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

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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.

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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.

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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-

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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

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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	<0.05 - 0.16	<0.05 - 0.09	<0.05 - 0.08	<0.05 - 0.05
2X	0.19	0.06	0.12	0.17
Melamine				
1X	<0.05 - 0.79	0.05 - 0.88	<0.05 - 1.2	<0.05 - 1.2
2X	1.1	1.4	1.8	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

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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.

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INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Cyromazine (Trigard®)

CODEX NO. 169

CODEX STATUS:

17 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:

14 No Canadian limit

Residue: _____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

14 No Mexican limit

Residue: _____

Crop(s)	Limit (mg/kg)

NOTES:

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

END OF DOCUMENT