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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

11 Mar 1998

MEMORANDUM

Subject: Cyromazine - 121301: Health Effects Division Risk Characterization for Use of the Chemical Cyromazine in/on Mangoes (5E4450), Crop Group 3: Bulb Vegetables (5F4576), Potatoes (6F4613), Cottonseed (5F4546), Sweet corn and Radishes (6F3332). Barcode: D242798, D242799, D242801, D242802

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The Health Effects Division (HED) of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The Registration division (RD) of OPP has requested that HED evaluate the toxicology and residue chemistry data and conduct dietary and worker risk assessments to estimate the risk to human health that will result from the use of cyromazine on mangoes, onions, green and dry bulb, potatoes and from inadvertent residues on cottonseed, sweet corn and radishes.

Novartis Crop Protection, Inc. has petitioned for permanent tolerances for residues of the insecticide/larvicide cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine) as follows:

| | |
|---|---|
| Mangos | 0.3 ppm |
| Onion, green | 2.0 ppm |
| Onions, dry bulb | 0.1 ppm |
| Potatoes | 0.8 ppm |

Additionally, tolerances are being requested for indirect or inadvertent as follows:

| | |
|---|---|
| Cotton, undelinted seed | 0.1 ppm |
| Corn, sweet, (K+CWHR) | 0.5 ppm |
| Corn, sweet, forage | 0.5 ppm |
| Corn, sweet, stover | 0.5 ppm |
| Radishes, root | 0.5 ppm |
| Radishes, tops | 0.5 ppm |

Meat and milk tolerances for residues of cyromazine are also being requested as follows:

| | |
|---|---|
| Milk | 0.05 ppm |
| Meat, Fat and Meat by-products* | 0.05 ppm |

*of beef, goat, hogs, horses and sheep

A summary of the findings and an assessment of human risk resulting from the proposed uses are provided in this document. The hazard assessment was provided by Albin Kocialski, of RAB1 Steve Dapson of TOX2; the residue chemistry data review by Jerry Stokes, of CEB2, Joel Garbus of CEB2, William Cutchin, of RAB2 and Andrew Rathman. of RAB1; the dietary risk assessment by Andrew Rathman, RAB1; the drinking water exposure assessment by James K. Wolf, Ph.D, of EFED; the occupational exposure assessment by Jeff Evans, of RAB1.

## I. EXECUTIVE SUMMARY

HED has reviewed toxicology and residue chemistry data submitted by Novartis Crop Protection, Inc. (formerly Ciba-Geigy Corp.) in accordance with the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and 40 CFR §158, to support pending registrations containing the active ingredient (ai) cyromazine as a technical product for use as an insecticide on mangoes, onions, potatoes and for inadvertent residues on cottonseed, sweet corn and radishes.

The HED Toxicological Endpoint Selection Committee (revised document dated 1/10/97) considered the No Observed Effect Level (NOEL) in the 6-month dog feeding study (MRID 00103193) of 0.75 mg/kg/day to be the appropriate end-point for establishing the reference dose (RfD) for cyromazine. An uncertainty factor (UF) of 100 was applied to account for interspecies extrapolation and intraspecies variability. FFDCA §408 provides that EPA shall apply an additional 10-fold margin of exposure (safety) for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the data base unless EPA determines that a different margin of safety will be safe for infants and children. The Hazard Identification Assessment Review Committee recommended (see 11/4/97 memo) that the 10 X factor to account for enhanced sensitivity of infants and children be removed. For chronic dietary risk assessment, an uncertainty factor of 100 is adequate because of the following:

(I) Developmental toxicity studies showed no increases sensitivity in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits.

(ii) A two generation reproduction toxicity study in rats showed no increased sensitivity in pups when compared to adults.

(iii) The toxicology data base is complete and there are no data gaps.

On this basis the RfD was calculated to be 0.0075 mg/kg/day utilizing the 100-fold uncertainty factor. The Committee recommended that a developmental neurotoxicity study in rats **not** be required.

The cancer classification for cyromazine is E (evidence of non-carcinogenicity for humans).

Toxicological endpoints of concern have been identified for chronic dietary exposure and short-term, intermediate-term and chronic (other than cancer) occupational or residential exposure. HED recommends the following endpoint be used for risk assessment purposes: The NOEL from the 6-month dog study (MRID 00103193) of 0.75 mg/kg/day for chronic dietary risk assessments, as well as for short-term, intermediate-term, and chronic (other than cancer) occupational and residential risk assessments. Since the endpoint for occupational and residential risk assessment is from an oral study , for dermal exposure scenarios a dermal absorption factor of 8% should be used. No acute dietary risk assessment is necessary because there were no toxicological effects attributable to a single exposure (dose) observed in oral toxicity studies including the developmental toxicity studies in rats or rabbits.

Anticipated residue values of 0.01 ppm for milk and meat, fat, and meat byproducts (except kidney) of cattle, goats, hogs, horses and sheep; and 0.04 ppm for kidney of cattle, goats, hogs, horses and sheep were used for the chronic dietary risk assessment. For crops tolerance level residues (except for cabbage at 0.05 ppm) were used. Percent crop treated values were used for a few crops.

A partially refined chronic dietary exposure analysis was performed. Because cyromazine has no residential uses, the aggregate exposure risk assessment is limited to food plus water. The chronic analysis showed that exposure from the tolerances proposed in the current actions under consideration plus the established tolerances for children (1-6 years old) (the subgroup with the highest exposure) would be 82% of the RfD, while the exposure for the general U.S. population would be 48% of the RfD. Based on the chronic dietary (food) exposures and using default body weights and water consumption figures, chronic drinking water levels of concern (DWLOC) for drinking water were calculated. For chronic exposure, based on an adult body weight of 70 kg and 2 L consumption of water per day, HED's level of concern from chronic exposure in drinking water is 136 $\mu$g/L. For children (10 kg and consuming 1L water/day), our level of concern for drinking water is 13.3 $\mu$g/L. Because the estimated chronic drinking water exposure for cyromazine is 9.63 $\mu$g/L, which is one-third (1/3) of the value of the 56-day concentration

estimated with the EFED screening model GENEEC. EFED and HED management determined that this better reflects results of monitoring data. Thus the potential residues in drinking water are not greater than HED's level of concern. **Therefore, the combined exposure of chronic dietary and drinking water exposure to cyromazine would be no greater than 100% of the RfD for children or the general U.S. population.**

The drinking water values were developed for use in eco-risk assessment and represent a reasonable upper-bound estimate for eco-risk assessment. It is expected they represent an even more substantial overestimate for human health chronic risk assessments. The chronic dietary analysis is also an overestimate of dietary exposure as 100 percent of most commodities were assumed to be treated with cyromazine. Therefore, even without further refinements, HED does not consider the combined aggregate chronic dietary/drinking water risk to exceed the level of concern.

Since there is no concern with acute risk, no Margin of Exposure (MOE) was calculated for acute exposure.

Occupational exposure risk estimates do not exceed HED's level of concern. MOE's for mixer/loaders are 375 for aerial application and 1500 for ground boom. MOE's for applicators are 1500 for aerial application and 1900 for ground boom. The MOE for flaggers is 500.

To provide for the periodic evaluation of the anticipated residues and percent crop treated, the Agency will require under Section 408 (b) (2) (E) new information on those crops for which percent crop treated was used every five years as long as the proposed tolerances remain in force. Additional residue data for meat and milk will not be required since the tolerances are based on the methods limit of quantitation and not on the actual residues present which were used in the anticipated residue calculations.

**The residue and toxicological data bases are adequate to support the tolerance under consideration here for mango in terms of human health risk. The data bases are adequate to support conditional registration and time-limited tolerances for onion, green and bulb; and potato, tuber in terms of human health risk. The data bases are also adequate to support tolerances for items for which registration is not required, these include secondary residues in meat and milk, as well as indirect or inadvertent residues in cotton, undelinted seed; corn, sweet (K+CWHR); corn, sweet, forage; corn, sweet, stover and radishes, roots and tops. In the case of cottonseed, additional data are required and a time-limited tolerance should be established for this commodity.** Novartis Crop Protection, Inc. has committed to obtain additional data for cottonseed and cotton gin byproducts that have been requested.

The registrant must also submit, upon EPA's request and according to a schedule determined by the Agency, such information as the Agency directs to be submitted in order to evaluate issues related to whether cyromazine shares a common mechanism of toxicity with any other substance

and, if so, whether any tolerances for cyromazine need to be modified or revoked.

## II. BACKGROUND

Cyromazine is a member of the triazine class of chemicals. Most of the chemicals of this class of chemicals are herbicides. Cyromazine is an insecticide/larvicide and therefore use of the chemical is different than most of the other triazines. For crops, use is generally throughout the season as a foliar spray. For onions, it is used as a seed treatment and for poultry, it is used as a feed through for fecal breeding flies. The two formulations under consideration here include Trigard a 75% wettable powder in water-soluble packets and Trigard OMC also a 75% wettable powder. Trigard OMC is not in water soluble packets and is intended for the seed treatment use of onions only.

## III. SCIENCE ASSESSMENT

### A. Identification of Active Ingredient

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

Common Name: Cyromazine

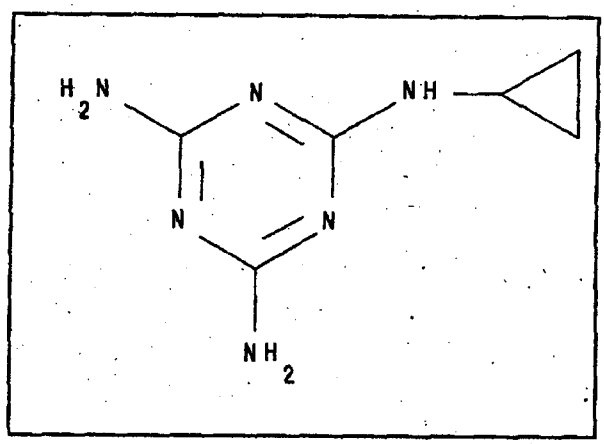
PC Code Number: 121301

CAS Registry No.: 66215-27-8

Empirical Formula: $C_6H_{10}N_6$

Molecular Weight: 166.18

Structural Formula:



## B. Human Risk Assessment

### 1. Hazard Assessment

Acute Toxicity for Cyromazine

| Guideline/Study | Results | Tox. Cat. |
|---|---|---|
| §81-1 Acute Oral Toxicity - Rat | $LD_{50}$ = 3387 mg/kg | III |
| §81-2 Acute Dermal Toxicity - Rabbit | $LD_{50}$ > 3100 mg/kg | III |
| §81-3 Acute Inhalation Toxicity - Rat | $LC_{50}$ >2.9 mg/kg | IV |
| §81-4 Primary Eye Irritation - Rabbit | Non-irritant | IV |
| §81-5 Primary Dermal Irritation - Rabbit | Mild irritant | IV |
| §81-6 Dermal Sensitization - Guinea Pig | Non-sensitizer | |

Chronic Toxicity for Cyromazine

| Guideline/Study | NOEL | LOEL |
|---|---|---|
| §83-1 6-Month chronic feeding - Dog | 30.0 ppm (0.75 mg/kg) | 300.0 ppm (7.5 mg/kg) based on decreased hematocrit and decreased hemoglobin |
| §83-1 2 Year oncogenicity feeding - Mouse | 50.0 ppm (7.5 mg/kg) | 1000.0 ppm (150.0 mg/kg) based on decreased body weight<br><br>Negative for oncogenicity in mouse at 3000.0 ppm (450.0 mg/km) |
| §83-3 Developmental - Rat | 100.0 mg/kg (maternal)<br><br>300.0 mg/kg (developmental) | 300.0 mg/kg (maternal) based on decreased body weight gain and clinical observations<br><br>600.0 mg/kg based on an increase of minor skeletal variations |

| Guideline/Study | NOEL | LOEL |
|---|---|---|
| §83-3 Developmental - Rabbit | 10.0 mg/kg (maternal)<br><br>≥ 60.0 mg/kg (developmental) HDT | 30.0 mg/kg (maternal) based on decreased body weight gain and food consumption<br><br>≥ 60.0 mg/kg (developmental) HDT (highest dose tested) |
| §83-4 2 Generation reproduction - Rat | 30.0 ppm (1.5 mg/kg) systemic<br><br>1000.0 ppm (50.0 mg/kg) reproductive effects | 1000.0 ppm (50.0 mg/kg) systemic based on decreased body weights associated with decreased food efficiency<br><br>3000.0 ppm (150.0 mg/kg) reproductive effects based on decreased body weights at birth thru weaning |
| §83-5 2 Year chronic feeding - Rat | 30.0 ppm (1.50 mg/kg) | 300.0 ppm (15.0 mg/kg) based on decreased body weights |
| §83-5 2 Year oncogenicity feeding - Rat | > 3000.0 ppm (150.0 mg/kg) Highest dose tested (HDT) - negative for oncogenicity at 3000.0 ppm (150.0 mg/kg) | |

**2. Dose Response Assessment**

**a. Special Sensitivity to Infants and Children**

FFDCA Section 408 provides that EPA shall apply an additional 10-fold margin of safety for infants and children in the case of threshold effects to account for pre- and post-natal toxicity and the completeness of the data base unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA risk assessment either directly through use of a margin of exposure analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans. In either case, EPA generally defines the level of appreciable risk as exposure that is greater than 1/100 of the no observed effect level in the animal study appropriate to the particular risk assessment. This 100-fold uncertainty (safety) factor/margin of exposure (safety) is designed to account for inter-species extrapolation and intra-species variability. HED believes that reliable data support using the 100-fold margin/factor, rather than the 1000-fold margin/factor, when EPA has a complete

data base under existing guidelines, and when the severity of the effect in infants or children, the potency or unusual toxic properties of a compound, or the quality of the data do not raise concerns regarding the adequacy of the standard margin/factor.

