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EPA SERIES 361

06/09/99

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

Memorandum

Subject: PP#7E4905. Cyromazine in/on Lima Bean. **Evaluation of Residue Data and Analytical Methodology.**

DP Barcode:	D242692	PRAT Case:	289171
Submission No.:	S536656	Caswell No.:	167B
Chemical No.:	121301	Class:	Insecticide
Trade Name:	Trigard	EPA Reg No.:	100-654
40 CFR:	\$180.414		
MRID No.:	443838-01		

TO: Robert Forrest/Sidney Jackson, PM Team 05  
RD (7505C)

FROM: William D. Wassell, Chemist  
RAB3/HED (7509C)

THRU: Stephen C. Dapson, Branch Senior Scientist  
RAB3/HED (7509C)

**Background:**

The petitioner, Dr. K.W. Dorschner, Coordinator, Interregional Research Project Number 4 (IR-4), on behalf of the IR-4 Project and the Agricultural Experiment Station of Georgia, proposes that tolerances for the combined residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine), and its metabolite, melamine (1,3,5-triazine-2,4,6-triamine), calculated as cyromazine, be established in/on the raw agricultural commodity (RAC) lima bean at 3.0 ppm.

Tolerances are established (40 CFR §180.414) for residues of cyromazine and its metabolite melamine in or on a variety of commodities. Information concerning the metabolism of cyromazine in/on plants and livestock were recently presented to the HED Metabolism Assessment Review Committee (MARC). The Metabolism Committee has determined that the cyromazine metabolite melamine no longer needs to be included in the tolerance expression for cyromazine (Memo, 4/15/98 J.B. Stokes, D245214). Currently established tolerances for cyromazine uses have been reassessed in light of this decision (Memo, 4/5/99, J.B. Stokes and T. Morton, D254881). Reassessed tolerance levels for residues of cyromazine range from 0.1 ppm (cotton, undelinted seed) to 7.0 ppm (leafy vegetables, except Brassica, crop group).

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## CONCLUSIONS

1. All product chemistry data requirements have been previously and adequately addressed. No additional data are needed for the proposed use. HED does not expect a residue problem for the impurities identified at or above 0.1% in the technical grade active ingredient when the formulation Trigard® is used as proposed on lima beans.
2. The petitioner has proposed the use of Trigard® (EPA Reg. No. 100-654) containing 75% cyromazine as the active ingredient (ai) on lima beans. The proposed directions for use of the product on lima beans are adequate. The rotational crop restrictions included on the label are adequate.
3. Plant metabolism data were not submitted in conjunction with this petition. The metabolism of cyromazine has been studied in celery, head lettuce, and tomatoes. The residue of concern is the parent compound cyromazine as determined by the HED Metabolism Committee on 11/4/97. The metabolism of cyromazine in plants is adequately understood and additional plant metabolism data are not required for this proposed use.
4. Livestock metabolism and feeding studies for cyromazine were not submitted in conjunction with this petition. As major livestock feedstuffs are not derived from lima beans, the nature and magnitude of the residue in livestock are not of concern for this petition.
5. Methods AG-408 and AG-417A are the tolerance enforcement methods for cyromazine as published in PAM, Vol II. These methods combined and with minor modifications comprise Method AG-621. The residue data for lima beans was generated using Methods AG-408 and AG-621. Methods AG-408 and AG-621 have been adequately validated for use as data collection methods for determination of residues of cyromazine in/on lima beans. Method AG-408 is adequate for enforcement of the proposed tolerance.
6. Recovery data for cyromazine via the FDA multiresidue methods have been previously submitted. These data have been forwarded to the FDA. Recovery of cyromazine through Protocol D is marginal.
7. Storage stability data were submitted in conjunction with this petition. RAB3 concludes residues of cyromazine in/on lima beans are stable during frozen storage for a maximum of 926 days. These storage stability data are adequate to show that residues of cyromazine did not degrade prior to analysis. The storage intervals for samples from the crop field trials ranged from 157 days to 967 days. For the submitted crop field trials, adjustment

of cyromazine residue levels for storage degradation is not necessary.

