



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

APR 14 1994

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Cyromazine, Larvadex™ 1% Premix Larvacide, (EPA Reg. No. 101-671).
Correspondence (3/11/94 and 3/30/94) from Ciba-Geigy Corporation.
MRID No. None; **CBTS No. 13365, 13480;**
DP Barcode: D200463, D201432.

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THROUGH: Debra Edwards, Ph.D., Chief
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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 (1,2,3-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 10/6/93 (W.D. Wassell, CBTS No. 12260) we stated: "After a review of the pertinent data (i.e. rotational crop data and studies in which crops were grown in soil amended with chicken manure containing ¹⁴C-cyromazine), we have determined corn is intended to be



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included in the Larvadex™ restriction concerning applications of cyromazine treated manure to small grain crops.". Ciba-Geigy Corporation in a letter dated 3/11/94 (Carolyn B. Bussey, Regulatory Manager) has asked the Agency to reconsider our position on this matter.

Detailed Considerations:

Cyromazine Uses:

Larvadex Premix (EPA Reg. No. 100-631):

Larvadex Premix (EPA Reg. No. 100-631) is registered for the control of certain fly species which develop in poultry manure. The active ingredient in the product is cyromazine. The product is blended with poultry feed in order to achieve a cyromazine concentration of 5 ppm. The cyromazine treated feed is fed to poultry as a "feed through" in order to deposit residues of the active ingredient in the poultry manure thereby controlling the fly population. This product is labeled for use in chicken layer and breeder operations only.

Poultry manure as a soil supplement is considered a valuable source of nitrogen and is utilized as such for a variety of crops. As the intention of the "feed through" is to deposit residues in the manure, the Agency has required the following restrictions to be included on the Larvadex Premix label: "Do not apply more than 3 tons of manure per acre per year. Do not apply to small grain crops that will be harvested or grazed or illegal residues may result.". These restrictions were required based upon studies in which poultry manure containing radiolabeled (¹⁴C) cyromazine was utilized as a supplement to soil in which crops were grown. At least one of the crops (spring wheat) showed uptake of residues and hence the restrictions. The uptake studies will be discussed in more detail elsewhere in this memorandum.

Larvadex 2SL (EPA Reg. No. 100-662):

Larvadex 2SL (EPA Reg. No. 100-662) is registered for topical applications to poultry manure in chicken layer and breeder operations for the control of certain fly species. The product is diluted with water to make a 0.1% spray mix. One gallon of the 0.1% spray may be applied per 100 square feet of area over the surface of the manure. This translates to an application rate of 0.0086 lbs ai/ 100 sq. ft. or 0.086 lbs ai/ 1000 sq. ft. Applications may be made every 21 days. If the product is used in conjunction with cyromazine treated feed, then applications are limited to a spot treatment of 20% of the manure surface. The following restrictions are included on the label: "Do not apply more than 4 tons of manure treated solely with Larvadex 2SL per acre per year. Do not apply more than 3 tons of manure treated with Larvadex 1% Premix and Larvadex 2SL as a spot treatment per acre per year. Do not apply to small grain crops that will be harvested or grazed or illegal residues may result.".

Other Cyromazine Formulations:

Other formulations containing cyromazine as the active ingredient include Trigard Insecticide (EPA Reg. No. 100-654) and Armor Insect Growth Regulator (EPA Reg. No. 100-656). The products are registered for leafminer control on a variety of crops including celery, lettuce, spinach, peppers, cucurbits and mushrooms. The following rotational crop restrictions are included on the label for Trigard Insecticide: "All crops on this label may be planted following harvest of a Trigard - treated crop. Do not rotate to any other crop except sweet corn or radishes. Do not plant sweet corn or radishes within 3 months after last application." These restrictions were required as a result of field rotational crop studies in which sweet corn and radishes were planted following celery which had received foliar applications. These data will be discussed in more detail elsewhere in the memorandum.

Practicality of Restrictions on the use of Poultry Manure:

Following discussions with agricultural specialists at the University of Delaware, University of Maryland Eastern Shore, Virginia Polytechnic Institute and State University and University of California - Davis, we have determined that restrictions placed on the Larvadex labels restricting the use of poultry manure to specific use rates (in tons per acre) and on certain crops are not practical. The primary basis for this conclusion is a question of control over the commodity. Does the poultry producer have control over the manure once it becomes treated with cyromazine? The answer to this question can be ascertained by reviewing some of the cultural practices associated with raising poultry.

