PP#2F4053

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

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

JAN 10 1997

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: Cyromazine. Revised Label for Trigard® 75W Insecticide. Spray Volume Changes Proposed For Crop Groups Leafy Vegetables (except Brassica) and Cucurbit Vegetables, and RACs Chinese Mustard, Pepper, and Tomato. No MRID's. CBTS#17600. DP Barcode# D230105. Chemical No. 121301. Case No. 003141.

From: Jerry B. Stokes, Chemist
Chemistry Branch I/Tolerance Petition Team 2
Health Effects Division (7509C)

Jerry B. Stokes

Through: Elizabeth Haeberer, Acting Chief
Chemistry Branch I/Tolerance Support
Health Effects Division (7509C)

Elizabeth T. Haeberer

To: Debbie McCall, Acting Section Head
Risk Characterization and Analysis Branch
Health Effects Division (7509C)

CIBA-GEIGY Corporation, Agricultural Division has submitted a revised label for the formulation Trigard® 75W Insecticide in regard to spray volumes of the carrier. The registrant proposes the phrase for ground applications, "minimum of 50 gallons of water" be replaced with "sufficient carrier to achieve adequate coverage". Tolerances for the combined residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), and its metabolite, melamine (1,3,5-triazine-2,4,6-triamine), all expressed as cyromazine are established under 40 CFR §180.414 in/on crop group leafy vegetables (except Brassica vegetables) at 10.0 ppm, the RAC Chinese mustard at 3.0 ppm, the RAC pepper at 4.0 ppm, the crop group cucurbit vegetables at 2.0 ppm, and the RAC tomato at 1.0 ppm. The petitioner also requests that aerial applications be allowed for the RAC tomato. The petitioner has not submitted additional residue data to support these requested changes.

RECOMMENDATION:

Although CBTS does not recommend for the requested "sufficient carrier to achieve adequate coveage", we can agree to a label minimum spray volume of 10 gal/A for ground applications for the RACs leaf lettuce, spinach, Chinese mustard, tomato, and the crop groups pepper and cucurbit vegetables. Also, according to CBTS comments (See memo of 04/02/93, R. Lascola), aerial application is allowed for the RAC tomato providing the minimum spray volume is 5 gallons of water per acre. The petitioner also submitted a Revised Section B for PP#6F3333 (tomato) dated 06/10/94 stating that the cyromazine formulation Trigard can be applied in a minimum of 5 gallons of water by air.

DETAILED CONSIDERATIONS:

DIRECTIONS FOR USE:

Request #1

The petitioner proposes that for ground applications of Trigard®75W Insecticide (a wettable powder containing 75% a.i. cyromazine), the specific volume of the spray carrier be undefined. The directions would read "sufficient carrier to achieve adequate coverage" in place of the phrase "a minimum of 50 gallons of water".

CBTS Comments:

The previously submitted residue data for the RACs leaf lettuce, spinach, Chinese mustard, tomato, and the crop groups pepper and cucurbit vegetables are summarized in the following table.

Application Rates	Spray Volume, gal/A	Maximum Residues, ppm		
		cyromazine	melamine	combined
Leaf lettuce, Data from MRID 419763-01 (PP#1F4016),				
Label directions: leafy vegetables (except Brassica), 5 applications/season at 0.125 lb a.i./A, 7-day PHI				
5 x 0.125 lb a.i./A (1X)	30	1.5, 2.4	1.4, 1.7	2.9, 4.1
"	20	3.3, 4.4	2.2, 2.7	5.5, 7.1
"	110	2.2, 1.1	0.4, 0.2	2.6, 1.3
"	16	3.8, 6.6	1.6, 1.5	5.4, 8.1
"	30	2.9, 2.6	2.1, 1.8	5.0, 4.4
"	20	1.7, 1.3	0.4, 0.5	2.1, 1.8
"	30	0.5, 0.7	0.3, 0.4	0.8, 1.1
"	5	7.6, 6.8	1.4, 1.6	9.0, 8.4
"	30	3.2, 3.3	1.2, 1.2	5.4, 5.5

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Application Rates	Spray Volume, gal/A	Maximum Residues, ppm		
		cyromazine	melamine	combined
Spinach, Data from MRID 419763-01 (PP#1F4016),				
Label directions: leafy vegetables (except Brassica), 5 applications/season at 0.125 lb a.i./A, 7-day PHI				
5 x 0.125 lb a.i./A (1X)	14.5	1.1, 1.1	0.5, 0.5	1.6, 1.6
"	20	1.8, 1.7	1.4, 1.3	3.2, 3.0
"	40	0.5, 0.4	0.2, 0.2	0.7, 0.6
"	110	1.9, 2.6	1.0, 1.0	2.9, 3.6
"	15.3	4.5, 7.6	1.2, 1.7	5.7, 9.3
"	110	4.2, 4.8	1.3, 1.2	5.5, 6.0
"	20	3.9, 6.9	2.4, 3.3	6.3,10.2
"	5	0.5, 1.9	0.2, 0.6	0.7, 2.5
"	30	3.7, 3.7	1.4, 1.4	5.1, 5.1
Chinese mustard, Data from MRID 411930-01 (PP#9E3781),				
Label directions: 7 applications/season at 0.125 lb a.i./A, 7-day PHI				
7 x 0.125 lb a.i./A (1X)	50	1.4, 1.6, 1.4, 1.7, 1.5, 1.4, 1.3, 1.3	0.2, 0.2, 0.3, 0.3, 0.2, 0.2, 0.2, 0.2	1.6, 1.8, 1.7, 2.0, 1.7, 1.5, 1.5, 1.5
Pepper, Data from Acc 260829 (PP#6F3342),				
Label directions: 6 applications/season at 0.125 lb a.i./A, 7-day PHI				
12 x 0.125 lb a.i./A (2X), bell	30	0.2, 0.1	0.2, 0.2	0.4, 0.3
", chili	30	0.2, 0.2	0.3, 0.2	0.4, 0.5
", bell	30	0.4, 0.4	0.4, 0.5	0.8, 0.9
", bell	36 (6) 60 (6)	0.3, 0.1	0.1, 0.1	0.4, 0.2
", tabasco	36.3	0.7, 1.0	0.5, 0.7	1.2, 1.7
", bell	55.6	<0.05, <0.05	0.06, 0.07	<0.11, <0.12
", chili	55.6	0.1, 0.1	0.1, 0.1	0.2, 0.2
", bell	60	0.1, 0.1	0.1, 0.1	0.2, 0.2
Cucurbit Vegetables, Data from MRID 421160-01 (PP#2F4053),				
Label directions: 6 applications/season at 0.125 lb a.i./A, 0-day PHI				
6 X 0.125 lb a.i./A (1X), cantaloupe	18	0.08, 0.06	0.12, <0.05	0.20, <0.11
", cantaloupe	30	<0.05, <0.05	<0.05, <0.05	<0.10, <0.10
", cantaloupe	24	0.09, 0.11	0.26, 0.29	0.35, 0.40
", cantaloupe	30	0.10, 0.16	0.17, 0.20	0.27, 0.36
", cantaloupe	15	0.18, 0.08	0.68, 0.52	0.86, 0.60

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Application Rates	Spray Volume, gal/A	Maximum Residues, ppm		
		cyromazine	melamine	combined
", cucumber	20	0.14, 0.19	1.6, 1.4	1.8, 1.6
", cucumber	33.8	0.19, 0.29	0.37, 0.47	0.56, 0.76
", cucumber	110	0.08, 0.06	0.13, 0.11	0.21, 0.17
", honeydew	30	<0.5, 0.06	0.05, 0.10	<0.10, 0.16
", honeydew	20	<0.05, 0.09	0.40, 0.88	<0.45, 0.97
", summer squash	30	0.07, 0.05	0.15, 0.15	0.22, 0.20
", zucchini	33.8	<0.05, <0.05	0.11, 0.08	<0.16, <0.13
", summer squash	110	<0.05, 0.08	0.05, 0.10	<0.10, 0.18
", summer squash	5	0.19, 0.09	0.25, 0.10	0.44, 0.19
", watermelon	20	0.10, 0.08	0.47, 0.81	0.57, 0.89
Tomato, Data from Acc 260565 (PP#6F3333),				
Label directions: 6 applications/season at 0.125 lb a.i./A, 0-day PHI				
11 X 0.5 lb a.i./A (7.3X)	110	0.12, 0.09	0.12, <0.05	0.24, <0.14
19 X 0.125 lb a.i./A (3.2X)	50	0.10, 0.07	0.05, 0.07	0.15, 0.14
13 X 0.125 lb a.i./A (2.2X)	50	0.07, 0.09	0.06, 0.09	0.13, 0.18
12 X 0.125 lb a.i./A (2X)	125	0.09, 0.07	<0.05, <0.05	<0.14, <0.12
12 X 0.125 lb a.i./A (2X)	20	0.19, 0.22	0.15, 0.21	0.34, 0.43
13 X 0.125 lb a.i./A (2.2X)	50	0.54, 0.44	0.10, 0.11	0.64, 0.55
11 X 0.125 lb a.i./A (1.8X)	110	0.14, 0.15	0.05, 0.06	0.19, 0.21
4 X 0.125 lb a.i./A (0.7X)	50	0.08, 0.12	<0.05, <0.05	<0.13, <0.17
4 X 0.125 lb a.i./A (0.7X)	10 (aerial)	0.07, <0.05	<0.05, <0.05	<0.12, <0.10
12 X 0.125 lb a.i./A (2X)	50	<0.05, <0.05	<0.05, <0.05	<0.10, <0.10

