

8/10/94

MEMORANDUM

SUBJECT: Cyromazine, Larvadex™ 1% Premix Larvacide, (EPA Reg. No. 101-671).
Review of 6(a)(2) data and correspondence (dated: 06/09/94, 06/13/94 and
06/17/94) from Ciba-Geigy Corporation.
MRID No. 432776-01, 432810-01, 432735-01; CBTS No. 14118, 14116,
14117; DP Barcode: D205836, D205837, D205838.

FROM: William D. Wassell, Chemist
Tolerance Petition Section I
Chemistry Branch I - Tolerance Support
Health Effects Division (7509C)

THROUGH: Richard A. Loranger, Ph.D., Chief
Chemistry Branch I - Tolerance Support
Health Effects Division (7509C)

TO: Phillip Hutton / Michael Mendelsohn, PM-18
Insecticide / Rodenticide Branch
Registration Division (7505C)

Background/Summary:

Larvadex® Premix (EPA Reg. No. 100-631) is registered for blending into poultry feed to control certain fly species which develop in poultry manure. The active ingredient in the product is cyromazine or *N*-cyclopropyl-1,3,5-triazine-2,4,6-triamine. Tolerances are established for residues of the active ingredient and its metabolite melamine (1,3,5-triazine-2,4,6-triamine) under 40 CFR §180.414 in or on various raw agricultural commodities. A feed additive tolerance is established for residues of cyromazine under 40 CFR §186.1400 at 5.0 ppm in or on poultry feed.

In 1993, the State of Maine was contacted by a grower wanting to know if a restriction on the product label which prohibited the application of poultry manure from animals fed Larvadex to fields in which "small grains" were to be planted included corn. Lebel R. Hicks, MS DABT, of the Maine Department of Agriculture, Food and Rural Resources, Board of Pesticides Control, contacted EPA for clarification of the restriction. In our memo of 04/14/94 (W.D. Wassell, DP Barcodes: D200463 and D201432) we stated that although it is not a violation of the label restriction to apply cyromazine-treated poultry manure to fields in which corn will be grown, the data base for cyromazine was not sufficient to determine if there would be residues of cyromazine or its metabolite melamine in corn.

In Maine, corn silage from fields amended with cyromazine-treated poultry manure is frequently fed to dairy cattle. The State of Maine and Ciba-Geigy determined that it would be appropriate to analyze bulk milk samples from cows fed corn silage grown in fields amended with cyromazine-treated poultry manure and bulk milk samples from cows fed corn silage grown in fields not amended with cyromazine-treated poultry manure and the corn silage from

these fields to determine if residues of either cyromazine or its metabolite melamine were present. The registrant has submitted the preliminary results of this monitoring study as 6(a)(2) data because residues of melamine have been detected in the raw milk samples. Our instructions from RD are to review the submitted data and determine its impact on the current Larvadex registrations.

Detailed Considerations:

The Department of Agricultural, Food and Rural Resources (DAFRR) of Maine has initiated a monitoring study for residues of cyromazine and its metabolite melamine in milk collected from various dairy farms. The purpose of the study was to determine if there is a transfer of residues of cyromazine and its metabolite melamine to the milk from dairy farms where cows are fed silage grown on fields amended with cyromazine-treated poultry manure. DAFRR identified two dairy farms in which the corn silage fed to the cows was grown in fields which had not been amended with cyromazine treated manure. We will refer to the milk and corn silage samples from these farms as "untreated" samples. Three farms in which the cows were fed corn silage grown in fields amended with cyromazine-treated poultry manure were also identified by DAFRR. We will refer to the corn silage and milk samples from these farms as "treated" samples. DAFRR collected samples of raw milk and corn silage from the five farms. Please note: the corn silage samples were collected after the analysis of the milk samples had been completed. The samples were halved and sent to Ciba-Geigy Corporation in Greensboro, NC and to the University of Maine in Orono, ME for analysis. The samples were analyzed for residues of cyromazine and its metabolite melamine by the Ciba-Geigy analytical method AG-403. A copy of the analytical procedure was not included in the current submission. As of this time, the University of Maine has not completed the analysis of the corn silage samples. Ciba-Geigy has stated that they will provide to the Agency the results of the corn silage analysis by the University of Maine as soon as they receive the information. Table 1 contains the sample analysis results from Ciba-Geigy and Table 2 contains the results of the sample analyses of the University of Maine.

2

Table 1. Residue Levels of Cyromazine and its Metabolite Melamine in Milk and Corn Silage from the State of Maine (Ciba-Geigy).