- 8a. Crop field trials for cyromazine in/on lima bean were conducted in GA and WI during 1990, CA and WA during 1991, NJ during 1992, and WI during 1993. RAB3 concludes the geographical representation of the lima bean field trials is adequate. We note these trials were conducted prior to the issuance of the guidance entitled: Number and Location of Domestic Crop Field trials (June 1994) and the Updated Livestock Feeds Table for Subdivision O. Residues of cyromazine are not expected to exceed 1.0 ppm in/on lima beans (in pod) when cyromazine is applied 6 times at a rate of 0.125 lbs ai/A with a PHI of 7 days. A revised Section F is required. The revised Section F should propose tolerances for "lima bean" in terms of residues of cyromazine only.
- 8b. HED now requires residue data for lima bean removed from the pod. The submitted crop field trials were conducted as per the guidance that was in effect at the time of the trials. As residue data are now required for the succulent beans without the pods, HED concludes an additional 2 crop field trials are required. HED would prefer that these field trials be conducted in major growing regions for lima beans. HED has no objections to the issuance of a time-limited tolerance for cyromazine in/on lima beans at 1.0 ppm and/or a conditional registration for the use while IR-4 generates the additional residue data.
9. Codex, Canadian or Mexican Maximum Residue Limits (MRLs) are not established for cyromazine in/on lima bean. Thus, harmonization is not an issue for this minor use petition.

#### **RECOMMENDATION**

Pending submission of a revised Section F as discussed in Conclusion 8a above, HED concludes there are no residue chemistry data requirements that would preclude the establishment of a time-limited tolerance for residues of cyromazine in/on lima bean at 1.0 ppm and/or a conditional registration while IR-4 generates the additional residue data discussed in Conclusion 8b above.

HED will now initiate a Human Health Risk Assessment for this use.

**DETAILED CONSIDERATIONS:**

**PRODUCT CHEMISTRY/CHEMICAL IDENTITY**

All product chemistry data for cyromazine have been previously submitted and reviewed (Memoranda, PP#9G2230, A. Rathman, 11/14/79; and 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 grade cyromazine (CGA-72662) is 95% pure. HED does not expect a residue problem for the impurities identified at or above 0.1% in the technical grade active ingredient when the formulation Trigard® is used as proposed on lima beans.

**DIRECTIONS FOR USE**

The petitioner has proposed the use of Trigard® Insecticide, EPA Reg. No. 100-654, for the control of leafminers on lima beans. This product contains 75% cyromazine as the active ingredient (ai) and is formulated as a wettable powder in water-soluble packets.

Trigard® is to be applied as a foliar spray at the rate of 1/6 lbs product (0.125 lbs ai/A) in a minimum of 5 gallons of water per acre by air or in a minimum of 10 gallons of water per acre by ground. Applications are to begin when leaf miners first appear and may be repeated at 7-day intervals. A 7-day preharvest interval (PHI) is proposed. The following restriction is included on the label: do not make more than 6 applications to one crop of lima beans. The total seasonal application rate is 1 lb product per acre (0.75 lbs ai/A).

**Rotational crop restrictions:**

The label for Trigard® allows 0-day plantback to those crops listed on the label. The label allows a 3-month plantback for sweet corn and radishes and a 300-day plantback interval for all other crops.

**RAB3 Comments/Conclusions:**

The proposed directions for use of Trigard® Insecticide, EPA Reg. No. 100-654, on lima beans are adequate. The rotational crop restrictions included on the label are adequate (Memo, 11/13/97, A. Rathman, PP#5F4546, D237716).

**NATURE OF THE RESIDUE - PLANTS**

Plant metabolism data were not submitted in conjunction with this petition. The metabolism of cyromazine has been studied in celery, head lettuce, and tomatoes (Memo, E. Haeberer, PP#5G3176, 2/4/85; Memo,

C. Dyrup, PP#5F3180, 3/20/85; and Memo, C. Dyrup, PP#6F3329 1/28/87). The residue of concern is the parent compound cyromazine. The metabolism of cyromazine in plants is adequately understood and additional plant metabolism data are not required for this proposed use.

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 plant metabolism data for cyromazine has been presented to the HED Metabolism Assessment Review Committee (MARC, meeting date: 11/4/97). The MARC determined that the residue of concern in plant commodities is the parent compound, cyromazine (Memo, 4/15/98 J.B. Stokes, D245214).

#### **RAB3 Comments/Conclusions:**

The metabolism of cyromazine has been studied in celery, head lettuce, and tomatoes. The residue of concern is the parent compound cyromazine as determined by the HED Metabolism Committee on 11/4/97. The metabolism of cyromazine in plants is adequately understood and additional plant metabolism data are not required for this proposed use.