Leaf lettuce has only one application at a low spray volume of 5 gal/A. The measured cyromazine residues at the proposed label rate and PHI were very close to the 10 ppm tolerance. Spinach likewise only has one trial at a spray volume of 5 gal/A and at the label rate and PHI. In this case the combined cyromazine residues were much lower than those observed with leaf lettuce.

The only trials for Chinese mustard were all conducted at a spray volume of 50 gal/A. The combined cyromazine residues at the label rate and PHI were one-half to two-thirds the 3.0 ppm tolerance.

The residue data for the RAC pepper has spray volumes ranging from 30 to 60 gal/A. However, these trials used 12 applications, not 6 as the label recommends. The PHI was 7 days. With the small hot

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pepper, the combined cyromazine residues reached 1.7 ppm. The tolerance is 4 ppm.

Field trials for the crop group cucurbits vegetables used spray volumes ranging from 5 (only 1 trial) to 110 gal/A at the label rate and 0-day PHI. With a spray volume of 20 gal/A, combined cyromazine residues reached 1.8 ppm. However a 5 gal/A trial with summer squash showed a combined cyromazine residue of 0.44 ppm.

Trials for the RAC tomato used approximately twice (ranging from 11 to 19) the allowable 6 applications. The spray volumes for ground applications ranged from 20 to 50 gal/A. The PHI was 0 day. Combined cyromazine residues reached 0.64 ppm in one trial using a 50 gal/A volume. The 20 gal/A trial gave slightly less residues at 0.43 ppm. One aerial application used a spray volume of 10 gal/A, but the total application was only two-thirds the maximum allowable label rate.

CBTS Conclusion:

CBTS cannot estimate the total residue levels for the proposed use based on the previously submitted field trial residue data for the subject commodities. Although several ground applications used spray volumes as low as 5 gallons/A, the data are insufficient to adequately assess the requested change, which does not specify a minimum spray volume. **However**, based on the available field trial residue data, **CBTS can agree to a label minimum spray volume of 10 gal/A for ground applications** for the RACs leaf lettuce, spinach, Chinese mustard, tomato, and the crop groups pepper and cucurbit vegetables. The phrase "sufficient carrier to achieve adequate coveage" should be replaced by the minimum 10 gal/A spray volume.

Request #2

The petitioner has requested that aerial applications be allowed on the RAC tomato.

CBTS Comment/Conclusion:

According to CBTS comments (See memo of 04/02/93, R. Lascola), aerial application is allowed providing the minimum spray volume is 5 gallons of water per acre. The petitioner also submitted a Revised Section B for PP#6F3333 (tomato) dated 06/10/94 stating that the cyromazine formulation Trigard can be applied in a minimum of 5 gallons of water by air.

cc: PP#6F3333, PP#6F3342, PP#9E3791, PP#1F4016, PP#2F4053, J. Stokes, G. LaRocca/L. Deluise (PM Team 13), E. Haeberer, RF, Circu.
RDI: TPT2:12/11/96:RLoranger:01/02/97:EHaeberer:01/02/97
7509C:CBTS:JStokes/js:CM#2:Rm803:305-7561:01/07/97

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H-1405

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

JUL 16 1993

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: MULTIRESIDUE METHOD (MRM) VALIDATION DATA FOR **CYROMAZINE (TRIGARD® AND LARVADEX®)**
[CBTS #s 12176 and 12177]{DP Barcodes #sD192978 and D192981}

From: Francis D. Griffith, Jr., Chemist
Chemistry Branch I - Tolerance Support
Health Effects Division (H-7509C)

To: Harvey K. Hundley, Section Head
Analytical Chemistry Section
Analytical Chemistry Branch
Biological and Economic Analysis Division (H-7503W)

Thru: Robert S. Quick, Section Head
Tolerance Petition Section - I
Chemistry Branch I - Tolerance Support
Health Effects Division (H-7509C)

Attached is the study for multiresidue method (MRM) validation data for cyromazine and its melamine and 1-methylcyromazine metabolites.

Chemical Name: N-cyclopropyl-1,3,5-triazine-2,4,6-triamine

Type: Insecticide

MRID #: 422243-05

Title: "Determination of Cyromazine and Its Major Metabolites By U.S. Food and Drug Administration (FDA) Multiresidue Protocols I, II, III, and IV"

Protocols Validated: I through IV

Chemicals Tested: Cyromazine, and the melamine and 1-methylcyromazine metabolites

Sponsoring Company: Ciba-Geigy Corporation, Agricultural Division
P.O. Box 18300
Greensboro, North Carolina 27419

Performing Laboratory: Ciba-Geigy Corporation, Agricultural Division
Residue Chemistry Department
Greensboro, NC 27419

PP#s: 2F4053 and 1F4016

40 CFR Ref: 180.414(a), (b), (c), and (d)

Cyromazine and its metabolites were not recovered through Protocol IV using fluorescence detection nor through the charcoal clean-up column in Protocol II. There was no recovery through the florisil clean-up columns as described in Protocol I due to the lack of sensitivity of cyromazine and its metabolites on an EC detector. CBTS notes the chromatography of cyromazine and its metabolites is not good and it is difficult to ascertain whether or not they would be present in various sample extracts. Recovery data were presented through 5 GC columns using EC and N/P detectors. FPD detectors were not used as the compounds contained neither phosphorus nor sulfur.

When analyzed through Protocol III cyromazine, per se, was recovered when the 2% DEGS column was used. Melamine and 1-methylcyromazine were not recovered at 1 ppm from tomatoes and lettuce using the method for Protocol III.

These data will be forwarded to FDA for more thorough review and will be printed in a future edition of PAM -I, Appendix I. Unless you or FDA find a problem with the recovery data that has been presented CBTS concludes they are acceptable and no additional cyromazine and its metabolite MRM recovery data will be required.

cc(without attachments):R.F.,Circu.,Reviewer(FDG),PP#1F4016,PP#2F4053,
PM-18(Hutton),PAM-II Coeditor(MJBradley),CyromazineSub.File.

H-7509C:CBTS:Reviewer(FDG):CM#2:Rm804Q:305-5826:FDG:7/15/93:edit:fdg:7/16/93.

RDI:SecHd:RSQuick:7/15/93:BrSrSci:RALoranger:7/15/93.

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

JUL 16 1993

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: PP# 1F4016 - **CYROMAZINE (TRIGARD®)** ON LEAFY VEGETABLES (EXCEPT BRASSICA CROP GROUP.
PP# 2F4053 - **CYROMAZINE (TRIGARD®)** ON CUCURBIT VEGETABLES CROP GROUP.
(MRID # 422243-05) [CBTS #s 11324 and 11327] {DP Barcodes D187702 and D187707}

From: Francis D. Griffith, Jr., Chemist
Chemistry Branch I - Tolerance Support
Health Effects Division (H-7509C)

To: Phillip O. Hutton, PM-18
Insecticide-Rodenticide Branch
Registration Division (H-7505C)

and

Albin Kocialski
Registration Section, CCB
Health Effects Division (H-7509C)

Thru: Debra F. Edwards, Ph.D., Chief
Chemistry Branch I - Tolerance Support
Health Effects Division (H7509C)

BACKGROUND

Ciba-Geigy Corporation, Agricultural Division has submitted this amendment consisting of a cover letter dated January 12, 1993, signed by N.B. Carrol and a supplementary Section D (multiresidue data) in response to deficiencies outlined in our reviews for PP# 1F4016 dated December 9, 1992, and for PP# 2F4053 dated December 23, 1992, by F.D. Griffith, Jr. In the cover letter the petitioner claims these data were submitted as part of the petitions for cyromazine on carrots and tomatoes. The deficiencies are the same for both reviews and will be repeated below in the body of this review as they appeared in our reviews, followed by the petitioner's response, then CBTS comments. Our conclusion and recommendation follow.

