UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
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AND TOXIC SUBSTANCES

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

7/25/2002

Memorandum

Subject: **PP#0E06219**; Cyromazine in/on Dry Beans. Review of Residue Data and Analytical Methodology.

DP Barcode:	D271622	PRAT Case:	293440
Submission No.:	S590374	Caswell No.:	167B
Chemical No.:	121301	Class:	Insecticide
Trade Name:	Trigard	EPA Reg No.:	100-654
40 CFR:	§180.414		
MRID No.:	452203-01		

TO: Robert Forrest/Shaja Brothers, PM Team 05
RD (7505C)

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

THRU: Stephen C. Dapson, Branch Senior Scientist
RAB3/HED (7509C)
07/29/2002

Background:

The petitioner, G. M. Markle, Associate Director, Interregional Research Project Number 4 (IR-4), on behalf of the IR-4 Project and the Agricultural Experiment Station of Georgia and Washington, proposes the establishment of tolerances for residues of cyromazine (N-cyclopropyl-1,3,5-triazine-2,4,6-triamine) in/on dry beans at 3.0 ppm. Dry beans are defined in 40 CFR §180.1(e) as *Cicer arietinum* (chick peas, garbanzo beans); *Lupinus* spp. (including sweet lupin, white sweet lupin, white lupin, and grain lupin); *Phaseolus* spp. (including kidney beans, lima beans, navy beans, pinto beans, snap beans, and wax beans); *Vigna* spp. (including asparagus beans, black-eyed pea, and cowpeas).

Tolerances are established (40 CFR §180.414) for residues of cyromazine in or on a variety of commodities ranging from 0.05 ppm (livestock commodities) to 7.0 ppm (leafy vegetables) and including lima beans at 1.0 ppm.

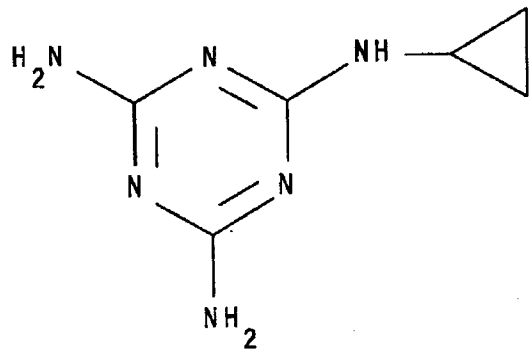

Figure 2: Cyromazine

Executive Summary of Residue Chemistry Deficiencies:

* Submission of a revised Section B/proposed label.
* Submission of a revised Section F.

Conclusions:

1. All product chemistry data for cyromazine have been previously submitted and reviewed. HED concludes no further product chemistry data are required for this use on dry beans.

2. The proposed directions for use of Trigard® Insecticide, EPA Reg. No. 100-654, on dry beans are not adequate. The petitioner has not provided crop field trial data for cowpea forage and hay. The proposed label/Section B should be revised to note that this product is not intended for use on cowpea.

3. 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 on dry beans.

4. Livestock metabolism studies for cyromazine were not submitted in conjunction with this petition. According to OPPTS 860.1000, lupin, seed is a feed item for beef and dairy cattle, poultry, and swine. Thus, the metabolism of cyromazine in livestock is of concern. Data concerning the metabolism of cyromazine in lactating goats and laying hens have been previously submitted. 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 livestock is adequately understood and additional livestock metabolism data are not required for this proposed use on dry beans.

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5a. 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 dry beans was generated using Method AG-621. Method AG-621 has been adequately validated for use as a data collection method for determination of residues of cyromazine in/on dry beans. HED concludes Method AG-408 is adequate for enforcement of the proposed tolerance.

5b. Adequate methods are available in PAM Vol. II for enforcement of the established tolerances for cyromazine in/on meat, milk, poultry, and eggs.

5c. 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.

6. Storage stability data for cyromazine in/on dry beans (navy beans) were submitted. HED concludes residues of cyromazine in/on navy beans are stable during frozen storage for a maximum of 414 days. Additionally, storage stability data for cyromazine in/on lima beans were previously submitted and reviewed. HED has previously concluded residues of cyromazine in/on lima beans are stable during frozen storage for a maximum of 926 days. The maximum storage interval for samples from the crop field trials was 387 days. These storage stability data in conjunction with the previously submitted data for lima beans 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 required.

7a. Crop field trials for cyromazine in/on black-eyed pea (1 trial - CA), pinto bean (3 trials - CO, ID, and WA), navy bean (1 trial - GA), kidney bean (1 trial - NE), and great northern bean (3 trials - WI) were conducted during 1998. HED concludes the geographical representation of the dry bean field trials is adequate. Residues of cyromazine are not expected to exceed 3.0 ppm in/on dry beans when cyromazine is applied 6 times at a rate of 0.125 lbs ai/A with a PHI of 7 days.

7b. HED notes one of the commodities defined in 40 CFR §180.1(e) as a dry bean is cowpea. According to OPPTS 860.1000, the raw agricultural commodities associated with cowpeas are seed, forage, and hay. Crop field trial data for cowpea forage and hay are not available and cowpea is not included on the proposed label/Section B. Therefore, tolerances should be established for residues in/on "beans, dry (except cowpea)". Thus, a revised Section F is required.