A common practice in the poultry industry is to collect the manure in deep pits that are generally not exposed to elements. The pits are ventilated with fans in order to partially dehydrate the manure. The dehydration measures facilitate the transportation and utilization of the manure as fertilizer. The pits are generally cleaned out after a period of one to five years. In some cases, the poultry producer will collect the manure for utilization on their own fields, but also many producers will hire a firm to empty the pit and haul the manure away. These firms sell the manure to other farmers for use as fertilizer. The University of Delaware has set up a poultry manure brokerage hot line for poultry producers that can not utilize all of the manure produced at their facilities. The University attempts to find farmers that need additional manure for fertilizer. In the State of California, poultry producers sell manure for use as fertilizer with most vegetable crops. They receive an average of approximately \$5 to \$10 per ton of manure.

Based upon this information, our conclusion is that the poultry producers do not have control over the utilization of the manure. Therefore, any restrictions placed on the utilization of the manure are not practical and cannot be enforced.

Residue Levels of Cyromazine in Poultry Manure:

Ciba-Geigy Corporation has submitted data (MRID No. 431832-01 and -02 or Ciba-Geigy Report No. ABR-85042) from a poultry feeding study in which residue levels of cyromazine were measured in poultry excreta. In this study, White Leghorn laying hens were fed a ration containing approximately 5.5 ppm cyromazine for a period of 56 days. Samples of excreta were collected periodically throughout the dosing period. Cyromazine residues in the excreta ranged from a minimum value of 2.4 ppm to a maximum value of 4.3 ppm during the dosing period. The average level of cyromazine in the excreta was reported to be 3.1 ± 0.5 ppm. The report does not indicate the moisture content of the manure, the analytical method that was utilized or values of fortification recoveries. We will assume the moisture content of the manure to be 74.8%. This figure was reported to CBTS by E.R. Collins, Jr., PhD, Professor of Waste Management at Virginia Polytechnic Institute and State University, College of Agricultural Engineering (teleconference between W.D Wassell and Dr. Collins, 4/5/94) as being the average moisture content of fresh poultry manure. Manure that is spread into the fields for fertilizer usually ranges in moisture content from 10 to 30% moisture, but can be as high as 60 to 70% moisture. We Note: The amount of manure spread into the fields will be dependent upon the manure's moisture content. At 70% moisture, manure will be spread at approximately 10 to 15 tons per acre, but at 20% moisture, the manure would be spread at a rate of 2 to 5 tons per acre. If the maximum value of 4.3 ppm and the average value of 3.1 ppm is adjusted to a moisture content of 20%, then the cyromazine levels become a maximum of 13.6 ppm and an average of 9.8 ppm.

In other studies conducted by Ciba-Geigy (Accession No. 257652), chickens were fed cyromazine in their ration at 5.0 ppm for periods of approximately 16 days, 3 days and 44 days. The levels of cyromazine and its metabolite melamine were reported as 16.7 ppm, 0.81 ppm and 28.7 ppm, respectively. These figures are corrected for procedural recoveries of less than 100% and for moisture content. If these values are adjusted to 20% moisture content, then the values become 13.4 ppm, 0.65 ppm and 23.0 ppm, respectively. We note that the ration fed to the animals was not analyzed for cyromazine levels, but the cyromazine levels in the manure are within the range of expected values.

Dr. Collins of Virginia Polytechnic Institute and State University has reported to CBTS that a 4 lb laying hen will produce an average of 0.21 lbs of excreta per day at 74.8% moisture content or 24.0 g/day at 0% moisture and 28.8 g/day at 20% moisture. If we assume the bird consumes 98 grams of feed per day, this translates to a dietary burden of 490 μ g of cyromazine per day. In a cyromazine metabolism study utilizing laying hens (Accession No. 257652, Ciba-Geigy Report No. ABR-79043), the registrant reports at a feeding level of 5.0 ppm cyromazine in the ration, the chicken excreta contained 75% of the administered dose as unaltered cyromazine. If we assume 75% of the administered dose is transferred to the excreta, then the amount in the excreta becomes 367 μ g of cyromazine. Therefore, CBTS has calculated a cyromazine level in the manure at 15 ppm (0% moisture) or 13 ppm (20% moisture). We note: our calculated values are approximately equivalent to the values reported by the registrant, but both the calculated values and the values from the feeding

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studies do not take into account residues added to the manure by topical applications of Larvadex 2SL.