EXECUTIVE SUMMARY OF RESIDUE CHEMISTRY DEFICIENCIES

- None -

CONCLUSION

CBTS Conclusion on **Residue Analytical Methods**

The petitioner has submitted the requested multiresidue method (MRM) recovery data for cyromazine and its metabolites using FDA protocols I through IV. The data are acceptable and have been forwarded to the EPA lab and to FDA for more review and publication in a future edition of the PAM I, Appendix I. The deficiencies are resolved. There are no remaining chemistry deficiencies for PP# 1F4016 and PP# 2F4053.

RECOMMENDATION

There being no remaining residue chemistry deficiencies for PP# 1F4016, TOX considerations permitting, CBTS recommends for the requested cyromazine and its principal metabolite melamine tolerance at 10 ppm on/in the leafy vegetables (except Brassica) crop group.

There being no remaining residue chemistry deficiencies for PP# 2F4053, TOX considerations permitting, CBTS recommends for the requested cyromazine and its principal metabolite melamine tolerance at 2 ppm on/in the cucurbit vegetables crop group.

DETAILED CONSIDERATIONS

RESIDUE ANALYTICAL METHODS

Deficiency (From PP#2F4053 and PP# 1F4016)

5b. CBTS reiterates that the petitioner needs to submit recovery data for cyromazine and melamine thru the FDA multiresidue methods. We suggest the petitioner provide these data using FDA Pesticide Analytical Manual Vol-I, Appendix II, Protocols A through E.

Petitioner's Response (MRID # 422243-05)

The petitioner submitted multiresidue method (MRM) recovery data for cyromazine and its melamine and 1-methylcyromazine metabolites in a study titled "Determination of Cyromazine and Its Major Metabolites By U.S. Food and Drug Administration (FDA) Multiresidue Protocols I, II, III, and IV" by R.K.Williams dated March 1, 1990 and coded ABR-88136.

CBTS Comments

While CBTS had suggested the MRM recovery data be generated using the newer MRM Protocols A through E, the petitioner informed us that he started generating these data in December 1987, using the guidance that at that time petitioners should use Protocols I through IV for MRM recovery data. For the chemicals tested for MRM recovery we agree

with the petitioner that the same recovery data would be generated whether Protocols I through IV, or Protocols A through E were used.

Cyromazine and its metabolites were not recovered through Protocol IV using fluorescence detection, nor through the charcoal clean-up column in Protocol II. There was no recovery through the florisil clean-up columns as described in Protocol I due to the lack of sensitivity of cyromazine and its metabolites on an EC detector. CBTS notes the chromatography of cyromazine and its metabolites is not good and it is difficult to ascertain whether or not they would be present in the various sample extracts. Recovery data were presented through 5 GC columns using EC and N/P detectors. FPD detectors were not used as the compounds contained neither phosphorous nor sulfur.

When analyzed through Protocol III cyromazine, per se, was recovered when the 2% DEGS column was used. Melamine and 1-methylcyromazine were not recovered at ppm from tomatoes and lettuce using the method for Protocol III.

The petitioner has presented requested MRM recovery data for cyromazine and its metabolites using FDA MRM protocols. Acceptable MRM recovery data were generated. These data will be forwarded to EPA's lab and to FDA for more thorough review and publication in a future edition of PAM-I, Appendix I. CBTS concludes that the deficiency 5b. in PP# 1F4016 and PP# 2F4053 is resolved. No additional cyromazine and its metabolites MRM recovery data are required.

There being no remaining residue chemistry deficiencies for PP# 1F4016 and PP#2F4053, TOX considerations permitting, CBTS recommends for the requested cyromazine and its principal metabolite melamine tolerance at 10 ppm on/in the leafy vegetables (except Brassica) crop group, and at 2 ppm on/in the cucurbit vegetables crop group.

cc:R.F.,Circu.,Reviewer(FDG),PP#1F4016,PP#2F4053.

H-7509C:CBTS:Reviewer(FDG):CM#2:Rm804Q:305-5826:7/15/93:edit:fdg:7/16/93.

RDI:SecHd:RSQuick:7/15/93:BrSrSci:RALoranger:7/15/93.

Agricultural Division
CIBA-GEIGY Corporation
P.O. Box 18300
Greensboro, North Carolina 27419-8300
Telephone 919 632 6000

CIBA-GEIGY

12 January 1993

To Dirk Griffith
for review on 2/10/93
RM

Mr. Phillip O. Hutton
Product Manager (18)
Registration Division (H7505C)
U. S. Environmental Protection Agency
401 M. Street, S.W.
Washington, DC 20460

Dear Mr. Hutton:

SUBJECT: PESTICIDE PETITION NUMBER 1F4016
TRIGARD, EPA REG. NO. 100-654
ADDITION OF LEAFY VEGETABLE USE - RESIDUE ISSUES
YOUR LETTER/REVIEW DATED 31 DECEMBER 1992

On 8 July 1991, CIBA-GEIGY requested a 10.0 ppm tolerance for the combined residues of cyromazine and its major metabolite melamine in or on the raw agricultural commodity crop group, leafy vegetables. This crop group excludes the Brassica vegetables. We have received the review (dated 12/31/92) of residue data and analytical method (MRID 419763-01), submitted in support of this petition.

This review indicates that CBTS cannot recommend for the requested cyromazine plus melamine tolerance on the leafy vegetables (except Brassica) crop group until CIBA-GEIGY submits recovery data for cyromazine and melamine through the FDA multiresidue methods. At this time we would like to reference this data which has been submitted in support of our pending petitions for cyromazine and melamine tolerance in carrots and tomatoes.

A multiresidue study was submitted on 17 February 1992, as volume 6 of 6, entitled "Determination of Cyromazine and Its Major Metabolites by U.S. Food and Drug Administration (FDA) Multiresidue Protocols, I, II, III, and IV" (ABR-88136, MRID 422243-05). For your use we have attached the Transmittal Document that accompanied this submission. This study was initiated 7 December 1987 and was conducted according to the FDA and EPA procedures in effect at that time. In 1989 the new PAM II appendix was issued, but the actual experiments described prior to and at this issuance are exactly the same. We have rereviewed this study and have determined that all pertinent data are included in this study and that it should satisfy the requirements.

At this time we ask that you consider this submission to complete the requirements for the establishment of the tolerance for the

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combined residues of cyromazine and melamine in or on the leafy vegetables crop group (except Brassica). Following establishment of this tolerance we further ask that you accept our application to amend the registration of Trigard Insecticide, EPA Reg. No. 100-654, to add use on leaf lettuce and spinach, which will complete the representative commodities for the leafy vegetables crop group. At this time we do not wish to add the other leafy vegetables covered under this crop group, but we may wish to add those commodities in the future.

We appreciate your continued cooperation in this matter, and look forward to resolving this action which has been pending since 1991. If you have questions regarding the information provided here, please call me at (919) 632-7178. Thank you for your assistance.

Sincerely,

N. Beth Carroll

N. Beth Carroll, Ph.D
Regulatory Manager

cc: Mike Mendelsohn

Attachment: Transmittal Document for subject MRMT study

RA Accession No.: 42224301 B

Vol. 1 of 6

Date Submitted: FEB 17 1992

MRID Number: NA

VOLUME 1 OF 6

TRANSMITTAL DOCUMENT

NAME AND ADDRESS OF SUBMITTER: CIBA-GEIGY Corporation
Agricultural Division
P.O. Box 18300
Greensboro, North Carolina 27419

REGULATORY ACTION: Submission of residue and animal metabolism data in response to EPA's Jan. 28, 1987 review of Pesticide Petition # 6F3329 for cyromazine in carrots and EPA's Feb. 12, 1987 review of Pesticide Petition #6F3333 for cyromazine in tomatoes.

TRANSMITTAL DATE: February 17, 1992

LIST OF SUBMITTED STUDIES:

VOLUME	TITLE OF STUDY	EPA GUIDELINE NO.
1 of 6	Transmittal Document	Not applicable
2 of 6 42224301	Residue Chemistry Response to EPA Review of January 28, 1987 for Cyromazine in Carrots	171-4
3 of 6 42224302	Metabolism of [Triazine-^{14}C]-Cyromazine in Lactating Goats	171-4
4 of 6 42224303	Residues of Cyromazine, Melamine, and 1-Methylcyromazine in Milk, Blood, and Tissues of Dairy Cows Receiving Cyromazine in Their Diet	171-4
5 of 6 42224304	Analytical Method for the Determination of 1-Methylcyromazine in Meat, Milk, and Blood by High Performance Liquid Chromatography Including Validation Data	171-4(d)

6 of 6 42224305 Determination of Cyromazine and Its Major Metabolites by U.S. Food and Drug Administration (FDA) . Multiresidue Protocols I, II, III, and IV 171-4

Carolyn B. Bussey
Name

Carolyn B. Bussey
Signature

COMPANY NAME: Agricultural Division, CIBA-GEIGY Corporation

COMPANY CONTACT: Carolyn B. Bussey (919) 632-2838
Name Telephone No.