The HED Hazard Identification Assessment Review Committee met on October 28, 1997 to evaluate the toxicological data base of cyromazine with special reference to the reproductive, developmental and neurotoxicity data. These data were re-reviewed specifically to address the sensitivity of infants and children from exposure to cyromazine as required by the Food Quality Protection Act (FQPA) In addition, the Committee also reassessed the doses and endpoints selected for acute dietary, chronic dietary (RfD) as well as occupational and residential risk assessments. The findings of this meeting are reported in a memorandum dated Nov. 4, 1997.

The Committee determined that a UF of 100 is adequate because

(i) Developmental toxicity studies showed no increased sensitivity in fetuses as compared to maternal animals following *in utero* exposures in rats and rabbits.

(ii) A two generation reproduction toxicity study in rats showed no increased sensitivity in pups when compared to adults.

(iii) The toxicology data base is complete and there are no data gaps.

Based upon a review of the currently available data base for Cyromazine, a developmental neurotoxicity study in rats was not recommended by the Committee. This determination was based upon the following evidence:

- The chemical class (triazine) does not generally target the central or peripheral nervous system.
- No indication of abnormalities in the development of the fetal nervous system, was observed in the prenatal developmental toxicity studies in either rats or rabbits, at maternally toxic oral doses up to 600 or 60 mg/kg/day, respectively.
- Clinical observations of inactivity and hyperactivity were noted in the prenatal developmental toxicity study in rats which was dosed by gavage, and an absolute brain weight decrease (not related to histopathology) was noted in the 2-year chronic study in rats. However, no other neurotoxic effects were observed in the clinical observation data, brain weights, or histopathology (nonperfused) of the nervous system in the subchronic and chronic toxicity studies with Cyromazine in several species.

## 3. Toxicological Endpoints

Based upon a review of the toxicology database for cyromazine, by the Toxicology Endpoint Selection (TES) Committee on November 7, 1995 and the Hazard Identification Assessment Review Committee on October 28, 1997, toxicology endpoints and dose levels of concern have been identified for use in risk assessments corresponding to the categories below.

### a. Acute Dietary (One Day)

There were no toxicological effects attributable to a single exposure (dose) observed in oral toxicity studies including the developmental toxicity studies in rats or rabbits. Therefore, a dose and an endpoint was not selected for this risk assessment.

### b. Chronic Dietary [Reference Dose (RfD)]

The study selected for the RfD was a 6-month toxicity (dog) (guideline §82-1b), MRID No. 00103193. Groups of male and female beagle dogs (4/sex/dose) were fed diets containing cyromazine at 0, 30, 300 or 3000 ppm (0, 0.75, 7.5 or 75 mg/kg/day, respectively) for 6 months. No treatment-related effects were observed in survival, clinical signs or body weight parameters. Pronounced effects on hematological parameters, were manifested as decreases in hematocrit and hemoglobin levels at 300 and 3000 ppm. The NOEL was 30 ppm (0.75 mg/kg/day) and the LOEL was 300 ppm (7.5 mg/kg/day) based on pronounced alterations in hematological parameters. The RfD was calculated to be 0.0075 mg/kg/day using an UF of 100. A 100 UF is adequate because; 1) the developmental toxicity studies showed no increased sensitivity in fetuses and compared to maternal animals following *in utero* exposures in rats and rabbits, 2) a two generation reproduction toxicity study in rats showed no increased sensitivity in pups when compared to adults, and 3) the toxicology data base is complete and there are no data gaps.

### c. Short Term, Intermediate Term and Chronic (Non-Cancer) Occupational and (dermal and inhalation)

Short term (1-7 days), intermediate term (7 days to several months) and chronic endpoints of concern were identified. The NOEL of 0.75 mg/kg/day from the 6 month feeding study in beagle dogs (MRID 00103193) was selected as the endpoint to be used for all exposure periods. This is based treatment related decreases in hematocrit and hemoglobin at the 7.5 mg/kg/day dose. Toxicity endpoints are established for the active ingredient for short-term, intermediate-term, and chronic occupational or residential exposure. A no observed effect level (NOEL) of 0.75 was selected from a six month dog feeding study in which pronounced hematological parameters were manifested as decreases in hematocrit and hemoglobin levels. These effects were observed during the first week of the study and were maintained throughout the study. An UF/MF of 100 is considered appropriate for this chemical. The UF is based on 100 to account for interspecies extrapolation and intraspecies variability. The factor of 100 (margin of exposure for occupational/residential exposures) is adequate because; 1) the developmental toxicity studies

showed no increased sensitivity in fetuses and compared to maternal animals following *in utero* exposures in rats and rabbits, 2) a two generation reproduction toxicity study in rats showed no increased sensitivity in pups when compared to adults, and 3) the toxicology data base is complete and there are no data gaps. Since an oral NOEL was selected, a dermal absorption factor of 8%, should be used in risk assessments. This dermal absorption factor was obtained from a 7.75% dermal absorption observed at 10 hours post treatment in a dermal absorption study. The dose identified for inhalation risk assessment from an oral study. Therefore; 1) the inhalation exposure component (i.e., mg/L) using a 100% absorption rate (default value) should be converted to a dose (mg/kg/day), 2) the dermal exposure component (i.e. mg/kg/day) using 8% dermal absorption may be combined with this converted dose (mg/kg/day), 3) this dose should then be compared to the oral NOEL of 0.75 mg/kg/day to calculate the Margin of Exposure.

d. Cancer Classification

Cyromazine has been classified a Group E (evidence of non-carcinogenicity for humans) chemical by the Cancer Peer Review Committee.

Summary of Toxicological Endpoints for Cyromazine

| Exposure Duration | Exposure Route | Endpoint and Toxicological Effect |
|---|---|---|
| Acute | Dietary | No effects attributable to a single dose. Therefore, no dose and endpoint were selected for risk assessment. |
| Short-Term (1-7 days) Occupational/Residential | Dermal/Inhalation[1] | NOEL: 0.75 mg/kg/day (decreases in hematocrit and hemoglobin levels at the 7.5 and 75 mg/kg/day dose levels in the 6-month dog study) |
| Intermediate-Term (one week to several months) Occupational/Residential | Dermal/Inhalation[1] | NOEL: 0.75 mg/kg/day (decreases in hematocrit and hemoglobin levels at the 7.5 and 75 mg/kg/day dose levels in the 6-month dog study) |

| Exposure Duration | Exposure Route | Endpoint and Toxicological Effect |
|---|---|---|
| Chronic-Term (greater than several months) Occupational/Residential | Dermal/Inhalation[1] | NOEL: 0.75 mg/kg/day (decreases in hematocrit and hemoglobin levels at the 7.5 and 75 mg/kg/day dose levels in the 6-month dog study) |
| Cancer | Dietary/Dermal/Inhalation[1] | Classified as E (evidence of non-carcinogenicity for humans) |
| Chronic (non-cancer) | Dietary | NOEL: 0.75 mg/kg/day (decreases in hematocrit and hemoglobin levels at the 7.5 and 75 mg/kg/day dose levels in the 6-month dog study) |

[1]The NOEL selected is from an oral study and therefore conversion to equivalent dermal and inhalation doses using appropriate absorption rates for there routs (i.e., 8% absorption for dermal and 100% for inhalation) was performed.

4. Dietary Exposure and Risk Assessment/Characterization

**a. Dietary Exposure (Food sources)**

**i. Directions for Use**

For potatoes, cyromazine is formulated as Trigard, a 75% WP, containing 75% cyromazine and is packaged as water-soluble packets. The product can be used for treatment of Colorado Potato Beetle or Leafminers. For Colorado Potato Beetle, Trigard is an insect growth regulator and is most effective for control of first and second instar larvae. Trigard does not control the adult beetles. Trigard is to be applied at 1/6 lb. (2.66 oz.) to 1/3 lb. (5.3 oz.) per acre as a foliar spray at beginning of egg hatch, using the higher rate for heavier infestations. If necessary, a second application may be made 10 to 14 days later. The product is to be applied is sufficient water for full coverage of the foliage by ground equipment and a minimum of 5 gallons of water per acre when applying by air. For Leafminers, Trigard is to be applied at the rate of 1/6 lb. (2.66 oz) per acre as a foliar spray. Use sufficient water to obtain full coverage by ground equipment and a minimum of 5 gallons of water per acre by air. Applications may be repeated at 7-day intervals or as necessary to maintain good control. A maximum of 2/3 lb. (0.5 lb. active ingredient) may be applied per acre per year. There is a 7-day PHI.

For onions, green and dry, cyromazine is formulated as Trigard OMC, as 75% WP, containing

75% cyromazine. The product is for control of onion maggots. The product is to be applied to the seed at the rate of 6.6 lbs. of product per 100 lbs. seed (4.95 lbs. active ingredient per 100 lbs. of seed). There is a PHI of 60-days.

For mangoes, English translation of the Mexican label was provided. The proposed use directions state that the product is to be applied to mangoes starting when the fruits are 1 inch long. The product is applied at a rate of 20-25 g (15-18.75 g active ingredient)/100 L at a volume of 500 l/ha. Including a feed attractant, hydrolyzed protein, in the spray is recommended to encourage consumption of the product by larvae. The product may be applied up to a maximum of 5 times per season at 15 day intervals with a 15 day PHI.

**ii. Nature of the Residue - Plants**

Studies for [$^{14}$C-(U)-triazine]-cyromazine metabolism in celery, lettuce, and tomato have been reviewed. These studies are summarized below. Identification of isolated residues in all studies was accomplished by thin layer chromatography (TLC) using co-chromatography techniques with 14C reference compounds of parent cyromazine and metabolite melamine. Additional reference compounds were not tested.

**Celery**

Celery crops were treated either by multiple foliar sprays or grown in soil amended with [U-ring-$^{14}$C]-cyromazine. Celery was harvested at maturity. In the study with the treated soil celery, the treatment rate of 0.9 lb a.i./A reflects the maximum expected runoff from celery spray treated 12 times at the use rate of 0.125 lb a.i/A.

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 was 60% (0.45 ppm) and melamine was 11% (0.08 ppm) of the residue. In the mature celery cyromazine was 43% (0.15 ppm) and melamine was 30% (0.10 ppm) of the radioactive residue.

**Head Lettuce**

Head lettuce crops were treated by multiple foliar sprays [U-ring-$^{14}$C]-cyromazine. Crops were harvested at maturity. Lettuce was treated at either 0.375 lb. a.i./A or at 1 lb. a.i./A. There was a 7-day PHI after the last treatment. From the 0.375 lb. rate cyromazine was 56% (1.43 ppm) and melamine was 16% (0.41 ppm) of the residue. From the 1 lb. rate cyromazine was 74% (2.72 ppm) and melamine was 11% (0.41 ppm) of the residue.

**Tomato**

Tomato crops were treated with [U-ring-$^{14}$C]-cyromazine. The formation of melamine is rapid as at the 0-day PHI some 11% of the residue is malamine, but cyromazine is the dominant residue.

