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

SEP 19 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: ID#105001: Response to Guidance for Terbufos Re-registration Standard issued in Sept. 1988. (DEB #5033).

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THRU: Philip V. Errico, Section Head Joel Carbis for P. Errico
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TO: William H. Miller, PM #16
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and

Reto Engler, Chief
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BACKGROUND

In September 1988, the Agency issued Guidance For The Re-registration Of Pesticide Products Containing Terbufos As The Active Ingredient in which 21 data gaps were listed in Table A. In response to these data gaps, the petitioner, American Cyanamid Company, submitted a cover letter dated 12/21/88 including a brief review and comments on these data gaps. The data gaps and the petitioner's responses are restated below, followed by DEB's comments/conclusions. The petitioner should receive a copy of this entire memorandum.

SUMMARY OF DATA GAPS REMAINING TO BE RESOLVED

Product Chemistry Chapter: §61-1, §61-2, §61-3, §62-1, §62-2, §62-3 and §63-2 to §63-20.

Residue Chemistry Chapter: §171-4: Metabolism studies in ruminants and poultry, residue analytical methods, storage stability data, magnitude of residues in sugar beet roots and tops, corn, processing study, corn forage and fodder, sorghum, and sorghum forage and fodder.

DETAILED CONSIDERATIONS

The Petitioner's Statement

In the Introduction section of the 12/21/88 letter, the registrant made the following statement:

> "American Cyanamid Company first obtained registration for COUNTER® systemic insecticide-nematicide in 1974, and updated the data base for it as required in the Terbufos Registration Standard of 1983. In part because COUNTER® is a mature product, and in part because the Agency has out-of-date information on acutal use of COUNTER®, we take this opportunity to set forth clarification and label amendments for the product:

1. We point out that there no longer are any aerial or ground applied broadcast uses for COUNTER®. These were SLN registrations which have expired. Cyanamid will not support renewal of these registrations and will not pursue Section 3 registrations for aerial or ground applied broadcast uses on any crop.

2. After study of the typical use of this mature product, Cyanamid wishes to retain uses in corn, sorghum and sugar beets. However, we wish to amend our label as follows:

   For corn (field, sweet, and pop), we wish to limit the applications to one treatment per season rather than the combination of at-planting and post-planting treatments which the label now allows. Eliminating the option for combinations of treatments will limit the maximum amount of product applied per acre per season and will eliminate the stated requirement for residue trials for combinations of at planting and post-planting treatments.

   For corn (field, sweet, and pop), we wish to lower the maximum use rate from 2.5 lb ai/acre to 1.3 lb ai/acre. The decrease in use rate will not affect the efficacy of this product against the pests for which it is labelled.

   For grain sorghum we wish to decrease the maximum use rate of the at-planting banded treatment from 3.9 lb ai/acre to 1.9 lb ai/acre.

Our comments on the various registration requirements are predicted on the above label amendments."

The Outstanding Data Gaps

The petitioner is requested to resolve the data gaps specified in the Product Chemistry Chapter (§61-1, §61-2, §61-3, §62-1, §62-2, §62-3, §63-2 thru §63-20) and Residue Chemistry Chapter (§171-4: storage stability data, magnitude of residues in sugar beet roots, sorghum and sorghum forage or fodder) of the Terbufos Registration Standard.

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The Petitioner's Response

The petitioner acknowledges the above data gaps and indicated that reports for filling these data gaps will be submitted in due time.

DEB's Comment/Conclusion

Since no data are provided with the current submission, DEB, therefore, concludes that these data gaps remain outstanding.

Data Gap §171-4: Metabolism Study in Ruminants and Poultry (Footnotes No.3 and 4)

"Metabolism studies using ruminants and poultry must be submitted. Animals must be dosed for at least 3 days with methylene-labeled ^{14}C-terbufos at a level high enough to permit identifications and quantification of ^{14}C-residues. Milk and eggs must be collected twice daily during the dosing period. Animals must be sacrificed within 24 hours of the final dose. The distribution and characterization of residues must be determined in milk, eggs, liver, kidney, muscle, and fat. Samples from these studies must also be analyzed using enforcement methods (including all FDA Multiresidue protocols [I-IV]) to ascertain that the methods are capable of adequately recovering and quantifying all residues of toxicological concern."

"Data depicting the nature of terbufos residues in swine are also required if the required metabolism studies with ruminants and poultry reveal that the metabolism of terbufos in these animals differs from that in rats."

The Petitioner's Response

The petitioner considers that these metabolism studies "would be of little value" because of the reasons quoted below:

1. "It appears to us that the main rationale for requiring these studies is to compare metabolism in ruminants and poultry with metabolism in rats. In fact, the Residue Chemistry Branch rejects our rat metabolism study, whereas the Toxicology Branch accepts that same study."