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

DEC 23 1992

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Subject: PP# 2F4053 - CYROMAZINE (TRIGARD®) ON CUCURBIT VEGETABLES CROP GROUP.
Review of Residue Data and Analytical Method.
(MRID # 421160-01)[CBTS # 9816]{DP Barcode D177550}

From: Francis D. Griffith, Jr., Chemist
Chemistry Branch I - Tolerance Support
Health Effects Division (H-7509C)

To; Phillip O. Hutton, PM-18
Insecticide-Rodenticide Branch
Registration Division (H-7505C)

and

Toxicology Branch - IR Support
Health Effects Division (H-7509C)

Thru: Debra F. Edwards, Ph.D., Branch Chief
Chemistry Branch I - Tolerance Support
Health Effects Division (H-7509C)

INTRODUCTION

Ciba-Geigy Corporation, Agricultural Division proposes a crop group tolerance for residues of its insecticide cyromazine, trade named Larvadex® and Trigard® (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine) and its principal metabolite, melamine (1,3,5-triazine-2,4,6-triamine) on the cucurbit vegetables crop group at 2 ppm.

Tolerances have been established for combined residues of cyromazine and its metabolite melamine calculated as cyromazine in eggs at 0.25 ppm (see 40 CFR 180.414(a)), in meat, fat, and meat by-products of poultry (from chicken layer hens and chicken breeder hens only) (see 40 CFR 180.414 (b and c)) at 0.05 ppm, and at 10 ppm in celery, and 5 ppm in head lettuce (see 40 CFR 180.414(d)).

Cyromazine, per se, tolerances are established in poultry feed at 5 ppm when cyromazine is used as prescribed in 40 CFR

186.1400(a, b, c, and d). Currently there are no cyromazine food additive tolerances.

No Registration Standard for cyromazine has been issued.

No Special Local Need (SLN) registrations have been granted. Recent Emergency Exemptions (Section 18) for use of cyromazine on potatoes (92-Fl-001, October 25, 1991, J. Abbotts; 92-Mi-0003, April 20, 1992, M.J. Nelson; and 91-Fl-0012, February 26, 1991, D. McNeilly) received favorable Chemistry Branch recommendations. For the 1992 Section 18s on potatoes cyromazine residues were not expected to exceed 3 ppm. An Emergency exemption for use of Trigard® (cyromazine) on tomatoes (see 91-Fl-0023, August 21, 1991, J. Abbotts) received favorable recommendation from Chemistry Branch. Cyromazine residues on tomatoes and tomato juice from this Emergency Exemption were not expected to exceed 1 ppm, 2 ppm in wet pomace, 30 ppm in dry tomato pomace, and 4 ppm in catsup. An Emergency Exemption for use of cyromazine on peppers with residues not expected to exceed 3 ppm also received a favorable recommendation from Chemistry Branch (see 91-TX-0026, July 24, 1991, A. Aikens).

CBTS has recommended for several cyromazine and its metabolite melamine tolerances in the following petitions which have not yet been established:

PP# 9E3791, 3 ppm on Chinese mustard,
PP# 9E3752, 3 ppm on Chinese cabbage,
PP# 6F3342, 4 ppm on peppers; and
PP# 5F3177, 10 ppm on mushrooms.

There are also a number of cyromazine petitions currently in reject status for a variety of deficiencies. They are as follows;

PP# 8F3633, 0.2 ppm on swine meat, fat, and meat by-products including kidney, and 0.4 ppm in swine liver,
PP# 6F3333, 1 ppm in tomatoes,
PP# 6F3329, 3 ppm in carrots,
PP# 6F3422, rotational crop tolerances of 0.05 ppm in cabbage, sweet potatoes, sugar beets (roots and tops), wheat grain, barley hay, sorghum forage, 0.5 ppm in wheat forage and straw, 0.2 ppm in wheat hay, 0.1 ppm in barley grain and forage, sorghum grain and fodder, and 1.5 ppm in barley straw, and
PP#5F3332, 0.5 ppm in radishes and 0.5 ppm in sweet corn ears, forage, and fodder, 0.01 ppm in milk, 0.05 ppm in bovine meat, fat, and meat by-products.

There is a co-pending petition, PP# 1F4016, currently under review for a cyromazine tolerance at 10 ppm on the leafy vegetable (except Brassica) crop group.

The cucurbit vegetables crop group is defined in 40 CFR 180.34(f)(9)(ix). The representative commodities for this crop grouping are cucumbers, melons (cantaloupe or muskmelon), and summer squash. Some of the other commodities in this crop group are Chinese waxgourd, pumpkin, Balsam pear, gourds (edible), citron melon, melons (including cantaloupe, casaba, crenshaw, honeydew, honey balls, mango melons, muskmelon, Persian melon), summer and winter squash, and watermelons.

EXECUTIVE SUMMARY OF CHEMISTRY DEFICIENCIES

- NEED MULTIRESIDUE METHODS RECOVERY DATA

CONCLUSIONS

1. CBTS Conclusions on **Product Chemistry/Chemical Identity**

   a. CBTS does not foresee a residue problem in the cucurbit vegetables crop group for the impurities identified at or above 0.1% in the TGAI cyromazine when Trigard® is used as directed.

   b. Ciba-Geigy has submitted the results of analysis for nitrosamines in the technical cyromazine. No nitrosamines were detected in cyromazine.

2. CBTS Conclusion on **Directions for Use**

   The petitioner has proposed an adequate set of directions for use of Trigard® containing 75% cyromazine active ingredient on the cucurbit vegetables crop group.

3. CBTS Conclusion on the **Nature of the Residue - Plants**

   The primary route for cyromazine metabolism is dealkylation of cyromazine to form melamine and cyclopropane. The nature of the residue in plants is adequately understood. The residues of concern are the parent cyromazine and its metabolite melamine.

4. CBTS Conclusion on the **Nature of the Residue - Livestock**

   a. Commodities in the cucurbit vegetables crop group are not considered to be livestock feed items. Thus, a full discussion on the nature of the livestock residue is not germane to this petition.

   b. However, CBTS notes that in non-ruminants; ie, hogs, horses, sheep, and poultry the nature of the cyromazine residue is adequately understood. The metabolic pathway in poultry is the same as in plants. The residues of concern are cyromazine and melamine.

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c. CBTS also notes that the nature of the cyromazine residue in ruminants is not adequately understood, but deficiencies noted in previous reviews need not be resolved for this petition.

5. CBTS Conclusion on **Residue Analytical Method**

a. There are adequate residue analytical methods in FDA's Pesticide Analytical Manual (PAM), Vol-II to gather the crop field trial residue data for cyromazine and its melamine metabolite on cucurbit vegetables and to enforce the proposed 2 ppm crop group tolerance.

b. CBTS reiterates that the petitioner needs to submit recovery data for cyromazine and melamine thru the FDA multiresidue methods. We suggest the petitioner provide this data using FDA Pesticide Analytical Manual Vol-I, Appendix II, Protocols A through E.

6. CBTS Conclusion on **Storage Stability**

Residues of cyromazine and melamine are stable in frozen storage for at least 24 months. There are adequate storage stability data to support the crop field trial residue data in this petition.

