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

OFFICE OF
PREVENTION, PESTICIDES,
AND TOXIC SUBSTANCES

MEMORANDUM

Date: October 14, 2005

Subject: Triadimenol. Registrants Response to Residue Chemistry Data Requirements. Field Corn, Cotton, and Wheat Processing Studies.

DP Barcode: D322336 PC Code: 127201
40 CFR §: 180.410 Chemical Class: Azole
MRID Numbers: 44519801, 44519802, and 44519803

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INTRODUCTION

In response to the Triadimenol Data Call-In (3/8/1996), Gustafson, Inc, has submitted data pertaining to the magnitude of triadimenol residues of concern in the processed commodities of field corn (1998; MRID 44519801), cotton (1998; MRID 44519802) and wheat (1998; MRID 44519803). These data are evaluated in this document for adequacy in fulfilling residue chemistry data requirements.

Triadimenol, β-(4-chlorophenoxy)-α-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol, is a systemic fungicide registered for use in the United States as a seed treatment for barley, corn, cotton, oats, rye, sorghum, and wheat. Additionally, an import tolerance on bananas has been established. Triadimenol end-use products are marketed in the U.S. under the trade name Baytan®. The reregistration of triadimenol is being supported by Bayer CropScience (Bayer), the basic producer. The triadimenol formulations registered for food/feed uses include wettable powder (WP), flowable concentrate (FlC), emulsifiable concentrate (EC), and soluble concentrate (SC) formulations.

Tolerances are established for residues of triadimenol and 1-(4-chlorophenoxy)-3,3-dimethyl-3- hydroxymethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanol (KWG 1342; calculated as triadimenol) in/on various plant commodities [40 CFR §180.450(a)]. The established tolerances for plant commodities range from 0.01 ppm (sorghum grain and fodder) to 2.5 ppm (green forage of oats, rye, and wheat). Tolerances are established for residues of triadimenol and its metabolites containing the chlorophenoxy moiety (calculated as triadimenol) in/on livestock commodities at 0.01 ppm (milk, and poultry commodities) and 0.1 ppm (fat, meat, and meat byproducts of cattle, goats, hogs, horses, and sheep).

Triadimenol and its butanediol metabolite (KWG 1342) are also regulated as metabolites of the fungicide triadimefon (40 CFR §180.410).

The reregistration requirements for plant metabolism have not been fulfilled. No metabolism studies with triadimenol have been submitted; however, metabolism studies with triadimefon have been received and reviewed. The Health Effects Division (HED) has examined the results of these studies and determined that the triadimefon residues of concern in/on apples, grapes, pears, pineapples, and raspberries for tolerance expression are triadimefon and triadimenol and for risk assessment are triadimefon, triadimenol, KWG 1323 [1-(4-chlorophenoxy)-3,3-dimethyl- 3-hydroxymethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone], and KWG 1342 (S. Ary, D314742, 11/23/2005). Of these compounds, triadimenol and KWG 1342 are currently regulated for plant commodities.

HED has determined that translation of metabolism data from triadimefon to triadimenol is not appropriate for the existing uses on cereal grains and cotton. The metabolism studies with triadimefon were conducted using a foliar application and triadimenol is used only as a seed treatment. Additionally, in the submitted triadimenol seed treatment wheat study, residues in grain were not identifiable due to the low activity found in wheat grain. Therefore, HED concludes that the nature of the residue in cereal grains and cotton is not adequately understood; however, based on chemical structure and the probable metabolic pathway of triadimenol, the residues of concern for tolerance expression and risk assessment are likely to be triadimenol, KWG 1342, and KWG 1732 in/on cereal grains (barley, corn, oats, rye, and wheat) and cotton. Separate metabolism studies with triazole-^{14}C and phenyl-^{14}C labeled triadimenol applied as a seed treatment to corn or wheat and cotton should be conducted to confirm the residues of concern. The residues of concern for tolerance expression and risk assessment for bananas are triadimenol and KWG 1342.

The Pesticide Analytical Manual (PAM) Vol. II does not contain a listing for triadimenol (February 1997 Index). However, the methods listed for triadimefon can be used for the determination of triadimenol, KWG 1323, KWG 1342, and KWG 1732. PAM lists two gas chromatography with mass spectrometry detection (GC/MS) methods (Methods I and II) for the determination of triadimenol and its free and conjugated metabolites in plant and livestock commodities. Both methods are common moiety methods. The reported limit of quantitation (LOQ) is 0.05 and limit of detection (LOD) is 0.01 ppm for both methods.