8. The addition of grain lupin treated with cyromazine to the diets of ruminants and poultry will not substantially increase the dietary burden to livestock. Thus, adjustment of the established livestock commodity tolerances for cyromazine are not required.

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

RECOMMENDATION

Pending submission of a revised Section B/proposed label (Conclusion 2) and a revised Section F (Conclusion 7b), 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 beans, dry (except cowpea) at 3.0 ppm.

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 (also referred to as CGA-72662) is 95% pure. HED concludes no further product chemistry data are required for this use on dry beans.

Directions for Use:

The petitioner has proposed the use of Trigard® Insecticide, EPA Reg. No. 100-654, for the control of leafminers on dry beans (including chickpea, kidney bean, mung bean, navy bean, black-eyed pea, grain lupin, adzuki bean, and 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 leafminers 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 dry beans. Do not make the last application within 7 days of harvest (cutting), or illegal residues may occur. The total seasonal application rate is 1.0 lb product per acre (0.75 lbs ai/A).

Rotational crop restrictions:

The label for Trigard® allows a 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.

HED Comments/Conclusions:

The proposed directions for use of Trigard® Insecticide, EPA Reg. No. 100-654, on dry beans are not adequate. The petitioner has not provided crop field trial data for cowpea forage and hay. The proposed label/Section B should be revised to note that this product is not intended for use on cowpea.

The rotational crop restrictions included on the label are adequate as per our previous review of cyromazine (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 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).

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.

HED 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 on dry beans.

Nature of the Residue - Livestock:

Livestock metabolism studies for cyromazine were not submitted in conjunction with this petition. According to OPPTS 860.1000, lupin, seed is a feed item for beef and dairy cattle, poultry, and swine. Thus, the metabolism of cyromazine in livestock is of concern. Data concerning the metabolism of cyromazine in lactating goats and laying hens have been previously submitted.

The livestock 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 livestock commodities is the parent compound, cyromazine (Memo, 4/15/98 J.B. Stokes, D245214).

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HED Comments/Conclusions:

The metabolism of cyromazine has been studied in lactating goats and laying hens. 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 livestock is adequately understood and additional livestock metabolism data are not required for this proposed use on dry beans.

Residue Analytical Methods:

Plant Commodities: 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 dry beans (black-eyed pea, pinto bean, navy bean, kidney bean, and great northern bean) was generated using Method 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. The analysis of samples is by HPLC with a UV Detector. The limit of quantification as demonstrated by fortification recovery data is 0.5 ppm for cyromazine in dry beans.

The fortification recovery data are summarized in Table 1.

Table 1. Fortification Recovery of Cyromazine from Dry Beans by Method AG-621

Matrix	Statistics	
Black-eyed Pea	Average	120%
	Fortification Levels (ppm)	0.50
	Recovery Range	NA
	Standard Deviation (n-1)	NA
	Number	1
Navy Bean	Average	78.8%
	Fortification Levels (ppm)	2.5
	Recovery Range	NA
	Standard Deviation (n-1)	NA
	Number	1

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Table 1. Fortification Recovery of Cyromazine from Dry Beans by Method AG-621		
Matrix	Statistics	
Kidney Bean	Average	67.0%
	Fortification Levels (ppm)	0.5
	Recovery Range	NA
	Standard Deviation (n-1)	NA
	Number	1
Pinto Bean	Average	71.9%
	Fortification Levels (ppm)	0.5 (1) and 1.0 (2)
	Recovery Range	69.8 to 74.3%
	Standard Deviation (n-1)	2.27%
	Number	3
Great Northern Bean	Average	78.0%
	Fortification Levels (ppm)	1.0 (1) and 2.0 (2)
	Recovery Range	73.1 to 80.9%
	Standard Deviation (n-1)	4.29%
	Number	3
Overall	Average	79.5%
	Fortification Levels (ppm)	0.5 to 2.5
	Recovery Range	67 to 120%
	Standard Deviation (n-1)	15.9%
	Number	9

HED Comments/Conclusions:

Plant Commodities: 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 dry beans was generated using Method AG-621. Method AG-621 has been adequately validated for use as a data collection method for determination of residues of cyromazine in/on dry beans. Additionally, HED concludes Method AG-408 is adequate for enforcement of the proposed tolerance.

Livestock Commodities: Adequate methods are available in PAM Vol. II for enforcement of the established tolerances for cyromazine in/on meat, milk, poultry and eggs.

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. 452203-01)

Storage stability data were submitted in conjunction with this petition. Untreated control samples of dry beans (navy beans) were fortified with cyromazine at 0.5 ppm and analyzed after frozen storage of 414 days. A fortification recovery sample was analyzed with the stored samples and served as the fresh recovery sample. The maximum storage interval for samples from the crop field trials was 387 days. The results of this study are summarized in Table 2.

Table 2. Storage Stability Data for Cyromazine in/on Navy Bean.