7. CBTS Conclusions on **Magnitude of the Residue - Crop Field Trials**

a. At the proposed PHI and application rate with an exaggerated maximum number of 8 applications for a total of 1 lb a.i. cyromazine applied the maximum total cyromazine residues on cantaloupe are 0.99 ppm at 0 day PHI. Residues of cyromazine plus melamine on cantaloupe are not expected to exceed the proposed cucurbit vegetables crop group tolerance of 2 ppm when Trigard® is used as directed.

b. At the proposed PHI and application rate with an exaggerated maximum number of 8 applications for a total of 1 lb a.i. cyromazine applied the maximum total cyromazine residues on cucumbers are 1.5 ppm. Residues of cyromazine plus melamine on cucumbers are not expected to exceed the proposed cucurbit vegetables crop group tolerance of 2 ppm when Trigard® is used as directed.

c. At the proposed PHI and application rate with an exaggerated maximum number of 8 applications for a total of 1 lb a.i. cyromazine applied the maximum total cyromazine residues on honeydew melons are 0.95 ppm. Residues of cyromazine plus melamine on honeydew melons are not expected to exceed the proposed cucurbit vegetables crop group tolerance of 2 ppm when Trigard® is used as directed.

d. At the proposed PHI and application rate with an exaggerated maximum number of 8 applications for a total of 1 lb a.i. cyromazine applied the maximum total cyromazine residues on watermelons are 1.1 ppm. Residues of cyromazine plus melamine on watermelons are not expected to exceed the proposed cucurbit vegetables crop group tolerance of 2 ppm when Trigard® is used as directed.

e. At the proposed PHI and application rate with an exaggerated maximum number of 8 applications for a total of 1 lb a.i. cyromazine applied the maximum total cyromazine residues on summer squash are 2.0 ppm. Residues of cyromazine plus melamine on summer squash are not expected to exceed the proposed cucurbit vegetables crop group tolerance of 2 ppm when Trigard® is used as directed.

f. The petitioner has presented an adequate amount of multi-year and geographically representative crop field trials for cyromazine on cantaloupes, cucumbers, honey dew melons, watermelons, and summer squash to support a crop group tolerance.

8. CBTS Conclusion on **Magnitude of the Residue - Processed Food/Feed**

There are no processed food or feed commodities associated with the commodities in the cucurbit vegetables crop group. Thus, no processing studies are required for cyromazine on the cucurbit vegetables.

9. CBTS Conclusion on **Magnitude of the Residue - Meat, Milk, Poultry, and Eggs**

Cucumbers, melons (cantaloupe or muskmelon), summer squash, watermelons, and the other commodities in the cucurbit vegetables crop group are not considered livestock feed items. There is little likelihood of secondary residues of cyromazine and melamine occurring in meat, milk, poultry, and eggs from the proposed use of Trigard®.

10. CBTS Conclusion on **Harmonization of Tolerances**

a. Compatibility is not a problem with Canadian and Mexican tolerances as these countries have no established cyromazine tolerances for any of the commodities in the cucurbit vegetables crop group.

b. Codex tolerances for cyromazine, per se, are established at Step 7B on melons, except watermelon at 0.2 ppm. Compatibility cannot be achieved with the Codex tolerance at this time due to the higher residues detected from the use in USA, and that the metabolite melamine is a significant portion of the total residue.

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RECOMMENDATION

CBTS cannot, at this time, recommend for the requested cyromazine plus melamine tolerance on the cucurbit vegetables crop group for the reason cited in the Executive Summary and further described in Conclusion 5b.

For further consideration the petitioner should be advised to resolve the deficiency noted above.

DETAILED CONSIDERATIONS

PRODUCT CHEMISTRY/CHEMICAL IDENTITY

All product chemistry data for cyromazine has been previously submitted and adequately reviewed (see memoranda in PP# 9G2230 by A. Rathman dated November 14, 1979; and in PP# 5F3177 by E. Haeberer dated February 13, 1985). The description of the starting materials, manufacturing process, formation of impurities, both actual and theoretical, and analysis of various batches of the technical material have been presented and reviewed. Technical cyromazine (CGA-72662) is 95% pure. CBTS does not foresee a residue problem in the crop group cucurbit vegetables for the impurities identified at or above 0.1% in the TGAI cyromazine when the formulation Trigard® is used as directed.

Ciba-Geigy has submitted the results of analysis for nitrosamines in the technical cyromazine. No nitrosamines were detected in cyromazine. CBTS (aka DEB) accepted the results of the study (see memorandum by K. Doctor dated January 27, 1989).

DIRECTIONS FOR USE

The petitioner proposes use of Trigard® 75W (EPA Reg. No. 100-654), a wetable powder containing 75% active ingredient cyromazine to control leafminer larvae in the cucurbit vegetables crop group. Trigard® is packaged in 2 pound bags only with the inner bag being a water soluble bag. The entire bag is mixed with water and applied as a foliar spray at a rate of 1/6 lb. Trigard® (0.125 lb a.i. cyromazine) per acre per application in 50 gallons water by ground equipment, and/or in 5 gallons water using aerial application. A maximum of 6 applications of Trigard® (0.75 lb cyromazine a.i.) can be made per cucurbit vegetable crop growing season. The initial Trigard® application is made when the leafminers first appear. The repeat application interval is 7 days and the PHI is 0 days; ie, harvest on the same day of the last application.

Rotational crop restrictions are do not rotate to any crops other then the cucurbit vegetables crop group, except corn and radishes, and then plant these 3 months after the last Trigard® application.

There is a restriction on use of Trigard® through any type of irrigation system.

The petitioner has proposed an adequate set of directions for use of Trigard® 75W (containing 75% cyromazine a.i.) on the cucurbit vegetable crop group.

NATURE OF THE RESIDUE - PLANTS

No new plant metabolism studies were submitted in this petition. [^{14}C-(U)-triazine]-cyromazine metabolism studies in the representative commodities celery and lettuce were presented and have been reviewed. A cyromazine metabolism study in tomatoes was also presented and reviewed (see memoranda in PP# 5G3176 by E. Haeberer dated February 4, 1985; in PP# 5F3180 by C. Deyrup dated February 8 and March 20, 1985; and PP# 6F3329 by A. Smith dated January 28, 1987). These studies are summarized as follows:

CELERY

Celery was treated at a rate of 0.25 lb (2X maximum proposed use rate) with ^{14}C-cyromazine 6 times (maximum application was 1.5 lbs a.i. cyromazine). Mature celery had total ^{14}C-cyromazine equivalent residues of 1.55 ppm at 14 days PHI. Cyromazine, per se, was 48.2% of the total radioactivity (0.744 ppm) and the metabolite melamine was 25.45% (0.388 ppm) of the residue.

In another study celery was grown to maturity in soil treated with ^{14}C-cyromazine at a rate 0.9 lb a.i. per acre. After 6 weeks of growth the celery stalks had 0.75 ppm of ^{14}C-cyromazine equivalents and at maturity the ^{14}C-cyromazine equivalents were 0.34 ppm. At 6 weeks cyromazine, per se, was 60.3% (0.45 ppm) and melamine was 10.7% (0.08 ppm) of the residue. In the mature celery cyromazine, per se, was 43% (0.146 ppm) and melamine was 30% (0.10 ppm) of the radioactive residue.

LETTUCE

Lettuce was treated with ^{14}C-cyromazine at a rate of 0.25 lb a.i. (2X the proposed application rate) 4 times for a total amount of 1 lb a.i. cyromazine. Total ^{14}C-cyromazine equivalent residues in mature head lettuce at 7 days PHI were 3.69 ppm. In the lettuce cyromazine, per se, was 74% (2.72 ppm) and melamine was 10.9% (0.41 ppm).

TOMATO

In the ^{14}C-cyromazine in tomato metabolism study tomatoes were treated with ^{14}C-cyromazine at a rate of 0.25 lb. (2X proposed use rate) 6 applications for a total amount of 1.5 lbs a.i. cyromazine. Total ^{14}C-cyromazine equivalent residues in tomatoes at 0 day PHI were 0.19 ppm, at 7 days PHI were 0.08 ppm ,and 0.12 ppm at 14 day PHI. The formation of melamine is rapid as at 0 day PHI melamine was 11% (0.021 ppm) while cyromazine was 76%

(0.15 ppm) of the residue. At day 7 cyromazine dropped to 41% (0.032 ppm) and melamine increased to 22% (0.018 ppm) of the radioactive residue. The residue profile changed only slightly at 14 days PHI as cyromazine was 39% (0.048 ppm) of the residue, and melamine increased slightly to 26% (0.03 ppm) of the residue. By 6 weeks the cyromazine portion of the total residue dropped to 37% (0.137 ppm) while melamine increased to 44% (0.163 ppm).

ROTATIONAL CROP ^{14}C-CYROMAZINE STUDIES

Various rotational crop ^{14}C-cyromazine studies have been reported and reviewed (see memorandum PP# 6F3422 by A. Smith dated January 28, 1987). In one study ^{14}C-cyromazine was applied to soil at a rate of 0.05 lb a.i. per acre and aged 30 days before wheat, sugar beets, and lettuce were planted. Mature lettuce, sugar beet tops and roots, and wheat grain each contained less then 0.009 ppm ^{14}C-cyromazine equivalents.