In conjunction with triadimefon reregistration, Bayer has proposed a GC/MS method (Report No. 106549) for enforcement of tolerances for residues of triadimefon, triadimenol, KWG 1342, KWG 1323, and KWG 1732 in/on barley, corn, cotton, oat, rye, and wheat commodities. The method has been successfully radiovalidated and has undergone independent laboratory validation. The reported method LOQ is 0.05 ppm for each analyte in cereal grains and 0.02 ppm in each analyte in cotton. Additionally, a GC method using a nitrogen phosphorus detector (NPD; Report No. 80488) is available for determination of residues of triadimenol, KWG 1342, and KWG 1323 and is adequate for the enforcement of the banana tolerance. The method has undergone a successful Agency method validation on tomatoes and was submitted to the FDA for publication in PAM Vol. II. The reported method LOQ is 0.01 ppm for each analyte.

CONCLUSIONS AND RECOMMENDATIONS

Processed Food/Feed

1. Field corn: The submitted data are adequate to fulfill the requirement for a field corn grain processing study. As triadimenol residues of concern were each below the LOQ (0.05 ppm) in/on corn grain grown from seed treated at 5x the maximum application rate, a corn grain processing study and tolerances for field corn processed commodities are not required.

2. Cotton: The submitted data are adequate to fulfill the requirement for a cottonseed processing study. As triadimenol residues of concern were each below the LOQ (0.02 ppm) in/on cottonseed grown from seed treated at 5x the maximum application rate, a cottonseed processing study and tolerances for cotton processed commodities are not required.

3. Wheat: The available wheat grain data do not fulfill the requirement for a wheat grain processing study. Residues of triadimenol and KWG 1342 were each <LOQ (<0.05 ppm) and residues of KWG 1732 were 0.11 ppm and 0.23 ppm in/on two samples of wheat grain grown from seed treated with triadimenol (FlC) at 5x the maximum rate. However, the treated grain was not processed. Instead, the registrant proposed translating data from a triadimefon wheat grain processing study; however, these data cannot be translated to triadimenol due to differences in the use patterns (seed treatment vs. late season foliar sprays) that are likely to impact the potential for concentration of residues in grain. The registrant should conduct a processing study using the available wheat grain grown from the seeds treated with triadimenol at 5x.

DETAILED CONSIDERATIONS

Residue Analytical Methods

Samples of field corn grain, cottonseed, and wheat grain were analyzed for residues of triadimenol, KWG 1342, and KWG 1732 at ABC Laboratories (Columbia, MO) using a

GC/MS method (Bayer Corporation Report No. 106549). This method has been proposed for enforcement of tolerances for triadimefon residues of concern and has undergone successful independent laboratory validation (J. Punzi; D222403, D227497, and D227543; 7/13/2000).

Briefly, residues are extracted under reflux in methanol:water (7:3, v:v) for 2 hours and then concentrated to an aqueous solution. The extract is then hydrolyzed with cellulase at 37 C overnight (at pH 5.5) and partitioned with dichloromethane:acetonitrile (3:2, v:v). The aqueous phase, containing KWG 1732, is reserved. The organic phase is dried using sodium sulfate and evaporated to dryness, and residues are redissolved in ethyl acetate, cleaned up by gel permeation chromatography, and separated by semi-preparative HPLC into two fractions: one containing triadimenol and the other containing KWG 1342. Triadimenol was determined directly by GC/MS; KWG 1342 was derivatized prior to GC/MS analysis. The reported LOQ was 0.05 ppm for each analyte in field corn and wheat grain and 0.02 ppm for each analyte in cottonseed.

The reserved aqueous phase, containing KWG 1732, is acidified to pH 1 (using concentrated HCl) and the residues are partitioned into ethyl acetate. The residues are then partitioned into 0.5 M sodium carbonate, acidified to pH 1, and repartitioned back into ethyl acetate. The residues are then evaporated to dryness, redissolved in methanol:dichloromethane (20:80; v:v), methylated with trimethylsilyl diazomethane, and cleaned up by silica gel solid phase extraction for analysis by GC/MS. Triadimefon was used as an internal standard for KWG 1732 analysis. The reported LOQ was 0.05 ppm for field corn and wheat grain and 0.02 ppm for cottonseed.