At day 7 cyromazine residue had decreased and melamine residue increased. The residue profile changed only slightly at 14 days PHI. By 6 weeks the cyromazine portion of the total residue had dropped and melamine residue continued to increase. Residues of cyromazine ranged from a maximum of 76% of the residue to a low of 37% of the residue with residues of melamine ranging from 11-44% of the residue.

The HED Metabolism Committee met to discuss cyromazine on 11/4/97. The conclusion of the committee was that only residues of cyromazine need to be regulated and used for risk assessment at this time.

**iii. Nature of the Residue - Livestock**

**Ruminants**

CIBA-GEIGY has submitted an animal metabolism study entitled, "Metabolism of [Triazine-14C]-Cyromazine in Lactating Goats", by Nicholas J. Tortora, 12/3/91, MRID# 422243-02.

Two lactating goats were dosed once daily with 150 mg of uniformly triazine ring-labeled 14C cyromazine, 42.9 μCi/mg) for four days. Goat #1 received 107 ppm; Goat #2 (Goat #85) received 75 ppm. Identification of the various metabolites was made by TLC, with MS confirmation. Residues in milk samples were analyzed by HPLC/LSC. Milk solids containing residues which were not released by the methanol were dissolved in water; however, these residues were not characterized.

Liver samples from both goats were analyzed by HPLC/LSC. Most of the residues were released in this initial extraction. Bound components were reextracted before a final combustion analysis of the remaining residue. Kidney and tenderloin samples were extracted in the same as the liver samples, with the exception that the bound residues were not reextracted. Omental fat samples were extracted initially in hexane, but only 0.85% of the activity was extracted. Samples were then extracted with acetonitrile, which released 97% of the activity.

In several cases (notably milk and fat samples) there were large portions of the extracted activity that were not characterized or identified. However, examination of the chromatograms shows that there are no unidentified peaks at levels exceeding the trigger values (10% TRR/0.05 ppm). Also, greater than 10% of the TRR was found in bound residues in both milk and liver samples. Bound residues in milk were released by dissolving the solids in water; bound residues in liver were released by the sequential use of acetonitrile, acetone, water, and methanol. Adequate steps were taken to release these residues.

The major residues in milk, meat, and meat by-products (except liver and kidney) are cyromazine and melamine. The major residues in liver and kidney are cyromazine, melamine, and 1-methylcyromazine.

**Poultry**

A 14C-cyromazine study in poultry had laying hens fed 5 ppm of 14C-cyromazine for 7 days. The egg whites had 0.09 ppm to 0.22 ppm of 14C-cyromazine equivalents and the egg yolks had 0.08 ppm to 0.15 ppm of 14C-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 egg white contained 25% melamine and 58% cyromazine. The egg yolk contained 5% melamine and 69% cyromazine. The cyromazine metabolic pathway in poultry is the same as in plants. The major residues are cyromazine and melamine. The study was not analyzed for 1-methyl cyromazine. However, HED does not expect this residue in poultry. HED concludes that it is a metabolite with ruminants only.

The HED metabolism Committee met to discuss cyromazine on 11/4/97. The conclusion of the committee was that only residues of cyromazine need to be regulated and used for risk assessment at this time.

**iv. Residue Analytical Methods**

Methods AG-408 and AG-417A are the tolerance enforcement methods as published in PAM, Vol II. These methods combined, and with minor modifications is Method AG-621. The residue data on the treated crops was analyzed by these methods. The crop matrix is extracted at reflux in methanol:water, acidified after cooling with dilute acid, partitioned with organic solvents, and then the water solubles are passed through an ion exchange column and a silica gel column for final cleanup before GLC analysis. The limit of quantitation is 0.05 ppm for cyromazine and 0.05 ppm for melamine expressed as cyromazine equivalents. These extraction and cleanup procedures are similar to the Methods AG-408 and AG-417, but AG-621 uses a gas chromatography for analysis, while the other methods use high pressure liquid chromatography for determination of cyromazine and melamine levels in the crop matrix.

Methods AG-408 and AG-417 as listed in FDA's Pesticide Analytical Manual (PAM), Vol-II are adequate to enforce the proposed tolerance. AG-621 is acceptable to support the crop field trial residue data for cyromazine and its melamine metabolite on RAC's.

Secondary residues of cyromazine, melamine, and 1-methylcyromazine could occur in animal commodities from the feeding of potato culls, potato processed waste, sweet corn forage and stover.

The petitioner has used method AG-403 to analyze residues in meat and milk. EPA has validated this method in the Agency laboratory for chicken meat and eggs. This method is very similar to the Method I in PAM II referenced in the petitioner submissions as AG-417 or AG-417A. The only major difference between the two methods is the use of a gel permeation chromatography (AG-403) vs. ion exchange chromatography (AG-417) for additional sample cleanup after the first ion exchange chromatographic sample cleanup common to both methods.

Method AG-403 has been radiovalidated for milk from a 14C goat metabolism. Method AG-403 is referenced as MRID#00128232 in the Agency files. The method AG-403 allows detection of cyromazine and melamine residues in milk at 0.01 ppm.

The PAM II enforcement method for the determination of cyromazine and melamine residues limit of quantitation (LOQ) is 0.05 ppm for each compound in meat, fat, and meat byproducts. Based on the estimation of expected cyromazine residues in animal commodities (See discussion Meat, Milk, Poultry, and Eggs, this memo), residues would be below the LOQ.

**v. Multiresidue Methods**

Data for cyromazine and its metabolites melamine and 1-methylcyromazine through the FDA multiresidue methods have been previously submitted for the FDA Pesticide Analytical Manual. Melamine and 1-methylcyromazine are not recovered by these methods. Cyromazine gives marginal recovery using Protocol D.

**vi. Storage Stability Data**

Storage stability data have been previously submitted for other crops and reviewed (See memo 01/28/87, A. Smith). 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. Samples removed from storage and reanalyzed reflected no significant changes in the residues. Residues of cyromazine and melamine are stable in frozen storage for at least 24 months. The treated potato field trial samples in this petition were stored from 5.5 to 12 months. The existing storage stability data for the listed crops are adequate to support the proposed use.

**vii. Crop Field Trials**

**Mangoes (MRID# 4344703-01-08)**

Data from six field trials conducted in Mexico showed residues of cyromazine ranging from 0.04 (below the limit of quantitation) to 0.25 ppm on day 0 and from <0.03 (non-detectable) to 0.10 ppm on day 28. No melamine residues were found in any sample. These results are contained in the data review of W. Cutchin (PP# 5E4450, 5/3/95). Therefore, the proposed tolerance level of 0.3 ppm is adequate.

**Onions (MRID# 437631-01)**

Data for onions (green and dry bulb) were submitted in connection with PP# 5F4576 and discussed in detail in the J. Stokes review dated 7/9/96. A total of eleven trials at the 1 and 2X application rate were submitted. Maximum cyromazine residues on green onions from the 1X

rate were 1.7 ppm and from the 2X rate were 2.0 ppm. Cyromazine residues in dry bulb onions were a maximum of 0.06 ppm at the 1 rate and <0.05 ppm at the 2X rate. From these data we conclude that the proposed tolerance levels for onion, green at 2.0 ppm and for onion, bulb at 0.1 ppm are adequate.

**Potatoes (MRID#'s 438262-02 and 438262-03)**

Data for potatoes were reviewed in the J. Stokes memo of 9/12/96 in connection with PP# 6F4613. Residue levels in samples from field trials using the proposed 0.75 lb a.i./A (1X) rate show average cyromazine residues of 0.23 ppm. The maximum value detected in the 1X samples was 0.75 ppm. Samples from the other application rates (0.75X-5X) show a fairly linear relationship with estimated (calculated) values of cyromazine residues all falling below 0.8 ppm. As a result, we conclude that the proposed tolerance of 0.8 ppm for potato, tuber is adequate.

**Cottonseed (MRID# 436944-01)**

The tolerance request for cottonseed is for inadvertent residues when cotton is planted as a rotational crop. A detailed review of the data is contained in the W. Cutchin memo of 2/15/96 of PP# 5F4546. Data are available from five studies conducted in CA(2), AZ(2) and TX. These studies show no detectable residues of cyromazine (<0.05 ppm) from a 1X application. These data were found deficient in that there were an inadequate number of studies and there were no data available for cotton gin byproducts (commonly called cotton gin trash). In a more recent review of this petition request (A. Rathman, 12/11/97), we had no objections to a time-limited rotational crop tolerance for residues of cyromazine 0.1 ppm noting the need for additional residue data and data for cotton gin byproducts for a permanent tolerance. The proposed time-limited rotational tolerance of 0.1 ppm is adequate. The company has committed to conduct the additional residue trials and obtain data for cotton gin byproducts requested in previous reviews.

**Sweet Corn and Radishes**

The data for sweet corn and radishes were originally reviewed in 1987 by A. Smith. Data of the level of parent vs. the metabolite melamine are not available in the branch files at this time. Therefore, we will use the levels found acceptable in the J. Garbus review of PP# 6F3332, 8/26/96 for the DRES calculations; these levels are also acceptable for tolerance setting purposes. These levels are the following:

| | |
|---|---|
| Corn, sweet (K+CWHR) | 0.50 ppm |
| Corn, sweet, forage | 0.50 ppm |
| Corn, sweet, stover | 0.50 ppm |
| Radishes, root | 0.50 ppm |
| Radishes, tops | 0.50 ppm |

**viii. Processed Food/Feed**

Processing studies were conducted where potatoes were processed into wet and dry peel, potato chips and potato granules. Average concentration factors for the various processed products were calculated to be the following: Wet peel - 0.4; dry peel - 3; potato chips - 1.7; potato granules - 2.4. Since the concentration factors for potato chips and potato granules were greater than 1, we used the highest average residue in the field trials (HAFTA = 0.48) to multiply by the mean concentration factors for these processed commodities to determine the highest expected residue in the processed items.

| | |
|---|---|
| Potato chips | 0.48 ppm x 1.7X = 0.8 ppm |
| Potato granules | 0.48 ppm x 2.4X = 1.15 ppm |

Since the maximum expected residue in potato chips is the same as the tolerance level required, no tolerances is needed for this processed commodity. For potato granules the concentration factor is below the 1.5X value that is generally used for setting tolerances for processed commodities.

**ix. Meat, Milk, Poultry, Eggs**

**Meat and Milk**

The only significant animal feed items from either published or proposed tolerances are potato culls, processed potato waste and sweet corn forage and stover. Since none of these items are fed to poultry, the established poultry tolerances need only be reevaluated on the basis of the established feed through use of Larvadex. Secondary residues could occur in meat, fat and meat byproducts of animals and in milk. Animal diets and the dietary burden to animals was discussed in detail in the J. Stokes review of PP# 6F4613, 9/12/96. At that time alfalfa was also a significant feed item, but has been removed from consideration (A. Rathman review dated 11/13/97). We have reexamined the animal diets considering only potato culls and sweet corn forage since this results in the highest dietary burden and find that maximum dietary burden for diary cattle would be 2.4 ppm and for beef cattle the maximum level would be 3.4 ppm; see the following table:

| COMMODITY | PERCENT DM | PERCENT IN DIET | LEVEL IN COMMODITY, ppm | DAILY DIETARY BURDEN |
|---|---|---|---|---|
| BEEF CATTLE | | | | |
| Potato culls | 20 | 75 | 0.8 | 3.0 |

| | | | | |
|---|---|---|---|---|
| Sweet corn forage (rotational) | 30 | 25 | 0.5 | 0.4 |
| | | | Total | 3.4 |
| DAIRY CATTLE | | | | |
| Potato culls | 20 | 40 | 0.8 | 1.6 |
| Sweet corn forage (rotational) | 30 | 50 | 0.5 | 0.8 |
| | | | Total | 2.4 |

A ruminant feeding study has been reviewed (R. Lascola, 4/2/93). In this study residues in milk appeared to plateau by day seven. Residue analyses were conducted for parent and the metabolites melamine and 1-methylcyromazine. Since the metabolism committee has determined that only residues of cyromazine need be considered in animal commodities unless the dietary burden to animals increases significantly, we have calculated the levels of cyromazine that might be present in milk, meat, liver and kidney. Very little residues were detected in fat, regardless of feeding level. Residue levels increase with increasing feeding levels and appear to be linear for milk and tissues (except fat). The table below shows the feeding levels and the amount of cyromazine detected along with calculations on the level of cyromazine to be expected for milk, meat, liver and kidney from the maximum dietary burdens from the table above.

| MEASURED RESIDUES FROM 10, 50, AND 100 PPM FEEDING LEVELS VS. CALCULATED VALUES | | |
|---|---|---|
| Feeding level, ppm | Cyromazine residues detected | Calculated levels from 2.4 ppm dairy diet and 3.4 ppm beef cattle diet |
| Milk (Day 7) | | |
| 10 | <0.04 | <0.02 |
| 50 | 0.20 | 0.01 |
| 100 | 0.50 | 0.01 |
| Meat (Day 28) | | |
| 10 | <0.05 | <0.02 |
| 50 | 0.12 | 0.01 |
| 100 | 0.25 | 0.01 |
| Liver (Day 28) | | |
| 10 | <0.05 | <0.02 |

| MEASURED RESIDUES FROM 10, 50, AND 100 PPM FEEDING LEVELS VS. CALCULATED VALUES | | |
|---|---|---|
| Feeding level, ppm | Cyromazine residues detected | Calculated levels from 2.4 ppm dairy diet and 3.4 ppm beef cattle diet |
| 50 | 0.12 | 0.01 |
| 100 | 0.21 | 0.01 |
| Kidney (Day 28) | | |
| 10 | 0.09 | 0.03 |
| 50 | 0.66 | 0.04 |
| 100 | 0.80 | 0.03 |

The following proposed tolerance levels for residues of cyromazine are adequate: 0.05 ppm for milk; 0.05 ppm for meat, fat and meat byproducts of cattle, goats, hogs, horses, and sheep. These levels are based on the limit of quantitation of the analytical method and overstate the actual maximum residues likely to be present in milk and animal tissues. As a result, the following anticipated residues should be used for chronic risk assessment: 0.01 ppm for milk; 0.01 ppm for meat, fat and meat byproducts (other than kidney) of cattle, goats, hogs, horses and sheep. With a level of 0.04 ppm in the kidney of cattle, goats, hogs, horses, and sheep.