In another study soil was treated with 6 applications of 0.25 lb. per acre (total of 1.5 lbs) ^{14}C-cyromazine and planted with various crops which included carrots and soybeans. Immature carrot roots had 0.03 ppm cyromazine equivalents while mature carrot tops had 0.05 ppm and mature carrot roots had <0.02 ppm cyromazine equivalents. For immature soybeans, the stalks had 0.02 ppm cyromazine equivalents 60 days after planting. The mature soybean stalks had 0.04 ppm, the pods had 0.05 ppm, and the soybeans had 0.03 ppm cyromazine equivalents residues.

These studies confirm that cyromazine residues in the soil are taken up by crops and translocated to the edible portion of the plants. The residues consist generally of free and bound forms of the parent cyromazine and its metabolite melamine.

SUMMARY

The primary route for cyromazine plant metabolism is dealkylation of cyromazine to form melamine and cyclopropane. Small amounts of several more polar metabolites form as plants approach maturity. Cyromazine residues in the soil are taken up by crops and translocated to the edible portion of the plants. Melamine forms rapidly. The nature of the residue in plants is adequately understood. The residues of concern are the parent cyromazine and its metabolite melamine.

NATURE OF THE RESIDUE - LIVESTOCK

No new livestock cyromazine metabolism studies were submitted in this petition. Commodities in the cucurbit vegetables crop group are not considered to be livestock feed items. Thus, a full discussion on the nature of the livestock residue is not germane to this petition.

Animal cyromazine metabolism studies have been presented in other petitions and adequately reviewed. We note that in rumi-

nants the nature of the cyromazine residue is not adequately understood. A significant portion of the residue in milk; ie, 34%, has not been identified and a major component in liver needs verification. One metabolic pathway identified is the same as in plants which is dealkylation of cyromazine to form melamine and cyclopropane. Another metabolite reported, but not confirmed in ruminants is 1-methylcyromazine.

In non-ruminants; ie, hogs, horses, sheep, and poultry the nature of the cyromazine residue is adequately understood. The ^{14}C-cyromazine study in poultry had laying hens fed 5 ppm of ^{14}C-cyromazine for 7 days. The egg whites had 0.09 ppm to 0.22 ppm of ^{14}C-cyromazine equivalents and the egg yolks had 0.08 ppm to 0.15 ppm of ^{14}C-cyromazine equivalents. Poultry tissues had <0.002 ppm to 0.003 ppm cyromazine equivalents. Cyromazine and melamine accounted for 77% to 85% of the residue in poultry. The cyromazine metabolic pathway in poultry is the same as in plants. The residues of concern are cyromazine and melamine.

RESIDUE ANALYTICAL METHODS

The primary residue analytical method used to gather the residue data on the representative commodities is titled "High Pressure Liquid Chromatographic Determination of Residues of Cyromazine and Melamine in Crops" dated July 15, 1983, and coded AG-408. Method AG-408 is modified by Method AG-417A which substitutes the anion exchange resin Dowex 1-8X for BioRex 9,which is no longer commercially available. The methods have been previously submitted and reviewed (see memorandum in PP# 5F3180 by C. Deyrup dated February 8, 1985).

In summary, for method AG-408 25 grams of crop are refluxed in 250 ml CH_3OH-H_2O (9+1) for 2 hours. A 5 gram aliquot of the extract is evaporated on a rotary evaporator at 40°C to the aqueous solution, diluted with 100 ml 0.1 N HCl, and cleaned-up first by partitioning 2 X 50 ml CH_2Cl_2 followed by 50 ml hexane, then the acidic solution is further cleaned-up on a cation exchange column of Dowex 50W-4. Cyromazine and melamine are eluted off the Dowex 50W-4 column in 20 ml of NH_4OH-CH_3OH (1+19). Additional clean-up, if necessary, is through an anion exchange column of Dowex 1-X8 with cyromazine and melamine being eluted off in 30 ml of NH_4OH-CH_3OH (1+3). Determination is by HPLC using a Waters 6000A pump, a 25 cm X 4 mm (id) column packed with LiChrosorb-NH_2, 10um particle size. The mobile phase solvent is isocratic ACN-H_2O (9+1) at a flow rate of 0.5 ml per minute and at ambient temperature. Detection is by UV at 214 nm. Under these conditions cyromazine elutes off at about 9.5 minutes and melamine elutes off about 13 minutes.

A Petition Method Validation (PMV) was requested for method AG-408 for cyromazine and melamine on lettuce (see memorandum in PP# 5F3180 by C. Deyrup dated March 13, 1985). Lettuce was to be spiked with cyromazine at 4 and 8 ppm and with melamine at 1 and 2 ppm. EPA recoveries through the first ion exchange clean-up

column ranged from 81% to 95% for cyromazine and ranged from 80% to 106% for melamine. EPA recoveries through the complete method for cyromazine ranged from 68% to 93% and for melamine recoveries ranged from 77% to 96%. The control samples used in the PMV showed 0.17 ppm cyromazine equivalents and 0.07 ppm melamine equivalent when the samples were analyzed after the first ion exchange cleanup, but neither cyromazine nor melamine were detected in control samples taken through the entire method (see memorandum in PP# 5F3180 by M.Law of ABC/BEAD dated May 8, 1985). EPA's limit of detection for cyromazine in the PMV was 0.05 ppm using both clean-up steps. CBTS (aka RCB) concluded the method was suitable to enforce the 5 ppm cyromazine tolerance in lettuce and the 10 ppm tolerance in celery. The methods were forwarded to FDA's Technical Editing Group and published in the Pesticide Analytical Manual, Vol-II as of June 1986.

Samples of cantaloupe were fortified with cyromazine and melamine at levels of 0.05 ppm, 0.1 ppm, 0.2 ppm, 0.5 ppm, 1.0 ppm, 2 ppm, and 5 ppm. Cyromazine recoveries from cantaloupe ranged from 66% to 123% ($X = 88\% \pm 16\%$, $n = 24$). Melamine recoveries from cantaloupe ranged from 71% to 136% ($X = 90\% \pm 18\%$, $n = 25$).

Samples of cucumbers were fortified with melamine and cyromazine at levels of 0.05 ppm, 0.1 ppm, 0.2 ppm, 0.5 ppm, 1 ppm, 2 ppm, and 5.0 ppm. Cyromazine recoveries ranged from 61% to 111% ($X = 83\% \pm 11\%$, $n = 30$). Melamine recoveries from cucumbers ranged from 67% to 126% ($X = 90\% \pm 12\%$, $n = 29$).

Samples of honeydew melon were fortified with cyromazine and melamine at levels of 0.05 ppm, 0.1 ppm, 0.2 ppm, 1 ppm, 2 ppm, and 5 ppm. Cyromazine recoveries ranged from 68% to 108% ($X = 82\% \pm 13\%$, $n= 11$). Melamine recoveries from honey dew melons ranged from 75% to 109% ($X = 90\% \pm 13\%$, $n = 10$).

Samples of summer squash were fortified with cyromazine and melamine at levels of 0.05 ppm, 0.1 ppm, 0.2 ppm, 0.5 ppm, 1 ppm, 2 ppm, and 5 ppm. Cyromazine recoveries ranged from 67% to 131% ($X = 88\% \pm 13\%$, $n = 34$). Melamine recoveries from summer squash ranged from 64% to 134% ($X = 97\% \pm 17\%$, $n = 34$).

Samples of watermelon were fortified with cyromazine and melamine at levels of 0.2 ppm, 0.5 ppm, 1 ppm, and 5 ppm. Cyromazine recoveries ranged from 64% to 89% ($X = 76\% \pm 10\%$, $n = 6$). Melamine recoveries from watermelons ranged from 65% to 93% ($X = 78\% \pm 13\%$, $n = 6$).

The overall recoveries for cyromazine from the representative commodities of the cucurbit vegetables ranged from 61% to 131% ($X = 85\% \pm 13\%$, $n = 105$). The overall recoveries for melamine from the representative commodities of the cucurbit vegetables ranged from 64% to 136% ($X = 92\% \pm 16\%$, $n = 104$).

The petitioner presented photocopies of 9 chromatograms for cyromazine and melamine standards at 0.25 ng, 0.6 ng, 1 ng, 2 ng,

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2.5 ng, 10 ng, and 20 ng. These standards were used to prepare the cyromazine and melamine standard curves. The petitioner presented a chromatogram for one control sample each of cantaloupe, cucumber, honey dew melon, summer squash, and watermelon. There were no unidentified analytical responses (UARs) in cantaloupe, cucumber, and summer squash that could interfere with the determination of either cyromazine or melamine. We noted an elevated base line with UARs in the control watermelon and honey dew melon; however these UARs should not interfere with the quantitation of cyromazine and melamine. The petitioner presented copies of chromatograms showing the 0.05 ppm spike in cantaloupe and cucumber, 0.2 ppm spike in honey dew melon and summer squash, and the 0.5 ppm spike in watermelon. We agree the limit of quantitation (LOQ) is in the 0.05 ppm range for both cyromazine and melamine, and that the minimum detection limit (MDL) is around 0.02 ppm. One chromatogram each for cantaloupe, cucumber, honeydew melon, summer squash, and watermelon showing field incurred residues was presented. The petitioner has presented adequate supporting chromatographic data.