2. "We understand that the purpose of metabolism studies is to identify the metabolites of toxicological concern. For terbufos, it is well known that these are the phosphorylated, cholinesterase-inhibiting compounds, therefore, additional studies would be of little value."

3. "Further, the Agency has valid studies on file which show that the total toxic residues in animal tissues, milk and eggs are lower than the limits of detection for each commodity. Based on these studies, terbufos was classified in Category 3 of 40 CFR 180.6(a). This classification means that there is no reasonable expectation of residues in animal tissues, milk, or eggs."

4. "Other lines of evidence also suggest to us that further metabolism work is not necessary. Studies on phorate, a homolog of terbufos, in the rat show virtually identical metabolic profiles for the two compounds. Therefore, we would expect the same to occur in the goat. Data have been submitted on the metabolism of phorate in the goat; metabolism in the rat and goat is similar. A poultry metabolism study is also being conducted with phorate."

DEB's Comments/Conclusions on the Petitioner's Response

DEB does not agree with the petitioner's comments because of the following reasons:

1. DEB did not reject the metabolism study on rats (see Table A on page 50 of the Guidance Document). The purpose of these studies is to identify the nature of the residues in the edible tissue of livestocks, milk and eggs. Furthermore, a rat metabolism study does not generally substitute for metabolism data on livestocks. Please refer to the Pesticide Assessment Guidelines, Sub-division O.

2. The metabolism of terbufos in livestocks is cited by the Agency as a data gap and it will remain so until relevant data are provided for our evaluation.

3. Classification in Category 3 of 40 CFR 180.6(a) may change to reflect the magnitude of the dietary burden to livestocks. Therefore, the nature of residues in livestock commodities must be elucidated.

4. The registrant may submit or reference any supporting studies as required by the Guidelines.

DEB, therefore, concludes that this data gap is still outstanding. However, the registrant should be told that the FDA multiresidue procedures do not need to be examined for their ability to determine the radiolabeled residue.

Data Gap §171-4: Residue Analytical Methods (Footnote No. 5)

"Residues of terbufos must be tested in representative plant commodities by multiresidue protocol IV (available from NTIS under order No. PB 8620373/AS). Also, each of the phosphorylated metabolites listed in the proposed tolerance definition must be tested by all four multiresidue protocols. In addition, methodology validation data pertaining to recovery of these individual metabolites from additional representative plant commodities are required. Additional analytical data for detection of terbufos residues of concern in animal products may be necessary upon receipt and evaluation of the animal metabolism data as described in footnote 3 and 4 of this table."

The Petitioner's Response

The petitioner agrees to test all residues of toxicological concern in Multiresidue Methods I, II and III. This includes parent, parent sulfoxide and sulfone, oxygen analogy and oxygen analogy sulfoxide and sulfone and will report the results by

12/22/89; however, "we see not scientific reason why any of these compounds should be tested in Multiresidue Method IV. None of these compounds has a fluorescent moiety."

DEB's Comment/Conclusion

The petitioner should be notified that FDA has revised the Appendix II of PAM I in April, 1989 under the topic of Protocols and Reporting Forms for Testing Chemicals Through FDA Multiresidue Methods and that this data gap should be resolved according to the revised protocols. Also, the FDA tables show that testing has been done on the parent compound, terbufos. Therefore, only the metabolites needed to be tested. At this time, DEB concludes that this data gap has been partially resolved.

Data Gap §171-4: Magnitude of Residues in Sugar beet Tops (Footnotes No.8)

"The registrant must propose an appropriate tolerance for residues of terbufos and its cholinesterase-inhibiting metabolites in or on sugar beet tops based on data depicting residues in or on sugar beet tops harvested at regular intervals through normal crop maturity following at-planting application of the 15% G formulation at 4.4 lb ai/field A (2.7 oz ai/1,000 ft of row, 20-inch row spacing) drilled in 2 inches to the side and 2 to 4 inches below the seed. Tests must be conducted in CA(23%), MN(20%) or ND(10%), ID(15%), and NE(7%) or CO(4%) or WY(3%) representing ca. 80% of 1985 U.S. sugar beet production (Agricultural Statistics 1986 p.76). The registrant must propose label amendments establishing a PHI; this PHI must be reflected in the data requested above and in all other data used to support the tolerance."

The Petitioner's Response

"We would like the Agency to reconsider this requirement. It appears to us that grazing on sugar beet tops is, according to the Agency, under the grower's control. Therefore, we propose to amend our label to prohibit grazing of the tops treated plants."