**Poultry**

For eggs and chicken tissue, the currently established tolerances should be revised by removing Section 180.414 (c) which is for residues of melamine in poultry tissue. The tolerances would be 0.25 ppm for eggs and 0.05 ppm for poultry meat, fat, and meat byproducts (from chicken layer hens and chicken breeder hens only). There are no poultry feed items that would require the poultry and egg tolerances to be raised. These tolerances are based on the feed through use of Larvadex.

**x. Water, Fish, and Irrigated Crops** - Not applicable

**xi. Food Handling** - Not applicable

**xii. Confined Accumulation in Rotational Crops**

Cyromazine is persistent in soils and residues will be present in many crops that are rotated to treated crops. Field studies have been submitted for a number of crops and tolerances are being proposed. For those crops with no tolerances established, a one year plant back interval is specified on the label.

### xiii. Field Accumulation in Rotational Crops

Rotational crop tolerances are being requested for cottonseed, sweet corn (K+CWHR), sweet corn forage and stover as well as radish, roots and tops (leaves). For a discussion of the data see under the Crop Field Trials section of this review.

### xiv. Tolerance Reassessment Table

Since the metabolite melamine is being removed from the tolerance expression, all established tolerances will need to be reevaluated at reregistration. We have commented only on the poultry tolerances in this review since residues of the parent and metabolite are in different subsections of the regulation.

### xv. Anticipated Residues

Meat and Milk: Tolerance levels are being set on the basis of the limit of quantitation of the analytical method. Even using maximum diets, residues in milk and animal tissues will not exceed 0.01 ppm (except for kidney). For kidney a value of 0.04 ppm is appropriate Percent crop treated values for sweet peppers (6%), tomatoes (28%), celery (27%), leaf lettuce (1%), lettuce unspecified (4%), and head lettuce (3%) were used in the DRES analysis. Tolerance levels were used for all crops except for cabbage at 0.05 ppm.

## b. Dietary Exposure (Drinking Water Sources)

### i. Ground Water

Based on review of environmental fate data (requirements listed under 40 CFR §158.290) by EPA's Environmental Fate and Effects division (EFED), cyromazine is somewhat mobile. Ground water estimates were made by James K. Wolf, Ph. D. of the Environmental risk Branch III using the SCI-GROW model.. The assumption of 6 applications of 0.125 lbs ai/A resulted in a calculated value of 1.6 $\mu$g/L.

### ii. Surface Water

Surface water estimates were also made by James K. Wolf, Ph. D. using the EFED GENEEC model. The assumptions of 6 applications of 0.125 lbs ai/A and three soil aerobic half-lives resulted in a calculated value of 28.9 $\mu$g/L. EFED and HED management have determined that this value devided by 3, better represents monitoring data. Thus 9.6 $\mu$g/L was used in HED's dringing water assessment. Three aerobic soil metabolism half-life values; 150, 300 and 450 days were used in the calculations. Since little difference in estimated concentrations were obtained, HED used the 450 day half-life, since it is the most conservative. Only a single soil aerobic metabolism half-life value of 150 days was actually available. When a single value is available EFED multiplies the single value times 3 (450 days) to consider uncertainty. The 300

days was considered to show that modle was generally insensitive to these long half-lives (≥ 150 days). No data were available for aquatic degradation, so it was not considered. Aquatic degradation would further reduce cyromazine concentrations in surface water.

**α Dietary Risk Assessment and Characterization**

**i. Chronic Risk**

A chronic dietary risk assessment is required for cyromazine. The RfD used for the chronic dietary analysis is 0.0075 mg/kg bwt/day.

Anticipated residue values for cyromazine of 0.01 ppm in milk and meat (other than kidney) and 0.04 ppm in kidney were used for this dietary risk assessment.

Chronic dietary exposure estimates (DRES) for cyromazine are summarize in Attachment I (run dated //). The DRES analysis utilized the anticipated residues calculated from field trial data for potatoes and animal commodities. The analysis also used percent crop treated for sweet peppers (6%), tomatoes (28%), celery (27%), leaf lettuce (1%), lettuce unspecified (4%), and head lettuce (3%). For all other crops, the value of 100% crop treated was used. The proposed and established cyromazine tolerances result in an Anticipated Residue Contribution (ARC) that is equivalent to the following percents of the RfD:

| | |
|---|---|
| U.S. Population | 47% |
| Hispanics | 42% |
| Non-Hispanics Others | 60% |
| Non-Nursing Infants (<1 year old) | 76% |
| Females (13+ years, nursing) | 48% |
| Children (1-6 years old) | 81% |
| Children (7-12 years old) | 65% |

The subgroups listed above are: (1) the U.S. population (48 states); (2) infants and children; and, (3) other subgroups for which the percentage of the RfD occupied is equal to, or greater than, that occupied by the subgroup U.S. population (48 states).

This chronic analysis for cyromazine is an over-estimate of dietary exposure with 100 percent of most of the commodities treated with cyromazine. Additionally, most of the residue values for crops include the metabolite melamine which is no longer of toxicological concern. This also results in an over-estimate of the risk. HED does not consider the chronic dietary risk to exceed the level of concern.

**ii. Carcinogenic Risk**

In accordance with the EPA proposed Guidelines for Carcinogenic Risk Assessment (April 10,

1996), cyromazine was characterized as "evidence of non-carcinogenicity for humans".

**iii. Acute Dietary Risk**

There were no toxicological effects attributale to a single exposure (dose) observed in oral toxicity studies including the developmental toxicity studies in rats or rabbits. Therefore, a dose and an endpoint was not selected for this risk assessment.

**iv. Drinking Water Risk (Chronic)**

OPP has calculated drinking water levels of concern (DWLOCs) for chronic (non-cancer) exposure to cyromazine in surface and ground water, the drinking water levels of concern are 136, 153, 13, and 146 ppb for the U.S. Population, Females, Children, and Males, respectively. To calculate the DWLOC for chronic (non-cancer) exposure relative to a chronic toxicity endpoint, the chronic dietary food exposure (from DRES) was subtracted from the RfD to obtain the acceptable chronic (non-cancer) exposure to cyromazine in drinking water. DWLOCs were then calculated using default body weights and drinking water consumption figures. Cyromazine has no residential uses; therefore, aggregate exposure is limited ot food plus water.

Estimated maximum concentrations of cyromazine in surface and ground water are 10 and 1.6 ppb, respectively. Estimated average concentrations of cyromazine in surface and ground water are 9.6 and 1.6 ppb, respectively. [Note: For the purposes of the screening-level assessment, the maximum and average concentrations in ground water are not believed to vary significantly.] The estimated average concentrations of cyromazine in surface and ground water are less than OPP's levels of concern for cyromazine in drinking water as a contribution to chronic aggregate exposure. Therefore, taking into account the present uses and uses proposed in this action, OPP concludes with reasonable certainty that residues of cyromazine in drinking water (when considered along with other sources of exposure for which OPP has reliable data) would not result in unacceptable levels of aggregate human health risk at this time.

OPP bases this determination on a comparison of estimated concentrations of cyromazine in surface waters and ground waters to back-calculated "levels of concern" for cyromazine in drinking water. These levels of concern in drinking water were determined after OPP has considered all other non-occupational human exposures for which it has reliable data, including all current uses, and uses considered in this action. The estimates of cyromazine in surface and ground waters are derived from water quality models that use conservative assumptions (health-protective) regarding the pesticide transport from the point of application to surface and ground water. Because OPP considers the aggregate risk resulting from multiple exposure pathways associated with a pesticide's uses, levels of concern in drinking water may vary as those uses change. If new uses (including crop or residential) are added in the future, OPP will reassess the potential impacts of cyromazine on drinking water as a part of the aggregate risk assessment process.

**d. Statement of the adequacy of the dietary exposure data base to assess infants' and children's exposure**

The dietary (food and water) exposure data base for cyromazine is adequate to assess infants' and children's exposure.

**5. Occupational and Residential Exposure Risk**

**a. Occupational and Residential Exposure**

**i. Summary of Use Patterns and Formulations: Occupational and Residential**

The information in two tables below is taken from Trigard 75% WP (enclosed in water soluble packets) and other sources as cited.

Registration Request for Use of Trigard in/on potatoes.

| Factors | Comments |
|---|---|
| Crop to be treated | potato |
| Pests | Colorado potato beetle |
| Application methods | Foliar applications using aerial and groundboom equipment. Aerial applications are suggested when ground conditions prohibit application by ground equipment. |
| Application rate | For leafminers and at the beginning of egg hatch for Colorado potato beetle - 0.125 lb ai per acre and 0.25 lb ai per acre for heavy infestations of Colorado potato beetle. |
| Maximum number of applications | Not more than 0.5 lb ai/A/year. |
| Percent Absorption | 8 percent [MRID 40168601] |
| Estimated Acreage of Application per Day | **Aerial** - 350, and **Ground boom** - 80 acres[1] |
| Manufacturer | Novartis Crop Protection, Inc. |

[1] The estimate of acreage used in this assessment of worker exposure are standard defaults representing acreage for aerial and ground boom applications to large scale production areas for potato production.

Registration Request for Use of Trigard in/on onions.

| Factors | Comments |
|---|---|
| Crop to be treated | onions (use site also includes garlic, great-headed garlic, leeks, Welch onions and shallots) |
| Pests | Used for onion maggots in soils having organic matter greater than 10%. |
| Application methods | Commercial seed treatment. |
| Maximum application rate | 4.95 lb ai/100 pounds of seed. |
| Maximum number of treatments | not known |
| Percent Absorption | 8 percent [MRID 40168601] |
| Average pounds of seed treated per day | not known |
| Manufacturer | Novartis Crop Protection, Inc. |

Toxicity endpoints are established for the active ingredient for short-term, intermediate-term, and chronic occupational or residential exposure. A no observed effect level (NOEL) of 0.75 was selected from a six month dog feeding study in which pronounced hematological parameters were manifested as decreases in hematocrit and hemoglobin levels. These effects were observed during the first week of the study and were maintained throughout the study. A dermal absorption rate of 8 percent was identified to be used in conjunction with this oral dose. This endpoint was also selected by the Hazard Identification Assessment Review Committee for use in inhalation exposure assessments.

Risk assessments are required for short-term, intermediate-term, and chronic exposure, where appropriate. Short and intermediate term exposures are expected for the use of cyromazine on potatoes. Information regarding the frequency and duration the seed treatment use is not known. However, the endpoint is the same for all exposure durations.

| TYPE OF TOXICITY | TOXICITY CATEGORY<br>Active ingredient |
|---|---|
| Acute Oral | III |
| Acute Dermal | III |
| Acute Inhalation | IV |
| Primary Eye | IV |
| Primary Dermal | IV |
| Dermal Sensitization | non-sensitizer |

### ii. Handler Exposures and Assumptions

HED's exposure assessment is based on the assumptions in the following table.