With the EPA PMV recovery data and the recovery data presented in this petition CBTS concludes that the petitioner has adequately validated residue method AG-408 to gather the magnitude of the cyromazine and melamine residues from the limit of quantitation (LOQ) of 0.05 ppm to above 5 ppm in the cucurbit vegetables crop group. This method has passed an EPA PMV and is in PAM-II as Method II as of June 1986. AG-408 is suitable to enforce the proposed 2 ppm crop group tolerance.

CBTS reiterates that the petitioner needs to submit recovery data for cyromazine and melamine thru the FDA multiresidue methods. We suggest the petitioner provide this data using FDA Pesticide Analytical Manual Vol-I, Appendix II, Protocols A through E.

STORAGE STABILITY

No new storage stability data were submitted with this petition. Storage stability data have been previously submitted and adequately reviewed (see memorandum in PP# 6F3329 by A. Smith dated January 28, 1987). In summary, field trial samples of head lettuce, leaf lettuce, celery, mushrooms, and tomatoes containing residues were analyzed and frozen at -15°C for periods from 9 to 24 months. When samples were removed from storage and reanalyzed there were no significant changes in the residues. CBTS reiterates that residues of cyromazine and melamine are stable in frozen storage for at least 24 months. There are adequate storage stability data to support the crop field trial residue data in this petition. Field trial samples in this petition were stored from 7 to 22 months.

MAGNITUDE OF THE RESIDUE - CROP FIELD TRIALS

The petitioner presented the magnitude of the residue data for cyromazine on the cucurbit vegetables crop group in a study titled " Residues of Cyromazine and Melamine in Cucurbit Vegetable Crop Group Resulting From Foliar Applications of Trigard" by W. T. Beidler, dated September 17, 1991, and coded ABR-91042. The MRID # is 421160-01.

CANTALOUPES

Magnitude of the cyromazine residue data were presented on cantaloupes for the 1986 and 1987 crop years from 5 field trials in Florida, North Carolina, Arizona, Colorado, and Texas. Residue data from these states represent cantaloupe production on 26,600 acres out of a national cantaloupe production on 86,350 acres (see Agricultural Statistics, 1981). The petitioner has presented an adequate amount of multi-year and geographically representative crop field trials for cyromazine on cantaloupes to support a crop group tolerance.

Cantaloupes were treated with Trigard® at the proposed use rate of 1/6 lb or 0.125 lb a.i. cyromazine per acre per application 8 times with a repeat application interval of 7 days. The maximum total cyromazine application was 1 lb. Three trials were also treated with an exaggerated application Trigard® at a rate of 1/3 lb or 0.25 lb (2X) a.i. cyromazine per acre per application 8 times with a repeat application interval of 7 days. In all trials a control plot that received no cyromazine applications was grown and harvested. Samples from the treated plots were grown to maturity and harvested at 0 day PHI, 7 days PHI, 14 days PHI, and 21 days PHI. Samples were frozen, then shipped with dry ice to the laboratory, and were stored in a freezer until sample preparation and analysis. Sample preparation followed the guidance in FDA's PAM-I, Section 141.

Cyromazine residue results in cantaloupe are as follows:

TABLE 1

Residues in PPM	PHI			
	0 Day	7 Day	14 Day	21 Day
Cyromazine				
1X	<0.05 - 0.73	<0.05 - 0.18	<0.05 - 0.4	<0.05 - 0.18
2X	0.2 - 0.53	0.21 - 1.3	0.09 - 0.43	<0.05 - 0.21
Melamine				
1X	<0.05 - 0.66	<0.05 - 0.68	<0.05 - 1.4	0.05 - 0.29
2X	0.33 - 1.3	0.21 - 1.3	0.1 - 1.8	<0.05 - 0.14

At the proposed PHI and application rate with an exaggerated maximum number of 8 applications for a total of 1 lb a.i. cyro-

mazine applied the maximum total cyromazime residues on cantaloupe are 0.99 ppm. The maximum residue was PHI and 1.8 ppm at a 14 day PHI. Residues of cyromazine plus melamine on cantaloupe are not expected to exceed the proposed cucurbit vegetables crop group tolerance of 2 ppm when Trigard® is used as directed.

CUCUMBERS

Magnitude of the cyromazine residue data on cucumbers were presented in this petition from the 1986 and 1990 crop years for 5 trials in Nebraska, California, Texas, North Carolina, and Michigan. Residue data from these states represent cucumber production on 63,400 acres out of a national celery production on 115,490 acres. (see Agricultural Statistics, 1991). The petitioner has presented an adequate amount of multi-year and geographically representative crop field trials for cyromazine on cucumbers to support a crop group tolerance.

Cucumbers in 4 of the trials were treated with Trigard® at the proposed use rate of 1/6 lb or 0.125 lb a.i. cyromazine 8 times in 3 trials and 6 times in 2 trials with a 7 day repeat application interval. Cucumber in the North Carolina trial were treated at a rate of 0.095 lb a.i. cyromazine 6 times. In 4 of the trials a separate plot was treated with Trigard® at an exaggerated rate of 0.25 lb. (2X) a.i. cyromazine 6 or 8 times with a repeat application interval of 7 days. The maximum total cyromazine application was 1 lb, or 2 lbs to the exaggerated rate plots. A separate cucumber control plot at each trial site was grown to maturity without cyromazine treatments, and sampled. Cucumber samples were harvested at 0 days, 7, 14, and 21 days after the last Trigard® application. Samples were frozen after harvest, then shipped with dry ice to the laboratory, and were stored in a freezer until sample preparation and analysis. Sample preparation followed the guidance in FDA's PAM-I, Section 141.

Cyromazine residue results on cucumbers are as follows:

TABLE 2

Residue in PPM	PHI			
	0 Days	6-7 Days	14 Days	21 Days
Cyromazine				
1X	0.11 - 0.24	<0.05- 0.29	<0.05- 0.24	<0.05- 0.24
2X	0.09 - 0.44	0.17- 0.36	<0.05- 0.27	0.07- 0.19
Melamine				
1X	0.18 - 1.3	0.11 - 1.6	0.11 - 1.5	0.1 - 1.4
2X	0.14 - 1.0	0.3 - 2.4	0.17 - 2.2	0.1 - 2.1

At the proposed PHI and application rate with an exaggerated maximum number of 8 applications for a total of 1 lb a.i. cyromazine applied the maximum total cyromazime residues on cucumbers are 1.5 ppm. The maximum residue was 1.7 ppm at a 6 days PHI. Residues of cyromazine plus melamine on cucumbers are not expected to exceed the proposed cucurbit vegetables crop group tolerance of 2 ppm when Trigard® is used as directed.

HONEYDEW MELON

Magnitude of the residue data for cyromazine and its melamine metabolite were presented on honeydew melons for the crop year 1986 from 2 trials in Arizona and California. The crop field trials for honeydew melon represent honeydew melon production on 21,500 acres out of a national honeydew melon production on 26,500 acres (see Agricultural Statistics, 1991). CBTS concludes the petitioner has presented an adequate amount of geographically representative honeydew melon crop field trials to support a crop group tolerance.

Honeydew melons were treated with Trigard® at the proposed use rate of 1/6 lb (0.125 lb a.i. cyromazine) 8 times with a repeat application interval of 7 days and PHIs of 0, 7, 14, and 21 days. The maximum total cyromazine applied was 1 lb. In one trial a separate plot was treated with Trigard® at an exaggerated rate of 1/3 lb. or 0.25 lb. (2X) a.i. cyromazine 8 times. At each trial site a separate control honeydew melon plot was planted, grown to maturity without cyromazine treatment, and harvested. Samples were harvested after the last Trigard® application at 0, 7, 14, and 21 days. Samples were frozen after harvest, shipped on dry ice to the laboratory, and stored frozen until sample preparation and analysis. Sample preparation followed the guidance in FDA's PAM-I, Section 141.

