152	136											
	LV	20[c]	17[c]											
100	HV	191	169	152										
	LV	25	22[c]	20[c]										
150	HV	256	254	229	208	191								
	LV	37	33	29	27	25								
200	HV	...[d]	...	305	277	254	235	218						
	LV	...	...	39	36	33	30	28						
250	HV	...	...	...	346	317	293	272	254	238				
	LV	...	...	...	45	41	38	35	33	31				
300	HV	...	...	...	416	381	352	327	305	286	269	254	241	229
	LV	...	...	...	53	49	45	42	39	37	35	33	31	29
350	HV	...	...	...	...	445	411	381	356	334	314	296	281	267
	LV	...	...	...	...	57	53	49	46	43	40	38	36	34
400	HV	...	...	...	...	...	469	436	407	381	359	339	321	305
	LV	...	...	...	...	...	60	56	52	49	46	44	41	39
450	HV	...	...	...	...	...	...	490	457	429	404	381	361	343
	LV	...	...	...	...	...	...	63	59	55	52	49	46	44
500	HV	...	...	...	...	...	...	...	508	476	448	424	401	381
	LV	...	...	...	...	...	...	...	65	61	58	54	52	49
550	HV	...	...	...	...	...	...	...	...	524	493	466	441	419
	LV	...	...	...	...	...	...	...	...	67	63	60	57	54
600	HV	...	...	...	...	...	...	...	...	...	538	508	481	457
	LV	...	...	...	...	...	...	...	...	...	69	65	62	59

[a] See text for full details of calculation. All values rounded to the nearest whole gallon. Based on standard dosage volumes of 0.7 gallon per 1,000 cu ft TRV for HV and 0.09 gallon for LV sprays. Trees which have a very dense foliar canopy may require slightly more spray volume than shown.

[b] Where small trees are interplanted with large trees in the same row, use only the large tree dimensions.

[c] LV applications of less than 25 gallons per acre are not generally recommended because of other factors affecting coverage.

[d] Data not given because the combination of this tree size on this planting density is unlikely.

Reference: Unrath, C. R., and T. B. Sutton. North Carolina State University, Raleigh, NC 27695. Bulletin AG 37.

The amount of a.i./acre can be calculated by using the volume of spray to run-off per acre found in the table above into the formula used in Procedure 1 (Step 3) above.

Procedure 4. For Low Volume (LV) and Ultra-low Volume (ULV) Applications to Orchards

Take the amount of a.i./A for orchard calculated from Procedure 1; the TRV estimated from Procedure 2; or the full leaf stage of canopy table from Procedure 3; and add to X gal of water/A for LV applications or Y gal of water and/or other solvent/A. X and/or Y is (are) determined by the petitioner to coincide with the proposed use. Less active ingredient/A is normally required for LV and ULV applications. The lower amount of active ingredient/A, if proposed, should be stated as a fraction of the high volume rate. Residue data must be submitted for all uses proposed on the label. Therefore, LV and/or ULV applications will not be allowed if residue data have been submitted for HV applications only.

DATE: February 5, 1988

SUBJECT: New Chemical Product Chemistry Review
RH-3866 (Technical)

REVIEWER: Maxie Jo Nelson, Ph.D., Chemist
Tolerance Petition Section I
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

PRODUCT MANAGER: Lois A. Rossi
P. M. #21
Herbicide-Fungicide Branch
Registration Division (TS-767C)

EPA Reg. No.:	707-ERN
Petition Nos.:	7F3476/7H5524
MRID/Acces. Nos.:	072895, 073596, 266075
RCB Nos.:	3110-3113

Common Name:	Myclobutanil (ANSI)
Trade Names:	Rally™, Systhane™, Nova™
Company Code Names:	RH-3866, RH-53,866
Applicant:	Rohm and Haas Company Philadelphia, PA
Type Product:	Fungicide

111

SUMMARY OF DEFICIENCIES FOR PRODUCT CHEMISTRY
(RH-3866 TECHNICAL)

The following additional information is required to satisfy data requirements of 40 CFR 158.120 for RH-3866 Technical:

1. §62-1 - Preliminary Analysis

   - Compositional analyses of 5 or more representative samples of RH-3866 Technical, with each sample taken from a different batch of the product.

   - Details on the verification of precision, accuracy, and limits of detection of the analytical method used to measure the composition of RH-3866 Technical.

2. §62-2 - Certification of Ingredient Limits

   - A revised Confidential Statement of Formula (EPA Form 8570-4, Rev. 2-85) for RH-3866 Technical with certification of ingredient limits based on analysis of representative samples from at least 5 different batches of technical product by analytical methodology validated for precision, accuracy, and limits of detection.

3. §62-3 - Analytical Methods to Verify Certified Limits

   - Details on the verification of precision, accuracy, and limits of detection of the analytical method used to measure the composition of RH-3866 Technical. (This information is stated to be in Appendix I of Report RWN-84-43A, but that Appendix is not with MRID/Acces. Nos. 072895 or 073596.)

4. §63-10 - Dissociation Constant

   - An explanation from the applicant as to why this information is claimed to be "not applicable". (If the technical product does not dissociate, a statement to that effect should be submitted.)