Assumptions for Worker Exposure Assessments

| Factors | Quantities/Units |
|---|---|
| Mixer/Loader and Applicator body weight | 70 kg |
| Flagger body weight | 70 kg |
| Application rate (Seed Treatment Aerial and Groundboom) | 0.125 - 0.25 lb ai/A |
| Acres treated per day (Aerial)<br>Acres treated per day (Groundboom) | 350 acres<br>80 acres[1] |
| Applicator unit exposure from Pesticide Handlers Exposure Database (PHED); (Aerial application; liquid; closed cab; with long-pants, long-sleeved shirt, and no gloves). | Dermal - 5.0 µg/lb ai handled[2]<br>Inhalation - 0.1 µg/lb ai handled[2] |
| Applicator unit exposure from PHED; (Ground boom application; liquid; open cab; with long-pants and long-sleeved shirt. No gloves). Inhalation exposure does not assume the use of a respirator. | 14 µg/lb ai handled[2] Inhalation - 0.7 µg/lb ai handled[2] |
| Mixer/loader unit exposure from PHED, (In support of Aerial and Ground applications; use of wettable powder enclosed in water soluble packets; wearing long pants and long-sleeved shirt. No gloves). Inhalation exposure does not assume the use a respirator. | Dermal - 21 µg/lb ai handled[2]<br>Inhalation - 0.1 µg/lb ai handled[2] |

| Factors | Quantities/Units |
|---|---|
| Airblast Applicator unit exposure from PHED; open cab; wearing long pants and long-sleeved shirt. No gloves). Inhalation exposure does not assume the use of a respirator. | Dermal - 390 µg/lb ai handled[2]<br>Inhalation - 4.5 µg/lb ai handled[2] |
| Flagger unit exposure from PHED; liquid applications by aircraft; Wearing long-sleeved shirt and long pants. No gloves. Inhalation exposure does not assume the use of a respirator. | Dermal - 11 µg/lb ai handled[2]<br>Inhalation - 0.35 µg/lb ai handled[2] |
| Personal protective equipment (PPE), per label.[3] | **For all labels:** long-sleeved shirt and long pants; chemical-resistant gloves. |

[1] Standard assumptions of the acreage treated per day given the crop.
[2] Source: Pesticide Handlers Exposure Database (PHED) V1.1, Surrogate Exposure Guide (May 97).
[3]Although handeler MOE's are acceptable for this use based on surrogate data without the use of gloves. Reduced PPE are not recommended at this time.

### iii. Post-Application Exposures & Assumptions - Occupational and Residential

Post application exposure is expected for workers involved in handset irrigation equipment in potato fields as well as for crop advisors scouting potato fields. Potatoes are harvested mechanically, however individuals sorting vines and other trash from potatoes may result in lower exposures than those involved in the activites mentioned above. There is a high potential for postapplication exposure for workers harvesting mangos. Post application exposure is unlikely for the seed treatment as the pesticide treated seed will be situated below the soil surface.

### iv. Handler Exposure Assessment (includes mixer/loaders, applicators and other handlers)

The table below, summarizes the HED/RAB1 estimates for total handler exposure for mixer/loaders, applicators and flaggers in the proposed use of cyromazine on potatoes. Usage data and surrogate data are not available to assess exposure for the use of cyromazine to treat onion seed. These handler estimates are based on the assumptions outlined in the following table.

Handler Exposure to Trigard WP Insecticide

| Job Function | Average Dermal Daily Dose for Trigard WP mg ai/kg bw/day | Dermal Short & Intermediate-Term MOE |
|---|---|---|
| Mixer/loaders | Aerial - 0.002<br>Ground boom - 0.0005 | Aerial - 375<br>Ground boom - 1,500 |
| Applicators | Aerial - 0.0005<br>Groundboom -0.0004 | Aerial - 1,500<br>Groundboom - 1,900 |
| Flaggers | 0.0015 | 500 |

MOE = NOEL/ADD (where NOEL = 0.75 mg/kg/day)

The exposure estimates in the above table are based on treatment of 350 acres per day by aerial and 80 acres per day by ground boom.

The following calculations were used to determine the expected worker exposures resulting from the handling and application of cyromazine (Trigard WP) to potatoes.

Example calculation (Dermal exposure for mixer/loaders supporting aerial applications).

$$0.25 \text{ lbs. ai applied/acre} \times 350 \text{ of acres treated/day} = 87.5 \text{ lbs ai/day}$$

$$5.0 \text{ µg/lb ai handled (PHED, Version 1.1)} \times 87.5 \text{ lbs ai/day} = 437.5 \text{ µg ai/day}$$

$$\frac{437.5 \text{ µg ai/day}}{70 \text{ kg bw}} = 6.25 \text{ µg ai/kg bw/day}$$

$$\frac{6.25 \text{ µg ai/kg bw/day}}{1000 \text{ µg/mg}} = 0.00625 \text{ mg ai/kg bw/day}$$

$$0.00625 \times 8\% = 0.0005 \text{ mg ai/kg bw/day}$$

### v. Post-Application Exposure Assessment

The petitioner did not provide post-application exposure sampling data. This should be considered a data gap.

### b. Occupational and Residential Risk Assessment/Characterization

### i. Risk from Dermal and Inhalation Exposures

The Agency does not generally have an occupational or residential concern unless MOEs are below 100 when the NOEL is based upon data generated in animal studies. The 100 accounts for interspecies extrapolation and intraspecies variability. FFDCA section 408 provides that EPA shall apply an additional 10-fold margin of safety for infants and children in the case of threshold effects to account for pre-and post-natal toxicity and the completeness of the data base unless EPA determines that a different margin of safety will be safe for infants and children. The additional 10X is not necessary for cyromazine (per Hazard I.D. Comm.) due to no increased sensitivity to fetuses (rats and rabbits) and pups (rats); therefore, HED's level of concern for cyromazine are for MOEs that are below 100. There are no residential uses registered for cyromazine.

### ii. Risk From Post-Application Exposures

The interim WPS, REI is 12 hours. Registration for potatoes and onions should be considered conditional until post application reentry exposure data are required consisting of Dislodgeable Foliar Residue data (132-1a) and Dermal and Inhalation exposure data (133-3 and 133-4 respectively). Because there are other uses of cyromazine that result in post-application exposure, the registrant should consider a reentry study design addressing all post-application exposures to cyromazine.

### iii. Restricted Entry Interval

See ii, above.

Other data gaps include the generation of mixer/loader/applicator data addressing the seed treatment use of cyromazine. These guidelines are dermal exposure at an indoor site (233) and inhalation exposure at an indoor site (234). This registration should be considered conditional pending the submission of these data as well as the reentry data for potatoes.

## 6. Aggregate Exposure and Risk Assessment/Characterization

### a. Acute Aggregate Exposure and Risk

There were no toxicological effects attributale to a single exposure (dose) observed in oral toxicity studies including the developmental toxicity studies in rats or rabbits. Therefore, a dose and an endpoint was not selected for this risk assessment.

### b. Short- and Intermediate-term Aggregate Exposure and Risk

Since there are no residential uses of cyromazine, no short- and intermediate-term aggregate risk

exists for cyromazine.

**c. Chronic Aggregate Exposure and Risk**

For the U.S. Population, 48% of the RfD is occupied by dietary (food) exposure. As noted above, potential chronic exposure from drinking water is at a level below OPP's level of concern.

**7. Other Food Quality Protection Act (FQPA) Considerations**

**a. Cumulative Risk**

Section 408 of FQPA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency considers "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." While the Agency has some information in its files that may be helpful in determining whether a pesticide shares a common mechanism of toxicity with any other substances, EPA does not at this time have the methodology to resolve the scientific issues concerning common mechanism of toxicity in a meaningful way. EPA has begun a pilot process to study this issue further through the examination of particular classes of pesticides. The Agency hopes that the results of this pilot process will enable it to develop and apply policies for evaluating the cumulative effects of chemicals having a common mechanism of toxicity. At present, however, the Agency does not know how to apply the information in its files concerning common mechanism issues to most risk assessments.

In the case of cyromazine, HED has not yet determined whether or how to include this chemical in a cumulative risk assessment. These tolerance determinations therefore does not take into account common mechanism issues. After EPA develops a methodology for applying common mechanism of toxicity issues to risk assessments, the Agency will develop a process (either as part of the periodic review of pesticides or otherwise) to reexamine those tolerance decisions made earlier.

On this basis, the registrant must submit, upon EPA's request and according to a schedule determined by the Agency, such information as the Agency directs to be submitted in order to evaluate issues related to whether cyromazine share(s) a common mechanism of toxicity with any other substance and, if so, whether any tolerances for cyromazine need to be modified or revoked.

**b. Endocrine Disruption**

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other endocrine effect...". The Agency is currently working with interested stakeholders, including other government agencies, public

interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disrupter effects.

**c. Determination of Safety (U.S. Population, Infants, and Children)**

Using the exposure assumptions described above, HED has concluded that the percentage of the RfD that will be utilized by chronic dietary (food only) exposure to residues of cyromazine ranges from 17 percent for nursing infants less than one year old, up to 82 percent for children 1-6 years old. Despite the potential for exposure to cyromazine in drinking water, HED does not expect the chronic aggregate exposure to exceed 100% of the RfD. Since there are no residential uses of cyromazine, no chronic residential exposure is anticipated. RAB1 concludes that there is a reasonable certainty that no harm will result to infants and children from chronic aggregate exposure to cyromazine residues.

**8. Data Requirements**

**a. Toxicology**

There are no toxicology data gaps.

**b. Residue Chemistry**

The only residue chemistry data gap for the crops under consideration here is for cotton. The data requirements were detailed in the William Cutchin review of PP# 5F4546 dated 2/15/97. For cotton, a total of 11 field trials are required, one each in Regions 2 and 6, three in Region 4, and four in region 8. Also data on cotton gin byproducts (commonly called gin trash) are required. Until these data are submitted and reviewed, a time-limited tolerance for cottonseed is required.

To provide for the periodic evaluation of the anticipated residues and percent crop treated, the Agency will require under Section 408 (b) (2) (E) new information on those crops for which percent crop treated was used every five years as long as the proposed tolerances remain in force. Additional residue data for meat and milk will not be required since the tolerances are based on the methods limit of quantitation and not on the actual residues present which were used in the anticipated residue calculations.

**c. Occupational/Residential Exposure**

Post-application reentry exposure data are required consisting of Dislodgeable Foliar Residue data (132-1a) and Dermal and Inhalation exposure data (133-3 and 133-4 respectively). Other data gaps include the generation of mixer/loader/applicator data addressing the seed treatment

use of cyromazine. These guidelines are dermal exposure at an outdoor site (231) and inhalation exposure at an outdoor site (232). This registration should be considered conditional pending the submission of these data as well as the reentry data for potatoes. Until these data are submitted and reviewed, conditional registrations and time-limited tolerances for potatoes and onions are required.

Attachment I - DRES Run

cc: with attachment A. Rathman, DRES (B. Steinwand)
cc: without attachment PP#5E4450, 5F4576, 6F4613, 5F4546, 6F3332
RDI: Team(1/22/98),M.Morrow(3/10/98)
A.Rathman:804K:CM#2:(703)305-7330:7509C:RAB1:3/11/98

Novartis Crop Protection, Inc.
P.O. Box 18300
Greensboro, NC 27419-8300

Tel 910 632 6000

NOVARTIS

January 22,1998

Mr. George LaRocca, PM 13
Office of Pesticide Programs - H7504C
Registration Division
U.S. Environmental Protection Agency
Crystal Mall 2, 2nd Floor
Arlington, VA 22202

**SUBJECT: 1)PP#5F4576 Petition for a Tolerance for Cyromazine In or on Bulb Vegetables.**

**2)EPA December 11, 1997 Memorandum—Cyromazine in/on Various Crops and Meat and Milk. Chemical #121301**

Dear Mr. LaRocca:

As discussed with Ms. Linda Deluise on January 21,1998 the proposed tolerance (PP#5F4576) for cyromazine in or on bulb vegetables ( onions)has been revised to include only cyromazine (reference to melamine has been deleted). Also, the proposed tolerance has been changed from 3.0 ppm to 2.0 ppm for green onions and from 0.3 ppm to 0.1 ppm for dry bulb onions. This is consistent with EPA's December 11,1997 memorandum.

This submission includes:

Three (3) copies of Section 408 (d) (2) (A) (vii) of Petition # 5F4576 .