DEB's Comment/Conclusion

DEB does not agree with the petitioner's response for the following reasons:

1. This data gap is based on the fact that the available data do not support the tolerance of terbufos and its cholinesterase-inhibiting metabolites in or on sugar beet tops at 0.1 ppm established under 40 CFR 180.352. The available data indicated that residues of 0.12 - 2.78 ppm were determined in/on three samples of sugar beet leaves harvested 40-91 days after in-furrow application of terbofos according to the proposed use. The registrant, therefore, must propose an appropriate tolerance for residues of terbufos and its cholinesterase-inhibiting metabolites in or on sugar beet tops based on adequate residue data, regardless of grazing restriction.

2. Sugar beet tops is an important feed item for livestock. Restriction of sugar beet tops as a feed item is no longer considered practical.

DEB, therefore, concludes that this data gap is still outstanding.

Data Gap §171-4: Magnitude of Residues in Corn (Footnotes No. 9, 10 and 11)

"Data are required depicting residues of concern in or on grain from field corn planted in 30-inch rows and harvested at normal crop maturity following application of the 15% G formulation in a band at-planting at 1.2 oz ai/1,000 ft of row and incorporated postemergence in a band at 2.4 oz ai/1000 ft of row (3.9 lb ai/field A seasonal use rate). Tests must be conducted in IL(17%) or IA(19%), IN (9%) or MI(3%) or OH(6%), MN(8%) or WI(4%), and NE(11%) or KS(2%) collectively representing ca. 80% of 1985 U.S. corn production (Agricultural Statistics 1986 p.32)."

"Data are required depicting residues of concern in or on grain from field corn grown in 30-inch rows and harvested 45 days after the last applications of the 15% G formulation, including a banded application at-planting of a 1.2 oz ai/1,000 ft of row, a postemergence banded application at cultivation at 1.2 oz ai/1000 ft of row, and a postemergence broadcast application of 1 lb ai/A applied by aerial or ground equipment (seasonal use rate of 3.6 lb ai/field A). Tests must be conducted in IA, NE, and NM, the states having SLN restrictions that allow the postemergence broadcast applications. Alternatively, the registrant may elect to cancel the SLN registrations for postemergence broadcast use on field corn."

"Data are required depicting residues of concern in or on K+CWHR from sweet corn planted in 30-inch rows and harvested at the PHI following the last of two applications of the 15% G formulation including a banded application at-planting at 1.2 oz ai/1,000 ft of row and a postemergence incorporated banded application of 2.4 oz ai/1000 ft of row (3.9 lb ai/field A seasonal use rate). Tests must be conducted in the states of FL(7%), IL(6%), MN(20%) or WI(20%), and OR(10%) or WA(10%) collectively representing ca. 70% of 1985 U.S. sweet corn production for fresh market and processing (Agricultural Statistics 1986 p.156). The registrant must propose label amendments establishing a PHI for sweet corn K+CWHR that is reflected in the data requested above. The data requested for field corn grain will be translated to support the tolerance for popcorn grain."

The Petitioner's Response

"The terbufos label will be amended to limit application to a single treatment at-planting or postemergence. Because the treatment will be restricted to one application per season, we believe that the requested studies are no longer necessary. (see the section of The Petitioner's Statement on p. 2 of this memo)."

DEB's Comments (See Conclusion on P. 9)

The original reasons for this data gap were specified on p. 20 of the Terbufos Registration Standard (9/25/87) as follows:

> "The data currently available are insufficient to assess the tolerances for terbufos residues of concern in or on field corn grain, popcorn grain and sweet corn K+CWHR because: (i) the method used to analyze residues in samples of field corn grain was not specified; (ii) data submitted for postemergence banded and broadcast applications to field corn did not represent the maximum seasonal use rate; and (iii) no data were submitted pertaining to postemergence banded applications to sweet corn."

The reviewer re-studied the residue data submitted previously and found: (i) The method used to analyze residues in samples of field corn grain was American Cyanamid Company's residue method M-336 which was considered adequate for enforcement purposes for corn grain and forage (see L. S. Propst's 10/31/80 memo in connection with PP#6F1765). (ii) Less than 0.05 ppm residues were determined in all corn grain samples (see the discussion of the next data gap below). (iii) The proposed label amendment (one application at 1.3 lb ai/A/season) will definitely reduce residue level, if any, in corn commodities. Therefore, DEB considers that the petitioner's comment on this data gap is reasonable. However, some additional data are needed on corn grain to address potential concentration in processed commodities (see DEB's Conclusion on P.9).

Data Gap §171-4: Magnitude of Residues in Corn Processed Commodities (Footnote 12)

"A processing study is required depicting terbufos residues of concern in products (starch, crude oil and refined oil from wet milling; grits, meal, flour, crude oil and refined oil from dry milling; and grain dust) processed from field corn grain bearing measurable, weathered residues. If residues concentrate in any product, appropriate food/feed additive tolerances must be proposed."