#### **NATURE OF THE RESIDUE - LIVESTOCK:**

Livestock metabolism studies for cyromazine were not submitted in conjunction with this petition. As major livestock feedstuffs are not derived from lima beans, the nature and magnitude of the residue in livestock are not of concern for this petition.

#### **RESIDUE ANALYTICAL METHODS:**

Methods AG-408 and AG-417A are the tolerance enforcement methods for cyromazine as published in PAM, Vol II. These methods combined and with minor modifications comprise Method AG-621. The residue data for lima beans was generated using Methods AG-408 and AG-621.

The analytical methods are described as follows: The crop matrix is extracted at reflux in 10% methanol:water. After cooling, the extract is acidified 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 analysis. For Method AG-408, analysis is by HPLC with a UV detector. For Method AG-621 the analysis is by GLC with a Nitrogen/Phosphorus Detector. The limit of quantification as demonstrated by fortification recovery data is 0.2 ppm for cyromazine by AG-408 and 0.05 ppm for cyromazine by AG-621.

The fortification recovery data for both methods are summarized in Tables 1 and 2.

Table 1. Fortification Recovery of Cyromazine from Lima Beans by Method AG-408		
Fortification Level (ppm)	Statistics	
0.2	Average	107%
	Recovery Range	78 to 145%
	Standard Deviation (n-1)	18.7%
	Number	18
0.5	Average	81.9%
	Recovery Range	59.8 to 116%
	Standard Deviation (n-1)	19.4%
	Number	15
1.0	Average	87.7%
	Recovery Range	70 to 141%
	Standard Deviation (n-1)	21.7%
	Number	18
2.0	Average	131%
	Recovery Range	126 to 136%
	Standard Deviation (n-1)	7.07%
	Number	2

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Table 2. Fortification Recovery of Cyromazine from Lima Beans by Method AG-621		
Fortification Level (ppm)	Statistics	
0.05	Average	93.8%
	Recovery Range	72 to 1119%
	Standard Deviation (n-1)	22.8%
	Number	5
0.5	Average	84.5%
	Recovery Range	77.3 to 94.8%
	Standard Deviation (n-1)	6.65%
	Number	5
5.0	Average	73.7%
	Recovery Range	67.0 to 79.6%
	Standard Deviation (n-1)	4.93%
	Number	5

**RAB3 Comments/Conclusions:**

Methods AG-408 and AG-417A are the tolerance enforcement methods for cyromazine as published in PAM, Vol II. These methods combined and with minor modifications comprise Method AG-621. The residue data for lima beans was generated using Methods AG-408 and AG-621. Methods AG-408 and AG-621 have been adequately validated for use as data collection methods for determination of residues of cyromazine in/on lima beans. Method AG-408 is adequate for enforcement of the proposed tolerance.

**MULTIRESIDUE METHODS:**

Recovery data for cyromazine via the FDA multiresidue methods have been previously submitted. These data have been forwarded to the FDA. Recovery of cyromazine through Protocol D is marginal (Memo, 7/16/93, F.D. Griffith, D192978).

**STORAGE STABILITY:** (MRID No. 443838-01)

Storage stability data were submitted in conjunction with this petition. In the submitted crop field trial studies, untreated control samples were fortified with cyromazine at levels ranging from 0.1 to 2.0 ppm and analyzed after frozen storage. The results of the 0.1 ppm

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fortification level were not used as recovery at this level was erratic. Procedure recovery samples were also analyzed with the storage samples. The maximum storage interval in the storage stability study was 926 days. The storage intervals for samples from the crop field trials ranged from 157 days to 967 days. The results of this study are summarized in Table 3.