5. §63-12 - pH

   - An explanation from the applicant as to why this information is claimed to be "not applicable". (A pH determination is required of substances which can be diluted or dispersed with water.)

6. §63-13 - Stability

   - Information on "consideration and discussion of the sensitivity of the active ingredient to metal ions and metal" and "the sensitivity of the active ingredient to sunlight" (see §63-13 Reporting Requirements, Product Chemistry Guidelines).

7. §63-2 thru §63-13 - Physical and Chemical Characteristics

   - The analytical methods (where applicable) used to generate the data reported for the §63 series need to be submitted or adequately referenced. Information provided should include the precision, accuracy, and limits of detection.

DETAILED CONSIDERATIONS

BACKGROUND

Product Chemistry data requirements for the registration of a pesticide product are listed in 40 CFR 158.120.

Each of those data requirements is cross-referenced to the Guidelines Reference Number in the Pesticide Assessment Guidelines, Subdivision D, Product Chemistry (October 1982; EPA-540/9-82-018), which provides detailed information on the types and minimum amounts of data/information an applicant must submit in support of registration.

The kind of data required by 40 CFR 158.120 for a technical product, and the Product Chemistry Guidelines Reference Numbers, are summarized below:

40 CFR 158.120 Data Requirement	Guidelines Ref. No.
Product Identity and Composition	§61-(1-3)
Analysis and Certification of Product Ingredients	§62-(1-3)
Physical and Chemical Characteristics	§63-(2-13)

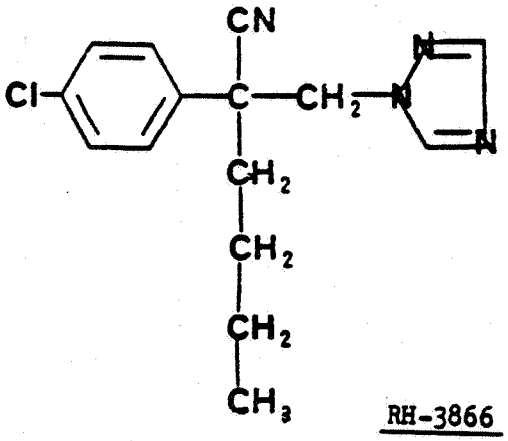
The data/information the applicant has submitted to fulfill these data requirements for registration of the technical grade of the active ingredient (RH-3866 Technical) are the subject of this review. Any existing data gaps are identified, and descriptions of the data/information needed to fill the data gaps are provided.

PRODUCT IDENTITY AND COMPOSITION

§61-1 - Product Identity and Disclosure of Ingredients

Myclobutanil is the ANSI-approved common name for a new fungicide for which registration is sought in the USA by Rohm and Haas Company, Philadelphia, PA.

The structure of myclobutanil is depicted below:



RH-3866

The chemical (CAS) name for myclobutanil is alpha-butyl-alpha-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile.

The trade names for myclobutanil are Rally™, Systhane™, and Nova™.

Rohm and Haas Company code numbers by which myclobutanil is known are RH-3866 and (earlier) RH-53,866.

Other identifying characteristics and codes are:

Empirical Formula:	$C_{15}H_{17}ClN_4$
Molecular Weight:	288.78
CAS Registry No.:	88671-89-0
Shaughnessy No.:	128857
Caswell No.:	723K

Rohm and Haas Company has applied for the registration of one technical product, RH-3866 Technical (EPA Reg. No. 707-ERN). Refer to Confidential Appendix D for disclosure of ingredients in this product.

RCB concludes no additional information is required to satisfy the data requirements of 40 CFR 158.120 - Product Identity and Disclosure of Ingredients (Guidelines Ref. No. §61-1) for RH-3866 Technical.

Information was obtained from MRID/Acces. No. 072895 (PP#4G3149, 9/18/84, Vol. 1, Sec. A) and (Caswell and Shaughnessy Nos.) from the C. Frick, RCB Tolerance Assessment System review of 9/10/87, PP#7G3479.

§61-2 - Description of Beginning Materials and Manufacturing Process

The data/information the registrant has submitted in response to this requirement are given and discussed in Confidential Appendix A.

RCB concludes (see Confidential Appendix A) no additional information is required to satisfy data requirements of 40 CFR 158.120 - Description of Beginning Materials and Manufacturing Process (Guidelines Ref. No. §61-2) for RH-3866 Technical.

§61-3 - Discussion of Formation of Impurities

The data/information the registrant has submitted in response to this requirement are given and discussed in Confidential Appendix B.

RCB concludes (see Confidential Appendix B) no additional information is required to satisfy data requirements of 40 CFR 158.120 - Discussion of Formation of Impurities (Guidelines Ref. No. §61-3) for RH-3866 Technical.

ANALYSIS AND CERTIFICATION OF PRODUCT INGREDIENTS

§62-1 - Preliminary Analysis

The data/information the registrant has submitted in response to this requirement are given and discussed in Confidential Appendix C.