The Petitioner's Response

"As mentioned above under Magnitude of Residues in Corn, the label will be amended to limit application to a single treatment. As stated earlier in this letter, Cyanamid will not pursue Section 3 registration for broadcast application by aerial or ground equipment. In support of this guideline criterion, the Agency has on file 25 residue studies (ACC. #232258; MRID #00137582) for single and multiple applications of terbufos in corn with sampling times ranging from 45 to 141 days. No residues were detected (detection level = 0.05 ppm) in grain samples from all treatments, and in 1983, the Agency waived the requirement for a processing study. In view of the data on file and the proposed label amendments, we believe that aprocessing study is not necessary."

DEB's Comment (see Conclusion on P.9)

The original reasons for this data gap were specified on p. 20 of the Terbufos Registration Standard (9/25/87) as follows:

> "The requirement for a corn processing study was waived in the terbufos Residue Chemistry Chapter dated 1/19/83 because residues were nondetectable in a single field corn grain sample harvested 144 days following an exaggered-rate (5X) at-planting treatment. Postemergence uses are currently registered which permit harvest of field corn grain 45 days posttreatment. Therefore, the available data are insufficient to assess the potential for concentration of terbufos residues of concern in the processed products of field corn."

DEB verified the data referred above and confirmed the petitioner's statement. However, this data gap was due to insufficient residue data to support the registered postemergence uses. DEB, therefore, considers that the request of additional residue data to assess the potential for concentration of terbufos residues of concern in the processed products of field corn is justified (see DEB's Conclusion on P. 9).

Data Gap §171-4: Magnitude of Residues in Corn Forage and Fodder (Footnotes 15 and 16)

"Data are required depicting terbufos residues of concern in or on forage and fodder of field corn grown in 30-inch rows and harvested 30 days after application of the 15% G formulation banded at-planting at 1.2 oz ai/1,000 ft of row and incorporated postemergence in a 2.4 oz ai/1,000 ft of row (seasonal use rate of 3.9 lb ai/field A). Tests must be conducted in IL(17%) or IA (19%), IN(9%) or MI(3%) or OH(6%), MN(8%) or WI(4%), and NE(11%) or KS(2%) collectively representing ca. 80% of 1985 U.S. corn production (Agricultural Statistics 1986 p.32)."

"Data are required depicting terbufos residues of concern in or on forage and fodder of field corn grown in 30-inch rows and harvested 45 days after the last three applications of the 15% G formulation, including a banded application at-planting of 1.2 oz ai/1,000 ft of row, a postemergence banded application at cultivation of 1.2 oz ai/1000 ft of raw, and a postemergence broadcast application of 1.0 lb ai/A applied by aerial or ground equipment (seasonal use rate of 3.6 lb ai/field A). Tests must be conducted in IA NE and NM, the states having SLN registrations that allow the postemergence broadcast applications. Alternatively, the registrant may elect to cancel the SLN registrations for postemergence broadcast use on field corn."

The Petitioner's Response

"As mentioned above under the section of Magnitude of Residues in Corn, application will be limited to a single treatment per season, either at-planting or postemergence. Therefore, we think that this study is no longer necessary."

DEB's Comment (see Conclusion on P.9)

The original reasons for this data gap were specified on p. 25 of the Terbufos Registration Standard (9/25/87) as follows:

> "The data now available are insufficient to assess these tolerances because only three samples represent both the maximum use rates for individual post-emergence banded application and the overall maximum seasonal use rates. None of the data represent maximum seasonal use rates for treatments involving postemergence broadcast applications."

Because this data gap was due to insufficient residue data to support the established tolerances on corn forage and fodder, DEB believes that the request for additional residues data to assess these tolerances is justified (see DEB's Conclusion below).

DEB's Conclusion

Since the petitioner plans to amend their label on field corn use by limiting to one application of Counter® per season and at 1.3 lb ai/A, DEB concludes that the petitioner should conduct trials on field corn in IL(17%) and IA(19%) reflecting postemergence applications at the rates of 1X (1.3 lb ai/A/season) and 5X. Samples of grain, forage and fodder should be collected at adequate PHI's for residue analysis. The adequacy of the established tolerances on corn grain, forage and fodder will be re-evaluated using the residue data so generated. If no residues (<0.05 ppm) are detected in all corn grain samples, the established 0.05 ppm tolerance on corn grain will be considered adequate and corn grain treated at the 5X rate should be processed to determine the need for food and feed additive tolerances.

At this time, the data gaps identified in the footnotes No. 9, 10, 11, 12, 15 and 16 of the Guidance for the Reregistration of Pesticide Products Containing Terbufos as the Active Ingredient (September 1988) are still considered outstanding.

cc: Circu., R.F., W.T.Chin, R.D.Schmitt, PMSD-ISB and Terbufos Reg. Std.
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