Table 3. Storage Stability Data for Cyromazine in/on Lima Bean					
Field Trial	Storage Period (Days)	Fortification Level (ppm)	Average Storage Recovery	Average Fresh Recovery	Corrected Recovery in Stored Sample <sup>1</sup>
GA-005	926	2.0	79%	100%	79%
WI-005	878	2.0	87%	89%	98%
CA-48	477	1.0	87%	92%	95%
		2.0	94%		102%
WA-10	481	1.0	82%	84%	98%
		2.0	79%		94%

<sup>1</sup> Corrected Recovery in Stored Sample =  $\frac{\text{Average Storage Recovery}}{\text{Average Fresh Recovery}} \times 100\%$

**RAB3 Comments/Conclusions:**

RAB3 concludes residues of cyromazine in/on lima beans are stable during frozen storage for a maximum of 926 days. The storage intervals for the crop field trials ranged from 157 days to 967 days. These storage stability data are adequate to show that residues of cyromazine did not degrade prior to analysis. For the submitted crop field trials, adjustment of cyromazine residue levels for storage degradation is not necessary.

**MAGNITUDE OF THE RESIDUE:** (MRID No. 443838-01)

Crop field trials for cyromazine in/on lima bean were conducted in GA and WI during 1990, CA and WA during 1991, NJ during 1992, and WI during 1993. All field trials except the 1990 trials were conducted with 6 applications of cyromazine at 0.125 and 0.25 lbs ai/A/application at 7 day intervals with a 7 day preharvest interval (PHI). The 1990 crop field trials were conducted with 8 applications of cyromazine at 0.125 and 0.25 lbs ai/A/application. An untreated control plot was also maintained at each site. Samples of lima beans in pod were collected from all trials and were analyzed for residues of cyromazine and its metabolite melamine. As melamine is no longer a residue of concern for cyromazine only the analyses for cyromazine residues will be discussed. All samples were analyzed according to

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Method AG-408 with the exception of samples from the 1993 WI trial which were analyzed according Method AG-621. These methods are described above. Residue levels of cyromazine in the samples from the untreated plots were below the limits of quantification of the methods. The results of these field trials are summarized in Table 4.

Table 4. Results of Field Trials for Cyromazine in/on Lima Bean in Pod.		
Field Trial ID	Application Rate (lbs ai/A)	Residue Levels (ppm)
GA005	0.125	0.54
	0.25	1.6
WI005	0.125	0.71
	0.25	1.7
CA48	0.125	0.28
	0.25	0.65
WA10	0.125	0.33
	0.25	1.37
NJ20	0.125	0.23
	0.25	0.45
WI11	0.125	0.40
	0.25	NA <sup>1</sup>

<sup>1</sup> Sample not analyzed.

**RAB3 Comments/Conclusions:**

RAB3 concludes the geographical representation of the lima bean field trials is adequate. We note these trials were conducted prior to the issuance of the guidance entitled: Number and Location of Domestic Crop Field trials (June 1994) and the Updated Livestock Feeds Table for Subdivision O. Residues of cyromazine are not expected to exceed 1.0 ppm in/on lima beans (in pod) when cyromazine is applied 6 times at a rate of 0.125 lbs ai/A with a PHI of 7 days. A revised Section F is required. The revised Section F should propose tolerances for the commodity "lima bean" in terms of residues of cyromazine only.

HED now requires residue data for lima bean without the pod. The submitted crop field trials were conducted as per the guidance that was

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in effect at the time of the trials. As residue data are now required for the succulent beans without the pods, HED concludes an additional 2 crop field trials are required. HED would prefer these field trials to be conducted in major growing regions for lima beans. HED has no objections to the issuance of a time-limited tolerance for cyromazine in/on lima beans at 1.0 ppm and/or a conditional registration for the use while IR-4 generates the additional residue data.

**MEAT, MILK, POULTRY, AND EGGS**

Livestock feeding studies were not submitted in conjunction with the subject petition. As major livestock feedstuffs are not derived from lima beans, the nature and magnitude of the residue in livestock are not of concern for this petition.

**OTHER CONSIDERATIONS**

Codex, Canadian or Mexican Maximum Residue Limits (MRLs) are not established for cyromazine in/on lima beans. Thus harmonization is not an issue for this minor use petition.

cc: PP#7E4905, W.D. Wassell, RAB3 Reading File.  
RDI: ResChem Team: 06/03/99; SDapson: 06/08/99.



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<b>Chemical:</b>	<b>Cyromazine</b>
<b>PC Code:</b>	<b>121301</b>
<b>HED File Code</b>	<b>11000 Chemistry Reviews</b>
<b>Memo Date:</b>	<b>06/09/99</b>
<b>File ID:</b>	<b>DPD242692</b>
<b>Accession Number:</b>	<b>412-01-0056</b>

**HED Records Reference Center**  
12/11/2000