Cyromazine residue results in honeydew melons are as follows:

TABLE 3

Residue in PPM	PHI			
	0 Day	7 Day	14 Day	21 Day
Cyromazine 1X 2X	<0.05 - 0.16 0.19	<0.05 - 0.09 0.06	<0.05 - 0.08 0.12	<0.05 - 0.05 0.17
Melamine 1X 2X	<0.05 - 0.79 1.1	0.05 - 0.88 1.4	<0.05 - 1.2 1.8	<0.05 - 1.2 2.1

At the proposed PHI and application rate with an exaggerated maximum number of 8 applications for a total of 1 lb a.i. cyromazine applied the maximum total cyromazime residues on honeydew

melons are 0.95 ppm. The maximum residue was 1.3 ppm at a 14 days PHI. Residues of cyromazine plus melamine on honeydew melons are not expected to exceed the proposed cucurbit vegetables crop group tolerance of 2 ppm when Trigard® is used as directed.

WATERMELONS

Magnitude of the residue data for cyromazine and its melamine metabolite were presented on watermelons for the crop year 1986 from one trial in California. The crop field trial for watermelons represent watermelon production on 11,500 acres out of a national watermelon production on 184,500 acres (see Agricultural Statistics, 1981). CBTS concludes the petitioner has presented an adequate amount of watermelon crop field trial data to support a crop group tolerance.

Watermelons were treated with Trigard® at the proposed use rate of 1/6 lb (0.125 lb a.i. cyromazine) 8 times with a repeat application interval of 7 days and PHIs of 0, 7, 14, and 21 days. The maximum total cyromazine applied was 1 lb. In the same trial a separate plot was treated with Trigard® at an exaggerated rate of 1/3 lb. or 0.25 lb. (2X) a.i. cyromazine 8 times. A separate control watermelon plot was planted, grown to maturity without cyromazine treatment, and harvested. Samples were harvested after the last Trigard® application at 0, 7, 14, and 21 days. Samples were frozen after harvest, shipped on dry ice to the laboratory, and stored frozen until sample preparation and analysis. Sample preparation followed the guidance in FDA's PAM-I, Section 141.

Cyromazine residue results in watermelons are as follows:

TABLE 4

Residue in PPM	PHI			
	0 Day	7 Day	14 Day	21 Day
Cyromazine				
1X	0.1 - 0.15	0.08 - 0.1	0.1 - 0.14	0.12 - 0.13
2X	0.38 - 0.42	0.14	0.13	0.1
Melamine				
1X	0.61 - 0.9	0.47 - 0.81	0.61 - 0.64	1.1
2X	1.7 - 1.9	1.1	1.0	1.1

At the proposed PHI and application rate with an exaggerated maximum number of 8 applications for a total of 1 lb a.i. cyromazine applied the maximum total cyromazime residues on watermelons are 1.1 ppm. The maximum residue was 1.2 ppm at a 21 days PHI. Residues of cyromazine plus melamine on watermelons are not expected to exceed the proposed cucurbit vegetables crop group tolerance of 2 ppm when Trigard® is used as directed.

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SUMMER SQUASH

Magnitude of the residue data for cyromazine and its melamine metabolite were presented on summer squash for the crop years 1986 (3), 1987, and 1990 (3) from 7 trials in New York, California, Texas, Florida, Georgia, Nebraska, and Michigan. CBTS conclude the petitioner has presented an adequate amount of multi-year and geographically representative summer squash crop field trials to support a crop group tolerance.

Summer squash was treated with Trigard® at the proposed use rate of 1/6 lb (0.125 lb a.i. cyromazine) per application in 4 trials 8 times for a total cyromazine application of 1 lb per crop growing season and in 3 trials 6 times for a total cyromazine application on 0.75 lb. The repeat application interval was 7 days and the PHIs was 0, 7, 14, and 21 days. In 4 trials a separate plot was treated with at an exaggerated rate of 1/3 lb Trigard® (2X or 0.25 lb a.i. cyromazine) per application 8 times with a repeat application interval of 7 days and PHIs of 0, 7, 14, and 21 days. One plot in a 1990 field trial was treated with Trigard® at an exaggerated rate of 1/3 lb or 0.25 lb a.i. cyromazine 6 times. Repeat application interval and PHIs were the same as for the 8 application exaggerated field trials. A separate summer squash control plot was planted at each trial site, grown to maturity without cyromazine treatment, and harvested. One field trial received 8 applications at the proposed use rate of 1/6 lb Trigard® per acre per application and a separate plot received the exaggerated application rate of 1/3 lb (2X) Trigard® per acre per application. Summer squash samples were harvested at 0, 7, 14, and 21-22 days after the last Trigard® application. Samples were frozen after harvest, then shipped on dry ice to the laboratory, and stored frozen until sample preparation and analysis. Sample preparation followed the guidance in FDA's PAM-I, Section 141.

Cyromazine residue results on summer squash are as follows:

TABLE 5

Residue in PPM	PHI			
	0 Day	7 Day	14 Day	21 Day
Cyromazine				
1X	0.06 - 1.1	<0.05 - 0.19	<0.05 - 0.28	<0.05 - 0.1
2X	0.1 - 2	<0.05 - 0.13	0.05 - 0.38	<0.05 - 0.52
Melamine				
1X	<0.05 - 0.99	<0.05 - 0.25	0.05 - 0.38	<0.05 - 0.13
2X	0.16 - 1.8	<0.05 - 0.29	0.17 - 0.34	0.05 - 0.37

At the proposed PHI and application rate with an exaggerated maximum number of 8 applications for a total of 1 lb a.i. cyromazine applied the maximum total cyromazime residues on summer

squash are 2.0 ppm at 0 day PHI. Residues of cyromazine plus melamine on summer squash are not expected to exceed the proposed cucurbit vegetables crop group tolerance of 2 ppm when Trigard® is used as directed.

MAGNITUDE OF THE RESIDUE - PROCESSED FOOD/FEED

There are no processed food or feed commodities associated with the commodities in the cucurbit vegetables crop group. Thus, no processing studies are required for cyromazine on the cucurbit vegetables.

MAGNITUDE OF THE RESIDUE - MEAT, MILK, POULTRY, AND EGGS

Cantaloupe, summer squash, cucumber, honey dew melons, and watermelons as well as the other commodities in the cucurbit vegetables crop group are not considered livestock feed items. There is little likelihood of secondary residues of cyromazine and melamine occurring in meat, milk, poultry, and eggs from the proposed use of Tri-gard®.

While poultry and ruminant cyromazine feeding studies are not needed from the proposed use of cyromazine we note that these studies have been previously submitted and reviewed (see memorandum in PP# 6F3422 by A. Smith dated October 5, 1987).

HARMONIZATION OF TOLERANCES

An **International Residue Limit Status Sheet** (IRL) is attached to this review.

Compatibility is not a problem with Canadian and Mexican tolerances as these countries have no established cyromazine tolerances for any of the commodities in the cucurbit vegetables crop group.

Codex tolerances for cyromazine, per se, are established at Step 7B on melons, except watermelon at 0.2 ppm. Compatibility cannot be achieved with the Codex tolerance at this time due to the higher residues detected from the use in USA, and that the metabolite melamine is a significant portion of the total residue.

ATTACHMENT: **International Residue Limit Status Sheet**

cc: R.F.,Circ,Reviewer(FDG),PP# 2F4053.
H-7509C:CBTS:Reviewer(FDG):CM#2:Rm804Q:305-5826:fdg:12/10/92:edit:fdg:12//92.
RDI:SecHd:RSQuick:12/21/92:BrSrSci:RALoranger:12/23/92.

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Cyromazine (Trigard®)

CODEX NO. 169

CODEX STATUS:

☑ No Codex Proposal Step 6 or above

Residue(if Step 8): Cyromazine

Step 7B

Crop(s)	Limit (mg/kg)
Melons, except Watermelon	0.2

PROPOSED U.S. TOLERANCES:

Petition No. 2F 4053

RCB Reviewer F.D. Griffith, Jr. 3 Dec 92

Residue: For 40 CFR 180.414(d) Cyromazine* and its metabolite Melamine

Crop(s)	Limit (mg/kg)
Cucurbit Crop Group	2

CANADIAN LIMITS:

☑ No Canadian limit

Residue: _____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

☑ No Mexican limit

Residue: _____

Crop(s)	Limit (mg/kg)

NOTES:

* N-cyclopropyl-1,3,5-triazine-2,4,6-triamine

END OF DOCUMENT

13544

R062886

Chemical:	**Cyromazine**
PC Code:	**121301**
HED File Code	**11500 Petition Files Chemistry**
Memo Date:	**08/05/2003 12:00:00 AM**
File ID:	**DPD230105; DPD192978; DPD192981; DPD187702; DPD187707; DPD177550**
Accession Number:	**412-04-0144**

HED Records Reference Center
06/29/2004