Ciba-Geigy has contended that the average cyromazine levels in poultry manure from a feeding level of 5 ppm cyromazine (1x feeding level) will be a maximum approximately 5 ppm (moisture content not specified). We assume this is for fresh manure, but our information indicates that the manure is frequently dried to a moisture content of approximately 20% prior to spreading in the fields. Obviously, if the 5 ppm level is corrected from approximately 75% moisture to 20% moisture, then a potential exists for much higher residue levels in the manure.

Larvadex 2SL (EPA Reg. No. 100-662) is registered for use as a topical spray to poultry manure. If the product is used in conjunction with the cyromazine feed through, then the applications are limited to no more than 20% of the surface area. If the topical sprays are made in the absence of the cyromazine feed through, then there is no limit to the amount of surface area which can receive the spray. Applications can be made on a 21-day schedule with no limit to the number of applications. Data (Ciba-Geigy report AGA-8130) submitted in conjunction with the request for the registration of the topical application show a maximum residue level of 31 ppm cyromazine in poultry manure following an application at a rate of 0.0078 lbs ai/ 100 sq. ft. on the day of the application. The moisture content of the manure is not specified, but most likely the moisture level was at 75% or higher. The data also show that the residue levels will decrease over time to approximately 13 ppm after 6 days. Presumably, this decrease is due to dilution by the addition of fresh manure. In our opinion, this data is not adequate to assess the likely residue levels resulting from applications on a 21 day schedule and/or in conjunction with the feed through cyromazine residues.

Application of Poultry Manure to Fields:

Application of poultry manure to cropland as a soil supplement is considered the most practical and economic means of "disposal" of this waste. In many crop production situations, poultry manure can effectively replace or significantly reduce the need for commercial fertilizers. Poultry manure is an important source of nitrogen, phosphorus, potassium, sulfur and micronutrients. Application of poultry manure as a fertilizer is generally based upon the nitrogen requirements of the crop to be planted. It has been reported to CBTS that typical application rates of poultry manure to cropland can range from 2 to 5 tons per acre with a moisture content of approximately 20%. If we estimate a cyromazine level of 15 ppm in the manure and the manure is applied at 5 tons per acre, then this translates to a cyromazine application rate of 0.15 lbs ai/A. This does not account for residues resulting from the topical applications to the manure.

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Cyromazine Residue Data:

Two studies (Accession No. 070915) pertaining to the uptake of residues by crops from soils amended with poultry manure containing cyromazine residues have been submitted to the Agency. In one of the studies (Ciba-Geigy Report No. ABR-82003), crops (lettuce, sugar beets and spring wheat) were grown in soil which had been amended with poultry manure to simulate an application rate of 5 tons per acre. The manure contained residues of radiolabeled (¹⁴C) cyromazine at a level of 5 ppm. This translates to an application rate of 0.05 lbs ai/A. The soil was aged for 30 days and transferred to the top three inches of pots containing untreated soil in the bottom 5 inches. At maturity lettuce and sugar beets did not contain detectable residues (<0.009 ppm Total Radioactive Residue (TRR)). However, the mature spring wheat straw contained 0.112 ppm TRR. This sample was extracted and residues of cyromazine and melamine were found at levels of 0.065 ppm and 0.0058 ppm, respectively. Wheat hulls and grain contained 0.078 ppm TRR and <0.009 ppm TRR, respectively. Residues in the hulls were not identified.

In another study (Ciba-Geigy Report No. ABR-81049), a field plot was treated with ¹⁴C-labeled cyromazine at a rate of 0.2 lbs ai/A and amended with the equivalent of 20 tons of poultry manure per acre. The manure was incorporated to a depth of 3 inches. The soil was aged for a period of 3 months and transferred to pots with either the top 3 inches of treated/amended soil and the lower 5 inches of untreated soil or a full 8 inches of treated/amended soil. The pots were planted with lettuce, carrots or spring wheat. At maturity, all of the indicator crops contained detectable ¹⁴C residues. For the crops planted in pots containing the top 3 inches only of the amended soil, lettuce leaves and carrot tops and roots contained residue levels of 0.03, 0.13 and 0.03 ppm TRR, respectively, while the wheat stalks and grain contained 0.23 and 0.15 ppm TRR, respectively. The residues in these samples were not identified. For the crops grown in a full eight inches of amended soil, lettuce leaves and carrot tops and roots contained 0.05, 0.27 and 0.06 ppm TRR, respectively. Again, the residues were not identified. For the wheat grown in the pots with the full 8 inches of amended soil, the stalks contained 0.76 ppm TRR and the grain contained 0.17 ppm TRR. Residues in the grain samples were not identified. Upon analysis, the wheat stalks contained residues of cyromazine at 0.12 ppm and residues of melamine at 0.22 ppm.