The registrant provided method validation and concurrent method recovery data for the GC/MS method from fortifications at the LOQ. These recovery data are presented in Table 1. These data indicate that the GC/MS method is adequate for data collection purposes.

Table 1. Recoveries of triadimenol and its metabolites KWG 1342, and KWG 1732 from fortified samples of untreated field corn grain, cottonseed, and wheat grain.

	Triadimenol		KWG 1342		KWG 1732	
Commodity	Fortification Level (ppm)	% Recovery [a]	Fortification Level (ppm)	% Recovery [a]	Fortification Level (ppm)	% Recovery [a]
Field corn Grain	0.05	76-84 (4)	0.05	86,88; 134, 142	0.05	88-102 (3)
Cottonseed	0.02	95-100 (3)	0.02	75-80 (3)	0.02	75-120 (3)
Wheat Grain	0.05	72-82 (3)	0.05	100-108 (3)	0.05	60, 62; 76

[a] Each value represents one sample unless otherwise indicated in parentheses; recovery values outside the acceptable 70-120% range are listed separately.

Storage Stability Data

Samples of field corn grain, cottonseed, and wheat grain were placed in frozen storage (temperature unspecified) within 4 hours of sample collection, and then shipped frozen to the analytical laboratory, where they were stored frozen (~-20 C) until analysis. Subsamples of the unginned cottonseed were removed from the freezer at the field trial site after approximately 3 months of storage; these subsamples were ginned, frozen, and then shipped to the analytical laboratory. Analyses were completed 82-96 days following collection for field corn grain samples, 201-236 days following collection for cottonseed samples, and 44-51 days following collection for wheat grain samples.

Storage stability data for triadimenol, KWG 1342, and KWG 1732 have been submitted by Bayer Corporation to satisfy reregistration data requirements for triadimefon. These data indicate that residues of triadimenol and KWG 1342 are stable in wheat grain for up to 2 years of at -20 C (S. Hummel; D168542 and D178884; 12/22/92) and residues of KWG 1732 are stable in wheat grain for up to 2.5 years at -20°C (J. Punzi; D222403, D227497, and D227543; 7/13/2000). These data are adequate to support the storage intervals and conditions of the samples from the submitted field corn grain, cottonseed, and wheat grain studies.

Magnitude of the Residue in Processed Food/Feed

Field Corn

Established tolerances: No tolerance has been established for triadimenol residues of concern in any field corn processed commodity. A tolerance of 0.05 ppm has been established for triadimenol residues of concern in/on field corn grain [§180.450(a)].

Use directions: The 2.65 lb/gal FlC formulation (EPA Reg. No. 7501-91) is registered for use on field corn as a seed treatment at 0.062 lb ai (1.0 oz ai) per 100 lb of seed. Application is to be made by mixing the dosage in 16 fluid oz of water per 100 lb of seed. The use of treated seed for feed, food or oil purposes is prohibited. A 45-day PHI has been established for forage.

Discussion of data: Gustafson has submitted data (1998; MRID 44519801) depicting the potential for concentration of triadimenol residues of concern in field corn processed commodities. Field corn seed was treated with the 2.65 lb/gal FlC formulation at 0.313 lb ai (5.0 oz ai) per 100 lb of seed (5x the maximum application rate) prior to planting. The treated seed was planted in IA six days after treatment. One sample of field corn grain grown from untreated seed and two samples of field corn grain grown from treated seed were collected at maturity, 177 days after planting. The field corn grain samples were placed in frozen storage within 2 hours of collection, and then shipped frozen to the analytical laboratory (ABC Laboratories), where they were stored frozen until analysis.

Field corn grain samples were analyzed for residues of triadimenol, KWG 1342, and KWG 1732. Residues were below the LOQ (<0.05 ppm) for each analyte in/on one sample of untreated field corn grain and two samples of treated field corn grain. Because no quantifiable residues were observed in/on corn grain following treatment at 5x the maximum application rate, a processing study was not conducted.

Study summary: The submitted data are adequate to fulfill the requirements for a field corn grain processing study. As triadimenol residues of concern were <LOQ in/on corn grain grown from seed treated at 5x the maximum application rate, a corn grain processing study and tolerances for field corn processed commodities are not required.

Cottonseed

Established tolerances: No tolerance has been established for triadimenol residues of concern in any cottonseed processed commodity. A tolerance of 0.02 ppm has been established for triadimenol residues of concern in/on cottonseed [§180.450(a)].