Maine Farm ID	Sample Type	Residue Levels (ppm) ¹	
		Cyromazine	Melamine
94001 (untreated)	Milk	<0.010	<0.010
	Corn Silage	<0.05	<0.05
94002 (untreated)	Milk	<0.010	0.013 ²
	Corn Silage	<0.05	<0.05
94003 (treated)	Milk	<0.010	<0.010
	Corn Silage	<0.05	<0.05
94004 (treated)	Milk	<0.010	0.053
	Corn Silage	<0.05	<0.05
94005 (treated)	Milk	<0.010	0.020
	Corn Silage	<0.05	<0.05

¹ Residue levels are the average of two values and melamine residues are reported as cyromazine equivalent residues.

² Residue results for this sample obtained by GC/MSD analysis.

Table 2. Residue Levels of Cyromazine and its Metabolite Melamine in Milk from the State of Maine (University of Maine).

Maine Farm ID	Residue Levels (ppm) ¹	
	Cyromazine	Melamine
94001 (untreated)	<0.005	<0.005
94002 (untreated)	<0.005	0.005
94003 (treated)	<0.010	0.008
94004 (treated)	<0.010	0.056
94005 (treated)	<0.010	0.017

¹ Residue levels are the average of two values and melamine residues are reported as cyromazine equivalent residues. Melamine residue levels are corrected for an average fortification recovery of 80%.

The University of Maine reports fortification of untreated milk samples was performed concurrent with the residue analysis. Recoveries of melamine from milk ranged from 61 to 94%. Recoveries of cyromazine from milk ranged from 59 to 78% with an outlier at 23% recovery. Ciba-Geigy does not report the results of any fortification recovery experiments.

CBTS Comments / Conclusions:

CBTS can conclude that the results of the sample analysis by the University of Maine seem to confirm Ciba-Geigy's results, but we are unable to determine the source of the melamine residues in the milk samples from the submitted data. Further, the results of this study do not alter our previous conclusions and data requirements concerning the use of Larvadex Premix and Larvadex 2SL (EPA Reg. Nos. 100-631 and 100-662, respectively). Ciba-Geigy Corporation has stated that they will provide additional data concerning this study as it becomes available. We note that as melamine and/or melamine resins are a common constituent of many materials such as adhesives, paper, textiles, plastic items and dinnerware, the melamine contamination of the milk samples may have come from sources other than animal feeds grown in fields amended with cyromazine-treated poultry manure.

In our memo of 04/14/94 (W.D. Wassell, DP Barcodes: D200463 and D201432), we stated that additional data is needed to evaluate the potential for uptake of cyromazine residues into crops planted in fields to which poultry manure containing cyromazine has been applied. The additional data requirements as stated in our 04/14/94 memo are restated below.

Additional Data Requirements:

CBTS recommends the following data be required of Ciba-Geigy in order to assess the potential for uptake of residues into crops grown in fields to which poultry manure containing cyromazine has been applied:

- i. The registrant should conduct a study in which Larvadex treated feed is fed to poultry as per the label directions. In this study, the manure should also be treated topically with Larvadex 2SL as per the label directions. The manure from these animals should be collected and analyzed for residues of cyromazine and its metabolite melamine. Due to the unusual nature of this study, we highly suggest that the registrant submit for review by CBTS a protocol outlining the procedures to be used in this study.
- ii. The registrant should conduct a study in which manure from birds not fed cyromazine treated feed is collected and topical applications of Larvadex 2SL are made to poultry manure as per the label directions. The manure should subsequently be analyzed for residues of cyromazine and its metabolite melamine. Due to the unusual nature of this study, We highly suggest that the registrant submit for review by CBTS a protocol outlining the procedures to be used in this study.
- iii. After a determination has been made concerning the magnitude of the residues of cyromazine in poultry manure, the registrant should conduct a confined residue uptake study in which crops are grown in soil that has been amended with manure containing

4

uniformly radiolabeled (^{14}C) cyromazine at an appropriate level. This study is being required because the submitted uptake studies are inadequate to delineate the nature of the residue as a result of the uptake of residues from soil amended with poultry manure containing cyromazine residues. The uptake study should be conducted according to current Chemistry Branch guidance for a confined rotational crop study with the exception that the soil should not be aged for an extended period of time and the soil should be analyzed for residues at the initiation of the study. Due to the unusual nature of this study, we highly suggest that the registrant submit for review by CBTS a protocol outlining the procedures to be used in this study.

- iv. Depending on the results of the uptake study, additional studies may be required. These studies could include limited field trials with representative commodities. If the limited field trials indicate the need for uptake tolerances, then an appropriate number of fields trials will be required in order to evaluate the magnitude of the resulting residues. If appropriate, ruminant commodity tolerances may also be required.

cc: WDWassell, RF, Circ., Cyromazine SF.
RDI: RSQuick: 08/09/94; MFlood: 08/10/94; RALoranger: 08/10/94;
7509C:CBTS:WDWassell:wdw:CM#2:Rm 804U:305-6135:08/09/94
Disk: WDW-3, File: FY94WDW.100