Completed Application for Pesticide Registration Form (8570-1).

We appreciate your assistance in processing this revised petition. Please contact me at (336) 632-2461 if you have any questions or comments.

Sincerely,

Richard Pence
Senior Regulatory Manager

cc:Linda DeLuise

M:\cyromazine\laroconi

*Please read instructions on reverse before completing form.*

Form Approved. OMB No. 2070-0060. Approval expires 05-31-98

United States
**Environmental Protection Agency**
Washington, DC 20460

[ ] Registration
[X] Amendment
[ ] Other

OPP Identifier Number: 250912

## Application for Pesticide - Section I

1. Company/Product Number: 100-632
2. EPA Product Manager: LaRocca
3. Proposed Classification: [ ] None [ ] Restricted
4. Company/Product (Name): Cyromazine
PM#: 13
5. Name and Address of Applicant *(Include ZIP Code)*:
Novartis Crop Protection, Inc.
P. O. Box 18300
Greensboro, NC 27419
[ ] *Check if this is a new address*
6. **Expedited Review.** In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:
EPA Reg. No. _____
Product Name _____

## Section - II

[ ] Amendment - Explain below.
[X] Resubmission in response to Agency letter dated 12/1/97
[ ] Notification - Explain below.
[ ] Final printed labels in response to Agency letter dated _____
[ ] "Me Too" Application.
[ ] Other - Explain below.

**Explanation:** Use additional page(s) if necessary. (For section I and Section II.)

Submit revised Section 408 (d)(2)(A)(vii) of PP # 5F4576 (Tolerance on Bulb Vegetables)

## Section - III

1. Material This Product Will Be Packaged In:

| Child-Resistant Packaging | Unit Packaging | | Water Soluble Packaging | | 2. Type of Container |
|---|---|---|---|---|---|
| [ ] Yes* [ ] No | [ ] Yes [ ] No | | [ ] Yes [ ] No | | [ ] Metal [ ] Plastic [ ] Glass [ ] Paper [ ] Other (Specify) |
| * *Certification must be submitted* | If "Yes" Unit Packaging wgt. | No. per container | If "Yes" Package wgt | No. per container | |

3. Location of Net Contents Information: [ ] Label [ ] Container
4. Size(s) Retail Container
5. Location of Label Directions: [ ] On Label [ ] On Labeling accompanying product
6. Manner in Which Label is Affixed to Product: [ ] Lithograph [ ] Paper glued [ ] Stenciled [ ] Other _____

## Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

| Name | Title | Telephone No. (Include Area Code) |
|---|---|---|
| Richard Pence | Sr. Regulatory Manager | (336) 632-2461 |

**Certification**

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

| 2. Signature | 3. Title | 6. Date Application Received (Stamped) |
|---|---|---|
| Richard Pence | Sr. Regulatory Manager | |
| 4. Typed Name: Richard Pence | 5. Date: January 22, 1998 | |

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete.

White - EPA File Copy (original) Yellow - Applicant Copy

## SECTION 408 (d) (2) (A) (vii)

## PROPOSED TOLERANCES FOR THE PESTICIDE CHEMICAL RESIDUE

Novartis Crop Protection hereby requests that tolerances be established for residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine) in or on the following raw agricultural commodities (RACs):

| RAC | Tolerance |
|---|---|
| Onions, green | 2.0 ppm |
| Onions, dry bulb | 0.1 ppm |

## SECTION 408 (d) (2) (A) (vii)

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| RAC | Tolerance |
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# End of Document

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

PP# 5F4576

Date 12/11/97

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: Cyromazine In/On Various Crops and Meat and Milk. Chemical # 121301.

From: Andrew R. Rathman, Chemist
Registration Action Branch I
Health Effects Division (7509C)

Through: Melba Morrow, Senior Scientist
Registration Action Branch I
Health Effects Division (7509C)

To: George Larocca, PM 13
Registration Division (7505C)

This memo covers the crop/tolerance combinations listed below. In the case of cotton, sweet corn and radishes, the tolerances are proposed as rotational crop tolerances with no purposeful use of cyromazine on those crops. The tolerance expression is for 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) in or on the following raw agricultural commodities (RACs):

| Petition Number | DP Barcode | RAC | Tolerance Level |
|---|---|---|---|
| PP# 5E4450 | D236184 | Mangoes | 0.3 ppm |
| PP# 5F4576 | D236189 | Onions, green | 3.0 ppm |
| | | Onions, dry bulb | 0.3 ppm |
| PP# 6F4613 | D236190 | Potato tubers | 1.5 ppm |
| PP# 5F4546 | D236187 | Cottonseed | 0.2 ppm |
| PP# 6F3332 | D236185 | Corn, sweet (K+CWHR) | 0.5 ppm |
| | | Corn, sweet, forage | 0.5 ppm |
| | | Corn, sweet, fodder | 0.5 ppm |
| | | Radish, root | 0.5 ppm |
| | | Radish, tops | 0.5 ppm |

In addition as part of PP# 6F3332 tolerances were proposed for residues of cyromazine and metabolite(s) in milk and tissues as listed below:

Amend §180.414(b) [residues of cyromazine alone] to include...

| | |
|---|---|
| Meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep | 0.05 ppm |
| Milk | 0.02 ppm |

Amend §180.414(c) [residues of melamine alone] to include...

| | |
|---|---|
| Meat, fat, and meat by-products of cattle, goats, hogs, horses, and sheep | 0.05 ppm |
| Milk | 0.02 ppm |

Create §180.414(e), for tolerances of 1-methylcyromazine (1-methyl-N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), calculated as cyromazine, in

| | |
|---|---|
| Liver and kidney of cattle, goats, hogs, horses, and sheep | 0.05 ppm |

These tolerance expressions were proposed in Ciba's response to review of the tomato and carrot petitions submitted on 6/10/94. They are to be found in Volume 5 of the submission containing revised Sections B and F.
[See J. Stokes, memo, 2/13/95]

[The submission of 6/10/94 contains these additional comments in regard to the proposed animal tissue tolerances.]

The petitioner has previously withdrawn the request to establish a tolerance on carrot. The exclusion of carrot from the dairy and beef cattle diets greatly reduces the need expressed previously by CBTS to increase petitioner's proposed milk tolerances of 0.02 ppm for cyromazine and 0.02 ppm for melamine to 0.05 ppm. The petitioner agrees with CBTS that the other tolerances for meat and meat by-products should be established at 0.05 ppm, and not at the petitioner's proposal of 0.1 ppm.
[See J. Stokes, memo, 2/13/95]

As part of the February 17, 1997 submission, the petitioner is requesting that the tolerance for residues of cyromazine in milk be raised to 0.04 ppm.

The HED metabolism committee met to discuss cyromazine on 11/4/97. The conclusion of the committee was that only residues of cyromazine need to be regulated and used for risk

assessment at this time. As a result of this decision, we have reevaluated the tolerance requests for the petitions currently under consideration. At some future time all the established cyromazine tolerances will need to be reevaluated to determine if the established levels are excessive because of the removal of melamine as a residue of concern.

**Conclusions**

1. As a result of the decision of the HED Metabolism Committee, the tolerance expression currently in 180.414 and in the petitions under consideration here needs to be revised to include the parent cyromazine only.

2. For those crops where purposeful use is proposed the tolerance levels need to be revised for potatoes and onions; however, the level previously proposed for mangos is acceptable since essentially all residues detected consisted of cyromazine. The following tolerances should be proposed for residues of cyromazine:

| | |
|---|---|
| Mango | 0.3 ppm |
| Onion, green | 2.0 ppm |
| Onion, bulb | 0.1 ppm |
| Potato, tuber | 0.8 ppm |

3. For those crops where inadvertent tolerances are being requested, tolerances should be established in a separate subsection as follows:

"Tolerances are established for the indirect or inadvertent residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), in or on the raw agricultural commodities when present therein as a result of the application of cyromazine to growing crops listed in paragraphs (x) of this section."

| | |
|---|---|
| Cotton, undelinted seed | 0.1 ppm |
| Corn, sweet, (K+CWHR) | 0.5 ppm |
| Corn, sweet, forage | 0.5 ppm |
| Corn, sweet, stover | 0.5 ppm |
| Radish, root | 0.5 ppm |
| Radish, tops (leaves) | 0.5 ppm |

4. No tolerances are required for the potato processing products chips and granules. Using the highest average field trial and the average concentration factor, residues in potato chips do not exceed the 0.8 ppm level required for potatoes and the concentration into potato granules is

below the 1.5X level where we generally set processed commodity tolerances.

5. For eggs and chicken tissue, the currently established tolerances should be revised by removing Section 180.414 (c) which is for residues of melamine in poultry tissue. The tolerances would be 0.25 ppm for eggs and 0.05 ppm for poultry meat, fat, and meat byproducts (from chicken layer hens and chicken breeder hens only).

6. As a result of the animal feed items potato waste and sweet corn forage being added to the animal diet at this time, the following meat and milk tolerances need to be proposed for residues of cyromazine: 0.05 ppm for milk; 0.05 ppm for meat, fat and meat byproducts of cattle, goats, hogs, horses, and sheep.

**Recommendations**

The petitioner should be requested to revise the Section F in all the petitions to remove melamine from the tolerance expression. Additionally, in many cases the levels being proposed need to be revised as a result of the removal of the metabolite melamine from consideration and the levels noted in Conclusions 2, 3 and 6 should be incorporated into the revisions.

**Detailed Considerations**

Mangoes (MRID# 4344703-01-08)

Data from six field trials conducted in Mexico showed residues of cyromazine ranging from 0.04 (below the limit of quantitation) to 0.25 ppm on day 0 and from <0.03 (non-detectable) to 0.10 ppm on day 28. No melamine residues were found in any sample. These results are contained in the data review of W. Cutchin (PP# 5E4450, 5/3/95). Therefore, the tolerance level of 0.3 ppm proposed is adequate with no revision needed.

Onions (MRID# 437631-01)

Data for onions (green and dry bulb) were submitted in connection with PP# 5F4576 and discussed in detail in the J. Stokes review dated 7/9/96. A total of eleven trials at the 1 and 2X application rate were submitted. Maximum cyromazine residues on green onions from the 1X rate were 1.7 ppm and from the 2X rate were 2.0 ppm. Cyromazine residues in dry bulb residues were a maximum of 0.06 ppm at the 1 rate and <0.05 ppm at the 2X rate. From these data we conclude that the tolerance level for onion, green should be 2.0 ppm and for onion, bulb the level should be 0.1 ppm.

Potatoes (MRID#'s 438262-02 and 438262-03)

Data for potatoes were reviewed in the J. Stokes memo of 9/12/96 in connection with PP# 6F4613. Residue levels in samples from field trials using the proposed 0.75 lb a.i./A (1X) rate

show average cyromazine residues of 0.23 ppm . The maximum value detected in the 1X samples was 0.75 ppm. Samples from the other application rates (0.75X-5X) show a fairly linear relationship with estimated (calculated) values of cyromazine residues all falling below 0.8 ppm. As a result, we conclude that the tolerance should be set at 0.8 ppm for potato, tuber.

Processing studies were conducted where potatoes were processed into wet and dry peel, potato chips and potato granules. Average concentration factors for the various processed products were calculated to be the following: Wet peel - 0.4; dry peel - 3; potato chips - 1.7; potato granules - 2.4. Since the concentration factors for potato chips and potato granules were greater than 1, we used the highest average residue in the field trials (HAFT = 0.48) to multiply by the mean concentration factors for these processed commodities to determine the highest expected residue in the processed items.

| | |
|---|---|
| Potato chips | 0.48 ppm x 1.7X = 0.8 ppm |
| Potato granules | 0.48 ppm x 2.4X = 1.15 ppm |

Since the maximum expected residue in potato chips is the same as the tolerance level required, no tolerances are needed for this processed commodity. For potato granules the concentration factor is below the 1.5X value that is generally used for setting tolerances for processed commodities.

Cottonseed (MRID# 436944-01)

The tolerance request for cottonseed is for inadvertent residues when cotton is planted as a rotational crop. A detailed review of the data is contained in the W. Cutchin memo of 2/15/96 of PP# 5F4546. Data are available from five studies conducted in CA(2), AZ(2) and TX. These studies show no detectable residues of cyromazine (<0.05 ppm) from a 1X application. These data were found deficient in that there were an inadequate number of studies and there were no data available for cotton gin byproducts (commonly called cotton gin trash). In a more recent review of this petition request (A. Rathman, 11/13/97), we had no objections to a time-limited rotational crop tolerance for residues of cyromazine and its metabolite melamine at 0.2 ppm noting the need for additional residue data and data for cotton gin byproducts for a permanent tolerance. Considering only residues of cyromazine, this time-limited rotational tolerance should be revised to 0.1 ppm. The company should be informed that the additional residue trials and data for cotton gin byproducts are still required.