Use directions: The 0.43 lb/gal EC formulation (EPA Reg. No. 7501-80) is registered for use on cotton as a seed treatment at 0.040 lb ai (0.6 oz ai) per 100 lb of seed. The use of treated seed for feed, food or oil purposes is prohibited.

The 2.65 lb/gal FlC formulation (EPA Reg. No. 7501-91) is registered for use on cotton as a seed treatment at 0.062 lb ai (1.0 oz ai) per 100 lb of seed. Application is to be made by mixing the dosage in 16 fluid oz of water per 100 lb of seed. The use of treated seed for feed, food or oil purposes is prohibited.

Discussion of data: Gustafson has submitted data (1998; MRID 44519802) depicting the potential for concentration of triadimenol residues of concern in cottonseed processed commodities. Cotton seed was treated with the 2.65 lb/gal FlC formulation at 0.313 lb ai (5.0 oz ai) per 100 lb of seed (5x the maximum application rate) prior to planting. The treated seed was planted in MS 13 days after treatment. One sample of cottonseed grown from untreated seed and two samples of cottonseed grown from treated seed were collected at maturity, 148 days after planting. The samples were placed in frozen storage within 1 hour of collection. Subsamples of the unginned cottonseed were removed from the freezer after approximately 3 months of storage; these subsamples were ginned, frozen, and then shipped to the analytical laboratory (ABC Laboratories), where they were stored frozen until analysis.

Ginned cottonseed samples were analyzed for residues of triadimenol, KWG 1342, and KWG 1732. Residues were below the LOQ (<0.02 ppm) for each analyte in/on one sample of untreated cottonseed and two samples of treated cottonseed. Because no quantifiable residues were observed following treatment at 5x the maximum application rate, a processing study was not conducted.

Study summary: The submitted data are adequate to fulfill the requirement for a cottonseed processing study. As triadimenol residues of concern were each below the LOQ (0.02 ppm) in cottonseed grown from seed treated at 5x the maximum application rate, a cottonseed processing study and tolerances for cotton processed commodities are not required.

Wheat

Established tolerances: No tolerance has been established for triadimenol residues of concern in any wheat processed commodity. A tolerance of 0.05 ppm has been established for triadimenol residues of concern in/on wheat grain [§180.450(a)].

Use directions: The 0.43 bl/gal EC formulation (EPA Reg. No. 7501-80), 2.65 lb/gal FlC formulation (EPA Reg. No. 7501-91), 2.6 lb/gal FlC formulation (EPA Reg. No. 3125-424), and 6.25% D formulation (EPA Reg. No. 7501-150) are registered for use on wheat as a seed treatment at 0.03 lb ai (0.5 oz ai) per 100 lb of seed. Application is to be made by mixing the dosage in 16 fluid oz of water per 100 lb of seed (FlC formulations only). The use of treated seed for feed, food or oil purposes is prohibited. A 40-day PHI has been established for forage. We note that the registrant has requested cancellation of the 6.25% D formulation (65 FR 24477, 4/26/00).

Discussion of data: Gustafson has submitted data (1998; MRID 44519803) depicting the potential for concentration of triadimenol residues of concern in wheat processed commodities. Wheat seed was treated with the 2.65 lb/gal FlC formulation at 0.16 lb ai (2.5 oz ai) per 100 lb of seed (5x the maximum application rate) prior to planting. The treated seed was planted in TX 18 days after treatment. The registrant noted that the treated seed did not grow as well as the untreated seed, and that the treated plot suffered ~40-50% loss due to winter freezing conditions. One sample of wheat grain grown from untreated seed and two samples of wheat grain grown from treated seed were collected at maturity, 308 days after planting. The wheat grain samples were placed in frozen storage within 4 hours of collection,

and then shipped frozen to the analytical laboratory (ABC Laboratories), where they were stored frozen until analysis.

Wheat grain samples were analyzed for residues of triadimenol, KWG 1342, and KWG 1732. Residues were below the LOQ (<0.05 ppm) for each analyte in/on one sample of untreated wheat grain. Residues of triadimenol and KWG 1342 were below the LOQ in/on two samples of treated wheat grain. Detectable residues of KWG 1732 were observed in the wheat grain samples at 0.11 ppm and 0.23 ppm.