RCB concludes (see Confidential Appendix C) the following additional information is required to satisfy data requirements of 40 CFR 158.120 - Preliminary Analysis (Guidelines Ref. No. §62-1) for RH-3866 Technical:

- Compositional analyses of 5 or more representative samples of RH-3866 Technical, with each sample taken from a different batch of the product.

- Details on the verification of precision, accuracy, and limits of detection of the analytical method (see Confidential Appendix E) used to measure the composition of RH-3866 Technical.

§62-2 - Certification of Ingredient Limits

The data/information the registrant has submitted in response to this requirement are given and discussed in Confidential Appendix D.

RCB concludes (see Confidential Appendix D) the following additional information is required to satisfy data requirements of 40 CFR 158.120 - Certification of Ingredient Limits (Guidelines Ref. No. §62-2) for RH-3866 Technical:

- A revised Confidential Statement of Formula (EPA Form 8570-4, Rev. 2-85) for RH-3866 Technical, with certification of ingredient limits based on analysis of representative samples from at least 5 different batches of technical product (ref. Confidential Appendix C) by analytical methodology validated for precision, accuracy, and limits of detection (ref. Confidential Appendix E).

§62-3 - Analytical Methods to Verify Certified Limits

The data/information the registrant has submitted in response to this requirement are given and discussed in Confidential Appendix E.

RCB concludes (see Confidential Appendix E) the following additional information is required to satisfy data requirements of 40 CFR 158.120 - Analytical Methods to Verify Certified Limits (Guidelines Ref. No. §62-3) for RH-3866 Technical:

- Details on the verification of precision, accuracy, and limits of detection of the analytical method used to measure the composition of RH-3866 Technical. (This information is stated to be in Appendix I of Report RWN-84-43A, but that Appendix is not with MRID/Acces. Nos. 072895 or 073596.)

PHYSICAL AND CHEMICAL CHARACTERISTICS

The physical and chemical properties test requirements for the technical grade of active ingredient are detailed in the Pesticides Assessment Guidelines, Subdivision D, Product Chemistry, §63-2 thru §63-13, and 40 CFR 158.120.

The applicant has submitted the following information to meet these data requirements for RH-3866 Technical:

§63-2 - Color:	Light yellow
§63-3 - Physical State:	Solid
§63-4 - Odor:	Odor of organosulfur compounds, moderately intense
§63-5 - Melting Point:	63-68°C
§63-6 - Boiling Point:	Not applicable, since the technical grade of the active ingredient is not a liquid at room temperature; 40 CFR 158.120(b)(7)
§63-7 - Density:	1.22 g/cc @ 23°C
§63-8 - Solubility:	For pure active ingredient in:

Water	142 ppm @ 25°C
Hexanes	<<1g/100g
Most Organics	>50g/100g

§63-9 - Vapor Pressure:	1.6×10^{-6} torr/25°C for pure active ingredient
§63-10 - Dissociation Constant:	Not applicable

§63-11 - Octanol/Water Partition Coefficient:	871/1 @ 25°C for pure active ingredient
§63-12 - pH:	Not applicable
§63-13 - Stability:	Stable at 25°C indefinitely; accelerated thermal stability studies (ARC) of RH-3866 showed no evidence of major instability below 300°C.

Information for §63-2 thru §63-13 was obtained from MRID/Acces. No. 072895 (PP#4G3149, 9/18/84, Vol. 1, Sec. A).

RCB concludes the following additional information is required to satisfy the data requirements of 40 CFR 158.120 (Guidelines Ref. Nos. §63-2 thru §63-13) on the Physical and Chemical Characteristics of the technical grade of RH-3866:

- §63-10 - Dissociation Constant - An explanation from the applicant as to why this information is claimed to be "not applicable". (If the technical product does not dissociate, a statement to that effect should be submitted.)

- §63-12 - pH - An explanation from the applicant as to why this information is claimed to be "not applicable". (A pH determination is required of substances which can be diluted or dispersed with water.)

- §63-13 - Stability - Information on "consideration and discussion of the sensitivity of the active ingredient to metal ions and metal" and "the sensitivity of the active ingredient to sunlight" (see §63-13 Reporting Requirements, Product Chemistry Guidelines).

- The analytical methods (where applicable) used to generate the data reported for the §63 series need to be submitted or adequately referenced. Information provided should include the precision, accuracy, and limits of detection.

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PRODUCT CHEMISTRY

Confidential Appendixes to RCB's review of the Product Chemistry data submitted in support of registration of RH-3866 Technical.

Confidential Appendixes

APPENDIX A: 7 pages

APPENDIX B: 4 pages

APPENDIX C: 5 pages

APPENDIX D: 3 pages

APPENDIX E: 5 pages

Myclobutanil residue chemistry review

Page _____ is not included in this copy.

Pages 122 through 128 are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

X Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

___ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

___ FIFRA registration data

___ The document is a duplicate of page(s) _____

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The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.

Myclobutanil residue chemistry review

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Pages 129 through 132 are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

X Identity of product impurities

X Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

___ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

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___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

X Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

___ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

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___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

___ A draft product label

X The product confidential statement of formula

___ Information about a pending registration action

___ FIFRA registration data

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The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

X Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

___ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

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