Sample ID	Storage Period (Days)	Fortification Level (ppm)	Storage Recovery	Fresh Recovery	Corrected Recovery in Stored Sample[1]
98SR025	414	0.5	78.0%	77.3%	101%
98SR026		0.5	82.4%		131%
98SR027		0.5	72.4%		93.6%
98SR028		0.5	83.4%		108%
98SR029		0.5	86.4%		112%
98SR030		0.5	80.6%		104%

[1] Corrected Recovery in Stored Sample = $\frac{\text{Storage Recovery}}{\text{Fresh Recovery}} \times 100\%$

Additionally, storage stability data for cyromazine in/on lima beans were previously submitted and reviewed (Memo, 6/9/99, W.D Wassell, D242692). HED has previously concluded residues of cyromazine in/on lima beans are stable during frozen storage for a maximum of 926 days.

HED Comments/Conclusions:

HED concludes residues of cyromazine in/on navy beans are stable during frozen storage for a maximum of 414 days. The maximum storage interval for samples from the crop field trials ranged was 387 days. These storage stability data in conjunction with the previously submitted data for lima beans 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 required.

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Magnitude of the Residue: (MRID No. 452203-01)

Crop field trials for cyromazine in/on black-eyed pea (1 trial - CA), pinto bean (3 trials - CO, ID, and WA), navy bean (1 trial - GA), kidney bean (1 trial - NE), and great northern bean (3 trials - WI) were conducted during 1998. All field trials were conducted with 6 applications of cyromazine at 0.125 lbs ai/A/application at 6 to 8 day intervals with a 7 ± 1 day preharvest interval (PHI). An untreated control plot was also maintained at each site. Samples of dry beans were collected at maturity from all trials and were analyzed for residues of cyromazine. All samples were analyzed according to Method AG-621 (described above). Residue levels of cyromazine in the samples from the untreated plots were not detected (<0.05 ppm). The results of the crop field trials are summarized in Table 3.

Table 3. Results of Field Trials for Cyromazine in/on Dry Beans.

Field Trial ID	Crop	Residue Levels (ppm)
98-CA-23	Black-eyed Pea	0.94, 1.2
98-CO-01	Pinto Bean	2.1, 1.5
98-GA-07	Navy Bean	0.64, 0.72
89-ID-03	Pinto Bean	1.1, 1.1
98-NE-03	Kidney Bean	0.74, 1.2
98-WA-19	Pinto Bean	<0.50, <0.50
98-WI-06	Great Northern Bean	0.70, 0.98
98-WI-07	Great Northern Bean	0.93, 1.1
98-WI-14	Great Northern Bean	1.2, 1.1

HED Comments/Conclusions:

HED concludes the geographical representation of the dry bean field trials is adequate. Residues of cyromazine are not expected to exceed 3.0 ppm in/on dry beans when cyromazine is applied 6 times at a rate of 0.125 lbs ai/A with a PHI of 7 days.

HED notes one of the commodities defined in 40 CFR §180.1(e) as a dry bean is cowpea. According to OPPTS 860.1000, the raw agricultural commodities associated with cowpeas are seed, forage and hay. Crop field trial data for cowpea forage and hay are not available and cowpea is not included on the proposed label/Section B. Therefore, tolerances should be established for residues in/on "beans, dry (except cowpea)". Thus, a revised Section F is required.

Meat, Milk, Poultry and Eggs:

The need for tolerances for secondary residues of cyromazine in meat, milk, poultry and eggs and anticipated residue estimates were discussed in detail in our risk assessment of 3/11/98 (Memo, A.R. Rathman, *et. al.*, D242798). In that review, it was concluded:

> *The following 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, and 0.04 ppm for 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). 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.*

HED Comments/Conclusions:

The addition of grain lupin treated with cyromazine to the diet of ruminant and poultry will not substantially increase the dietary burden to livestock. Thus, adjustment of the established livestock commodity tolerances for cyromazine are not required.

International Harmonization Issues:

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

cc: W.D. Wassell, RAB3 Reading File.
RDI: SKnizner: 08/16/2001; SDapson: 7/17/2002

INTERNATIONAL RESIDUE LIMIT STATUS

Chemical Name: N-cyclopropyl-1,3,5-triazine-2,4,6-triamine	Common Name: Cyromazine	☐ Proposed tolerance ☐ Reevaluated tolerance ☐ Other	Date: 8/16/2001

Codex Status (Maximum Residue Limits)	U. S. Tolerances
☐ No Codex proposal step 6 or above X No Codex proposal step 6 or above for the crops requested	Petition Number: 0E06219 DP Barcode:D271622 Other Identifier: none
Residue definition (step 8/CXL):cyromazine	Reviewer/Branch: W. D. Wassell
	Residue definition: cyromazine only

Crop (s)	MRL (mg/kg)	Crop(s)	Tolerance (ppm)
		beans, dry (except cowpea)	3.0

Limits for Canada	Limits for Mexico
☐ No Limits X No Limits for the crops requested	☐ No Limits X No Limits for the crops requested
Residue definition: cyromazine and the metabolite 1,3,5-triazine-2,4,6-triamine	Residue definition: cyromazina

Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)

Notes/Special Instructions:
S.Funk, 08/27/01.

Rev. 1998