Sweet Corn and Radishes

The data for sweet corn and radishes were originally reviewed in 1987 by A. Smith. Data of the level of parent vs. the metabolite melamine are not available in the branch files at this time. Therefore, we will use the levels found acceptable in the J. Garbus review of PP# 6F3332, 8/26/96 for the DRES calculations. These levels are the following:

| | |
|---|---|
| Corn, sweet (K+CWHR) | 0.50 ppm |
| Corn, sweet, forage | 0.50 ppm |
| Corn, sweet, fodder* | 0.50 ppm |
| Radishes, root | 0.50 ppm |
| Radishes, tops | 0.50 ppm |

* Note: The proper terminology now for this tolerance is "corn, sweet, stover."

Meat, Milk, Poultry and Eggs

The only significant animal feed items from either published or proposed tolerances are potato culls, processed potato waste and sweet corn forage and stover. Since none of these items are fed to poultry, the established poultry tolerances need only be reevaluated on the basis of the established feed through use of Larvadex. Secondary residues could occur in meat, fat and meat byproducts of animals and in milk. Animal diets and the dietary burden to animals was discussed in detail in the J. Stokes review of PP# 6F4613, 9/12/96. At that time alfalfa was also a significant feed item, but has been removed from consideration (A. Rathman review dated 11/13/97). We have reexamined the animal diets considering only potato culls and sweet corn forage since this results in the highest dietary burden and find that maximum dietary burden for diary cattle would be 2.4 ppm and for beef cattle the maximum level would be 3.4 ppm; see the following table:

| COMMODITY | PERCENT DM | PERCENT IN DIET | LEVEL IN COMMODITY, ppm | DAILY DIETARY BURDEN |
|---|---|---|---|---|
| BEEF CATTLE | | | | |
| Potato culls | 20 | 75 | 0.8 | 3.0 |
| Sweet corn forage (rotational) | 30 | 25 | 0.5 | 0.4 |
| | | | Total | 3.4 |
| DAIRY CATTLE | | | | |
| Potato culls | 20 | 40 | 0.8 | 1.6 |
| Sweet corn forage (rotational) | 30 | 50 | 0.5 | 0.8 |
| | | | Total | 2.4 |

A ruminant feeding study has been reviewed (R. Lascola, 4/2/93). In this study residues in milk seemed to plateau by day seven. Residue analyses were conducted for parent and the metabolites melamine and 1-methylcyromazine. Since the metabolism committee has determined

that only residues of cyromazine need be considered in animal commodities unless the dietary burden to animals increases significantly, we have calculated the levels of cyromazine that might be present in milk, meat, liver and kidney. Very little residues were detected in fat, regardless of feeding level. Residue levels increase with increasing feeding levels and appear to be linear for milk and tissues (except fat). The table below shows the feeding levels and the amount of cyromazine detected along with calculations on the level of cyromazine to be expected for milk, meat, liver and kidney from the maximum dietary burdens from the table above.

| MEASURED RESIDUES FROM 10, 50, AND 100 PPM FEEDING LEVELS VS. CALCULATED VALUES | | |
|---|---|---|
| Feeding level, ppm | Cyromazine residues detected | Calculated levels from 2.4 ppm dairy diet and 3.4 ppm beef cattle diet |
| Milk (Day 7) | | |
| 10 | <0.04 | <0.02 |
| 50 | 0.20 | 0.01 |
| 100 | 0.50 | 0.01 |
| Meat (Day 28) | | |
| 10 | <0.05 | <0.02 |
| 50 | 0.12 | 0.01 |
| 100 | 0.25 | 0.01 |
| Liver (Day 28) | | |
| 10 | <0.05 | <0.02 |
| 50 | 0.12 | 0.01 |
| 100 | 0.21 | 0.01 |
| Kidney (Day 28) | | |
| 10 | 0.09 | 0.03 |
| 50 | 0.66 | 0.04 |
| 100 | 0.80 | 0.03 |

Since tolerances are currently being proposed for combined residues of cyromazine and melamine in milk and meat, fat and meat byproducts, a revised Section F will be required. While the limit of quantitation for the method is 0.05 ppm, the limit of detection is at or about 0.01 ppm. Based upon the limit of quantitation of the method, we recommend that the following tolerance levels be proposed for residues of cyromazine: 0.05 ppm for milk; 0.05 ppm for meat, fat and meat byproducts of cattle, goats, hogs, horses, and sheep. If anticipated residues are required for risk assessment, we recommend the following levels be used: 0.01 ppm for milk; 0.01 ppm for

meat, fat and meat byproducts (other than kidney) of cattle, goats, hogs, horses and sheep. And a level of 0.04 ppm in the kidney of cattle, goats, hogs, horses, and sheep.

For eggs and chicken tissue, the currently established tolerances should be revised by removing Section 180.414 (c) which is for residues of melamine in poultry tissue. The tolerances would be 0.25 ppm for eggs and 0.05 ppm for poultry meat, fat, and meat byproducts (from chicken layer hens and chicken breeder hens only).

cc: PP#s 5E4550 ,6F3332, 5F4546, 6F4613 5F4576, Rathman (2 copies)
RDI:G.Kramer:12/10/97:M.Morrow:12/11/97
7509C:RAB1:ARR:12/11/97

# End of Document

PP#5F4576

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

JUL 9 1996

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Memorandum

Subject: PP#5F4576: Cyromazine In/On Crop Group 3: Bulb Vegetables. CBTS#'s 16896, 16973 and 17150. MRID#'s 437631-00 and 437631-01. DP Barcode#'s D219197 and D225580. Chemical No. 121301.

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

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

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

CIBA-GEIGY Corporation, Agricultural Division proposes that tolerances for the combined residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), its metabolite, melamine (1,3,5-triazine-2,4,6-triamine), all expressed as cyromazine be established in/on Crop Group 3: Bulb Vegetables at 5.0 ppm. The representative crops in Crop Group 3: Bulb Vegetables are onions, green and onions, dry bulb. The group also consists of garlic, leek, onion (Welch), and shallot. The petitioner has provided residue data for green onions, and fresh and dry bulb onions. Tolerances for the combined residues of cyromazine and melamine are established under 40 CFR §180.414. Currently there are no cyromazine food additive tolerances. No Registration Standard for cyromazine has been issued.

**CONCLUSIONS**

1. All product chemistry data requirements have been previously and adequately addressed. No additional data are needed for the proposed use as a seed treatment for onions.

2a. The petitioner has proposed the use of Trigard® containing 75% cyromazine active ingredient (a.i.) on the Crop Group 3: Bulb

Vegetables. The label does not state a minimum PHI for green onions or other fresh bulb vegetables. There are some 45-day cultivars of green onions and green shallots. The submitted field residue data do not support the early cultivars. Therefore, a 60-day PHI for green onions and green shallots should be stated on the label. A revised Section B is needed.

2b. Tolerances are not yet established for sweet corn and radishes as rotational crops (pending PP#6F3332). Until such tolerances are established, rotation to sweet corn and radishes should not be allowed. A revised Section B is needed.

3. 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 for the proposed use as a seed treatment for onions. The residues of concern are the parent cyromazine and its metabolite melamine.

4. Commodities in the Crop Group 3: Bulb Vegetables are not considered significant livestock feedstuffs. Thus, a discussion on the nature of the livestock residue is not germane to this petition.

5a. There are adequate residue analytical methods in FDA's Pesticide Analytical Manual (PAM), Vol-II to enforce a crop group tolerance for cyromazine and its melamine metabolite on Crop Group 3: Bulb Vegetables.

5b. Recovery data for cyromazine and its metabolite melamine through the FDA multiresidue methods have been previously submitted for the FDA Pesticide Analytical Manual.

6. Residues of cyromazine and melamine are stable in frozen storage from 9 to 24 months in head lettuce, leaf lettuce, celery, mushrooms, and tomatoes. The treated onion seed and field trial samples in this petition were stored from 2 to 19 months. Storage stability data are adequate to support the subject petition.

7. Field trial residue data are from the major onion-growing states. The submitted field trial data are adequate to support the proposed use on the Crop Group 3: Bulb Vegetables. The proposed 5.0 ppm tolerance will adequately cover any expected residues from the proposed use. In fact, the residue data suggests that the proposed 5.0 ppm tolerance be decreased to 3.0 ppm. However, the residue data also show greater than a 5X difference of residues on green onions vs. maturity onions. Therefore, according to 40 CFR §180.40 (g) a crop tolerance is not appropriate. Instead two separate tolerances should be established. A 3.0 tolerance can be established for **onions, green,** while a 0.3 ppm tolerance can



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be established for **onions (dry bulb only)** . According to 40 CFR §180.1(h) onions, green include green onions, leeks, spring onions or scallions, Japanese bunching onions, green shallots, and green eschalots. Onions (dry bulb only) include garlic, onions (dry bulb only), and shallots (dry bulb only). No additional field trial data are needed. A revised Section F is needed.

8. There are no processed food commodities or feedstuffs considered with the commodities in the Crop Group 3: Bulb Vegetables. (See Table II (September 1995) of the Residue Chemistry Guidelines. Thus, no processing studies are required for the proposed use.

9. Commodities in the Crop Group 3: Bulb Vegetables are not considered significant feedstuffs. There is no reasonable expectation of finite secondary residues of cyromazine and melamine occurring in meat, milk, poultry, and eggs from the proposed use.

10. Compatibility is not a problem with Codex, Canadian and Mexican limits as there are no established cyromazine limits for any of the commodities in the Crop Group 3: Bulb Vegetables.

**RECOMMENDATION**

CBTS cannot recommend for the requested 5.0 ppm cyromazine (plus metabolite melamine) tolerance on the Crop Group 3: Bulb Vegetables. Instead two separate tolerances should be established. A 3.0 tolerance can be established for **onions, green,** while a 0.3 ppm tolerance can be established for **onions (dry bulb only)** . According to 40 CFR §180.1(h) onions, green, include green onions, leeks, spring onions or scallions, Japanese bunching onions, green shallots, and green eschalots. Onions (dry bulb only) include garlic, onions (dry bulb only), and shallots (dry bulb only). **A revised Section F is needed. Also, a revised Section B with a 60-day PHI for green onions and green shallots, and deleting rotation to sweet corn and radishes should be submitted.**

A DRES run can be initiated using the suggested 3.0 ppm tolerance for **onions, green** and 0.3 ppm for **onions (dry bulb only).** For dehydrated onion flakes the combined residues of cyromazine and melamine were 0.25 ppm at the 1X label rate and 0.38 ppm at the 2X label rate. Based on the residues of the field samples (1X: 0.12 ppm, 2X: <0.11 ppm) for the dried onion bulb, the processing yields concentrations factors of 2 and 3.5, respectively. The concentration factor typically used in the Agency DRES runs is 9. **Therefore,** the DRES run should use a lower concentration factor of **3 instead of 9** for dehydrated onion flakes.

DETAILED CONSIDERATIONS

PRODUCT CHEMISTRY/CHEMICAL IDENTITY

All product chemistry data for cyromazine have been previously submitted and adequately reviewed (see memos in PP# 9G2230, A. Rathman, 11/14/79; and in PP# 5F3177, E. Haeberer, 02/13/85). 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 expect a residue problem in the Crop Group 3: Bulb Vegetables for the impurities identified at or above 0.1% in the TGAI cyromazine when the formulation Trigard® is used as directed.

DIRECTIONS FOR USE

The petitioner proposes use of Trigard®OMC, a wettable powder containing 75% a.i. cyromazine as a seed treatment to control onion maggots in the Crop Group 3: Bulb Vegetables for crops grown in soil with organic matter >10%. Trigard®OMC is applied at the rate of 6.6 lb of formulated product per 100 lb of seed (5 lb a.i. per 100 lb seed). The label also restricts concurrent applications at planting time of insecticide products which have activity against the onion maggot. This would also restrict applications of other cyromazine formulations.

The label does not state a minimum PHI for fresh green onions, or other fresh bulb vegetables. There are some 45-day cultivars of green onions and green shallots. The submitted field residue data do not support the early cultivars. A 60-day PHI should be stated on the label for green onions and green shallots. A revised Section B should be submitted.