The registrant did not process seed from the above 5x field trial; instead, Gustafson cited a wheat processing study submitted by Bayer Corporation to fulfill reregistration requirements for triadimefon (1996; MRID 44029301). In that study, mature wheat grain was harvested 35 days following the last of two foliar broadcast applications of a 50% WP triadimefon formulation (EPA Reg. No. 3125-340) at 0.9 lb ai/A/application (ca. 4x the maximum seasonal use rate for triadimefon). At the processing facility (Texas A&M University Food Protein and Development Center, Bryan, TX), aspirated grain fractions were collected (data for aspirated grain fractions are not presented here) and wheat grain samples were processed into bran, wheat germ, flour, middlings, and shorts, using a small-scale processing procedure which simulated normal commercial processing conditions. The residues of triadimenol, KWG 1342, and KWG 1732 found in wheat grain and its processed commodities are presented in the Table 2. These data indicate that the combined residues of triadimenol, KWG 1342, and KWG 1732 concentrate by 2.1x in wheat bran but do not concentrate in wheat flour, middlings, shorts, or germ.

Table 2. Residues of triadimenol, KWG KWG 1342, and KWG 1732 in the processed commodities of wheat grain harvested at maturity (35 days) following the last of two foliar applications of triadimefon at 4x the maximum seasonal triadimefon rate (MRID 44029301).

Grain					
Bran					
Flour					
Middlings					
Shorts					
Germ					

[a] Each residue value represents a single sample.

However, these data cannot be translated to triadimenol because of differences in the use patterns of the two compounds. The use of triadimefon on wheat, which Bayer is no longer supporting, involves late season foliar applications that are more likely to result in surface residues in/on wheat grain, as suggested by the concentration of residues in bran in the above study. However, the use of triadimenol as a seed treatment is unlikely to result in the concentration of residues in the outer seed coat. To assess the potential for the concentration of triadimenol residues in wheat grain, the registrant should conduct a processing study using the available wheat grain grown from the 5x treated seeds.

Study summary: The available wheat grain data do not fulfill the requirement for a wheat grain processing study. Residues of triadimenol and KWG 1342 were each <LOQ (<0.05 ppm) and residues of KWG 1732 were 0.11 ppm and 0.23 ppm in/on two samples of wheat

grain grown from seed treated with triadimenol (FlC) at 5x the maximum rate. However, the treated grain was not processed. Instead, the registrant proposed translating data from a triadimefon wheat grain processing study; however, these data cannot be translated to triadimenol due to differences in the use patterns (seed treatment vs. late season foliar sprays) that are likely to impact the potential concentration of residues. The registrant should conduct a processing study using the available wheat grain grown from the seeds treated with triadimenol at 5x.

AGENCY MEMORANDA CITED IN THIS REVIEW

DP Barcodes: D168542 and D178884
Subject: Triadimefon (109901): Storage Stability Data, PAM Multiresidue Methods, Product Chemistry Data. CBRS Nos. 8566 and 9929.
From: S. Hummel
To M. Wilhite/B. Sidwell
Dated: 12/22/92
MRIDs: 41976601, 41976602, and 42307801-42307803

DP Barcodes: D222403, D227497, and D227543
Subject: Triadimefon. Independent Laboratory Validation, Radiovalidation Data, and Storage Stability Data.
From: J. Punzi
To: B. Chambliss
Dated: 7/13/2000
MRIDs: 43870101, 44038901, 44041001, and 44041002

MASTER RECORD IDENTIFICATION NUMBERS

The citations for the MRID documents referred to in this review are presented below.

44029301 Grace, T. (1996) BAYLETON 50WP - Magnitude of the Residue in Wheat Processed Products: Lab Project Number: BL19WH02: 107130: PR95322. Unpublished study prepared by Bayer Corp.; Texas A&M University; and Maxim Technologies, Inc. 2508 p.

44519801 Shen, S. (1998) Determination of Residues of Baytan 30 in Processed Field Corn Fractions: Lab Project Number: 96-003: 963HI: 43514. Unpublished study prepared by ABC Labs., Inc. and Gustafson Research and Development Center. 458 p.

44519802 Shen, S. (1998) Determination of Residues of Baytan 30 in Processed Cotton Fractions: Lab Project Number: 96-001: 963HG: 43516. Unpublished study prepared by ABC Labs., Inc. and Gustafson Research and Development Center. 452 p.

44519803 Shen, S. (1998) Determination of Residues of Baytan 30 in Processed Wheat Fractions: Lab Project Number: 96-002: 963HH: 43513. Unpublished study prepared by ABC Labs., Inc. and Gustafson Research and Development Center. 462 p.