Additional field rotational crop studies (Accession No. 260663, PP#6F3332) have been submitted in conjunction with a request for rotational crop tolerances in or on sweet corn that has been rotated to fields in which cyromazine treated celery had been harvested. In these studies, celery had been treated with 12 to 15 applications of cyromazine at a rate of 0.125 or 0.25 lbs ai/A. Applications were on an approximate 7 day schedule. Sweet corn was planted 15 to 48 days after the last application. The registrant has requested a 0.5 ppm tolerance for residues of cyromazine and its metabolite melamine in or on sweet corn ears, forage and fodder as a result of the data. This petition is currently in reject status. In our opinion, this data does not apply to the current situation and cannot be used to estimate the

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potential for residues in corn planted in fields amended with cyromazine treated poultry manure.

In conjunction with a request for a foliar use of cyromazine on tomatoes, the registrant has requested tolerances in crops to be planted in fields in which cyromazine treated tomatoes had been harvested (PP#6F3422). The rotational crop tolerances had been requested for a variety of commodities including cabbage, sweet potatoes, sugar beets, wheat, barley and sorghum at various levels. The proposed use for cyromazine on tomatoes included a maximum of 12 applications at a rate of 0.125 lbs ai/A. Residue data has been submitted in conjunction with this request (see Accession Nos. 263320 and 263321). This petition is currently in reject status. Again, these data do not apply to the current situation, but the studies submitted in conjunction with PP#6F3422 and PP#6F3332 show that the potential exists for the uptake of residues into crops from fields treated with cyromazine.

Current Situation:

The State of Maine inquired of the Agency whether corn was to be included in the restriction on the Larvadex Premix label concerning the planting of "small grains" into fields in which poultry manure from cyromazine fed poultry had been spread. CBTS has concluded that it is intended that corn was to be included in the restriction for small grains (see our memo of 10/6/93, W.D. Wassell, CBTS No. 12260). Ciba-Geigy has requested that the Agency reconsider this decision based upon various grounds. The registrant has stated that corn is not a small grain and that the potential for uptake is very small based upon the label restrictions and the residue levels of the active ingredient in the manure. CBTS agrees with the registrant's contention that traditionally corn is not considered a small grain, but the restriction was based upon the confined uptake studies performed by the registrant. In an uptake study, indicator crops such as a small grain, a leafy vegetable and a root crop are planted in order to determine the potential for uptake of residues. The small grain crop is representative of all field grain crops including crops such as sorghum, wheat and corn. In conjunction with the rejection rate analysis, CBTS has made available a memorandum entitled "Guidance on How to Conduct Studies on Rotational Crops" (2/23/93). This memorandum states that "... rotational crop restrictions will be set at the interval appropriate to each tested crop group with the longest interval being applied to other (untested) rotated crops.". This is why we have concluded that the "small grain" restriction was intended to include corn. Earlier in this review, we have concluded that any restrictions imposed on the utilization of poultry manure from birds fed cyromazine treated feed are not practical. The reason is that the manure is not under the control of the poultry producers. We have also shown that the residue levels in the manure will most likely exceed the 5.0 ppm level which the registrant has contended will be present.

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Conclusions:

1. Based upon the data that has been submitted to the Agency, CBTS can conclude that if poultry manure containing cyromazine residues is spread into fields in which corn (or other commodities) are to be grown the potential exists for the uptake of residues into this (these) crop(s).
2. CBTS also concludes that it is not a violation of the use directions for Larvadex Premix and Larvadex 2SL to spread poultry manure containing cyromazine residues into fields in which corn will be grown, because technically corn is not a small grain.
3. We further conclude 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 are outlined 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 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.

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