Rotational crop restrictions:

The submitted label for Trigard®OMC allows 0-day plantback to those crops listed on the label, i.e., celery, head and leaf lettuce, spinach, Chinese mustard and cabbage (Florida use only), peppers, and cucurbits. The label allows a 3-month plantback for sweet corn and radishes.

Cyromazine and/or melamine residues available in the soil for uptake by any of the above 0-day plantback crops would be adequately covered by the established tolerances on these individual crops. Tolerances are not yet established for sweet corn and radishes as rotational crops (pending PP#6F3332). Until such tolerances are established, rotation to sweet corn and radishes should not be allowed. A revised Section B is needed.

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 memo of 02/04/85, E. Haeberer; memos of 02/08/85 and 03/20/85, C. Deyrup; memo of 01/28/87, A. Smith).

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 Crop Group 3: Bulb Vegetables are not considered to be significant feedstuffs. Thus, a full discussion on the nature of the livestock residue is not germane to this petition.

RESIDUE ANALYTICAL METHODS: MRID#437631-01

The residue analytical method used to gather the residue data on the representative commodities is titled "Analytical Method for the Determination of Cyromazine and its Metabolite Melamine Residues in Crops by Gas Chromatography with a Nitrogen/Phosphorous Detector in the Nitrogen Specific Mode" dated January 1, 1995, and coded AG-6218. According to the petitioner this method involves consolidation of and modifications to Methods AG-408 and AG-417A, which have been previously submitted and reviewed (See memo of 02/08/85, C. Deyrup). In summary, the crop matrix is extracted at reflux in methanol:water, acidified after cooling with dilute acid, partitioned with organic solvents, and then the water solubles are passed through an ion exchange column and a silica gel column for final cleanup before GLC analysis. This extraction and cleanup procedures are similar to the Methods AG-408 and AG-417, but AG-621 uses a gas chromatography for analysis, while the other methods use high pressure liquid chromatography for determination of cyromazine and melamine levels in the crop matrix. However, Methods AG-408 and AG-417 as listed in FDA's Pesticide Analytical Manual (PAM), Vol-II are adequate to enforce the proposed 5.0 ppm crop group tolerance. AG-621 is acceptable to support the crop field trial residue data for cyromazine and its melamine metabolite on bulb

vegetables. Adequate data has been previously submitted for the FDA multiresidue methods using Protocols A through E.

STORAGE STABILITY: MRID#437631-01

Storage stability data have been previously submitted and adequately reviewed (See memo 01/28/87, A. Smith). 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. Samples removed from storage and reanalyzed reflected no significant changes in the residues. Residues of cyromazine and melamine are stable in frozen storage for at least 24 months. The treated onion seed and field trial samples in this petition were stored from 2 to 19 months. Existing storage stability data are adequate to support the subject petition.

MAGNITUDE OF THE RESIDUE: MRID#437631-01

Field trial residue data from the major onion-growing states have been submitted accounting for >80% of the US green and bulb onion production. (See summary table, Attachment 1).

The field trial residue data for plots treated at 1X and 2X the proposed maximum application rate show that the proposed 5.0 ppm tolerance will adequately cover any combined residues of cyromazine plus melamine in harvested bulb vegetables as the highest field weathered residue after the maximum proposed application rate is 2.7 ppm for fresh, green, immature onions harvested at a 60-day PHI. The average is approximately 0.8 ppm. The green onions were harvested from 60 to 75-day PHI's. The mature bulbs, both fresh and dried, were harvested from 98 to 207 day PHI's. The proposed 5.0 ppm tolerance will adequately cover any expected residues from the proposed use. In fact, based on the residue data CBTS suggests that the proposed 5.0 ppm tolerance be decreased to 3.0 ppm. However, the residue data show greater than a 5X difference of residues on green onions vs. maturity onions. Therefore, according to 40 CFR §180.40 (g) a crop tolerance is not appropriate. Instead two separate tolerances should be established. A 3.0 tolerance can be established for **onions, green,** while a 0.3 ppm tolerance can be established for **onions (dry bulb only).** According to 40 CFR §180.1(h) onions, green, include green onions, leeks, spring onions or scallions, Japanese bunching onions, green shallots, and green eschalots. Onions (dry bulb only) include garlic, onions (dry bulb only), and shallots (dry bulb only). No additional field trial data are needed. A revised Section F is needed. Also, a revised Section B with a 60-day PHI for green onions should be submitted.

Processed Commodities:

There are no processed food commodities or feedstuffs considered in the Crop Group 3: Bulb Vegetables. [See Table II (September 1995)



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of Residue Chemistry Guidelines]. Thus, no processing studies are required for the proposed use. However, the petitioner submitted residue data from the two CA trials for dehydrated onion flakes. Combined residues of cyromazine and melamine were 0.25 ppm at the 1X label rate and 0.38 ppm at the 2X label rate. Based on the residues of the field samples (1X: 0.12 ppm, 2X: <0.11 ppm) for the dried onion bulb, the processing yields concentrations factors of 2 and 3.5, respectively. The concentration factor typically used in the Agency DRES runs is 9.

NOTE: The DRES run should use a lower concentration of 3 instead of 9.

MEAT, MILK, POULTRY, AND EGGS

Commodities in the Crop Group 3: Bulb Vegetables are not considered significant feedstuffs. There is no reasonable expectation of finite secondary residues of cyromazine and melamine occurring in meat, milk, poultry, and eggs from the proposed use of cyromazine (Trigard®OMC) as an onion seed treatment.

OTHER CONSIDERATIONS

An International Residue Limit Status Sheet (IRL) is attached to this review. Compatibility is not a problem with Codex, Canadian and Mexican tolerances as there are no established cyromazine tolerances for any of the commodities in the Crop Group 3: Bulb Vegetables.

Attachment 1: Field Trial Summary Table
Attachment 2: International Residue Limit Status Sheet

cc with Attachments 1 and 2: PP#5F4576, J. Stokes, G. LaRocca/L. Deluise (PM Team 13), E. Haeberer, RF, Circu.
RDI: EHaeberer:06/27/96:RLoranger:07/03/96:EZager:07/08/96
7509C:CBTS:JStokes/js:CM#2:Rm803:305-7561:07/09/96

| Site | Field Trial Summary Table for Onions<br>Residues, Cyromazine/Melamine/Combined Cyromazine and Melamine * | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Seed, Pelleted | | | Whole Plant | | | Fresh Bulb | | | Dried Bulb | | |
| NY | 9600 | na | 9600 | 0.43, 0.44 | 0.46, 0.42 | 0.89, 0.087 | <0.05, <0.05 | 0.14, 0.15 | <0.19, <0.20 | <0.05, <0.05 | 0.07, 0.06 | <0.12, <0.11 |
| NY (2X) | 21000 | na | 21000 | 0.76 | 0.64 | 1.4 | <0.05 | 0.11 | <0.16 | <0.05 | 0.06 | <0.11 |
| MI | 10800 | na | 10800 | 0.24, 0.43 | 0.07, 0.10 | 0.31, 0.55 | <0.05, <0.05 | <0.05, <0.05 | <0.10, <0.10 | <0.05, <0.05 | 0.08, 0.07 | <0.13, <0.12 |
| TX | 8000, 10400 | na, na | 8000, 10400 | 0.36, 0.33 | <0.05, <0.05 | <0.41, <0.38 | <0.05, <0.05 | <0.05, <0.05 | <0.10, <0.10 | <0.05, <0.05 | <0.05, <0.05 | <0.10, <0.10 |
| GA | 6600 | na | 6600 | 0.06, 0.11 | 0.09, 0.12 | 0.16, 0.23 | <0.05, <0.05 | <0.05, 0.06 | <0.10, <0.11 | <0.05, <0.05 | 0.07, 0.10 | <0.12, <0.15 |
| CA | 10000, 10200 | na, na | 10000, 10200 | 0.74, 0.91 | 0.11, 0.12 | 0.85, 1.0 | 0.08, <0.05 | 0.18, 0.18 | 0.24, <0.21 | 0.06, <0.05 | 0.06, 0.07 | 0.12, <0.12 |
| CA (2X) | 20300, 17900 | na, na | 20300, 17900 | 2.0 | 0.22 | 2.2 | 0.13 | 0.23 | 0.36 | <0.05 | 0.06 | <0.11 |
| CO | 8600 | na | 8600 | 1.7, 1.7 | 1.0, 1.0 | 2.7, 2.7 | <0.05, <0.05 | 0.10, 0.06 | <0.15, <0.11 | <0.05, <0.05 | 0.07, 0.10 | <0.12, <0.15 |
| OR | 14,100, 12,400 | na, na | 14,100, 12,400 | 0.14, 0.18 | 0.12, 0.12 | 0.27, 0.30 | <0.05, <0.05 | <0.05, <0.05 | <0.10, <0.10 | <0.05, <0.05 | <0.05, <0.05 | <0.10, <0.10 |
| OR (2X) | 22,200, 22,200 | na, na | 22,200, 22,200 | 0.39 | 0.14 | 0.52 | <0.05 | <0.05 | <0.10 | <0.05 | <0.05 | <0.10 |
| ID | 11,500 | na | 11,500 | 0.30, 0.23 | 0.13, 0.09 | 0.43, 0.31 | <0.05, <0.05 | 0.06, 0.07 | <0.11, <0.12 | <0.05, <0.05 | 0.06, 0.06 | <0.11 <0.11 |
| Average (1X) | 10,200 | na | 10,200 | 0.52 | 0.25 | 0.77 | <0.05 | <0.09 | <0.14 | <0.05 | <0.07 | <0.12 |
| Average (2X) | 20,700 | na | 20,700 | 1.05 | 0.33 | 1.4 | <0.08 | <0.13 | <0.21 | <0.05 | <0.06 | <0.11 |
| Maximum (1X) | 14,100 | na | 14,100 | 1.7 | 1.0 | 2.7 | 0.06 | 0.18 | 0.24 | 0.06 | 0.10 | 0.16 |
| Maximum (2X) | 22,200 | na | 22,200 | 2.0 | 0.64 | 2.2 | 0.13 | 0.23 | 0.36 | <0.05 | 0.06 | <0.11 |

* PHI's: seed, pelleted, 1 to 41 days; whole plant, 60 to 75 days; bulbs, fresh and dried, 98 to 207 days





Attachment 1

ATTACHMENT 2

# INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL cyromazine

CODEX NO. _____

CODEX STATUS:

|X| No Codex Proposal Step 6 or above

Residue(if Step 8): _____

| Crop(s) | Limit (mg/kg) |
|---|---|

PROPOSED U.S. TOLERANCES:

Petition No. PP#6G4615

RCB Reviewer J. Stokes

Residue: Cyromazine + metabolite Melamine

| Crop(s) | Limit (mg/kg) |
|---|---|
| bulb vegetables | 5.0 |

CANADIAN LIMITS:

|X| No Canadian limit

Residue: _____

| Crop(s) | Limit (mg/kg) |
|---|---|

MEXICAN LIMITS:

|X| No Mexican limit

Residue: _____

| Crop(s) | Limit (mg/kg) |
|---|---|

NOTES:

ATTACHMENT 2

# INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL cyromazine

CODEX NO. _____

CODEX STATUS:

|X| No Codex Proposal Step 6 or above

Residue(if Step 8): _____

| Crop(s) | Limit (mg/kg) |
|---|---|

PROPOSED U.S. TOLERANCES:

Petition No. PP#6G4615

RCB Reviewer J. Stokes

Residue: Cyromazine + metabolite Melamine

| Crop(s) | Limit (mg/kg) |
|---|---|
| bulb vegetables | 5.0 |

CANADIAN LIMITS:

|X| No Canadian limit

Residue: _____

| Crop(s) | Limit (mg/kg) |
|---|---|

MEXICAN LIMITS:

|X| No Mexican limit

Residue: _____

| Crop(s) | Limit (mg/kg) |
|---|---|

NOTES:

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# END OF DOCUMENT

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# R062477

| | |
|---|---|
| **Chemical:** | **Cyromazine** |
| **PC Code:** | **121301** |
| **HED File Code** | **11500 Petition Files Chemistry** |
| **Memo Date:** | **07/03/2003 12:00:00 AM** |
| ***File ID:*** | **DPD242798; DPD242799; DPD242801; DPD242802; DPD240184; DPD236189; DPD236190; DPD236187; DPD236185; DPD219197; DPD225580** |
| **Accession Number:** | **412-04-0138** |

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