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OFFICE OF
PREVENTION, PESTICIDES
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OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

Date: April 5, 2008

SUBJECT: **Ingredient:** Prothioconazole **Title:** Amended Registration for Use on Peanuts. Summary of Analytical Chemistry and Residue Data. Decision No. 383255. 40 CFR §180.626.

PC Code: 113961
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Petition Nos.: None
Assessment Type: None
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Registration No.: 264-825
Regulatory Action: Amended Section 3
Reregistration Case No.: None
CAS No.: 178928-70-6

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Rec'd RRC 5/21/08

Executive Summary

Prothioconazole, 2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3 H -1,2,4-triazole-3-thione, is a systemic demethylation inhibitor fungicide which belongs to the triazolinthione class of fungicides (Group 3). In the U.S., a 4 lb/gal flowable concentrate (FlC) formulation of prothioconazole is registered to Bayer CropScience for use on various food/feed crops and is marketed under the trade name PROLINE™ 480 SC Fungicide (EPA Reg. No. 264-825). This formulation is currently registered for use on peanuts as broadcast foliar applications at up to 0.178 lb ai/A/application, at minimum retreatment intervals (RTIs) of 14 days, for a maximum seasonal use rate of 0.71 lb ai/A/season. The label specifies a 14-day preharvest interval (PHI) and prohibits the grazing or feeding of treated hay to livestock. Bayer has requested an amendment to the label directions on peanuts to allow for inclusion of either an in-furrow application at planting or a banded application at emergence at 0.178 lb ai/A; the maximum seasonal rate will remain unchanged.

Permanent tolerances have been establishment for the combined residues of prothioconazole and its metabolite prothioconazole-desthio, calculated as parent, in/on various plant commodities at levels ranging from 0.02-17 ppm, including tolerances at 0.02 ppm on peanut and 6.0 ppm on peanut hay. Tolerances on animal commodities have also been established for the combined residues of prothioconazole, prothioconazole-desthio, and conjugates that can be converted to either of these two compounds by acid hydrolysis, calculated as prothioconazole.

The nature of prothioconazole residues in plants and animals is adequately understood based on the available wheat, peanut, sugar beet, goat and poultry metabolism studies. In plants, the residues of concern include prothioconazole and its metabolite prothioconazole-desthio, both for purposes of tolerance enforcement and risk assessment. In animal commodities, the residues of concern for purposes of risk assessment include prothioconazole, prothioconazole-desthio, the 4-hydroxy prothioconazole metabolite, and conjugates that can be converted to any of these three compounds by acid hydrolysis.

The contribution of triazole derivatives [1,2,4-triazole, triazole alanine (TA), and triazole acetic acid (TAA)] from the use of prothioconazole on peanuts to the aggregate exposure for human-health risk assessment has been previously considered to be below HED's level of concern (DP# 322215, M. Doherty, 2/07/2006).

Adequate LC/MS/MS methods are available for enforcing prothioconazole tolerances in plant commodities (Bayer Method RPA JA/03/01) and animal commodities (Bayer Report No. 200537). In the submitted peanut field trials, combined prothioconazole residues in/on peanuts and peanut hay were determined using a slightly modified version of the enforcement method. The method was also adequately validated in conjunction with the analysis of field trial samples. For combined residues, the validated limits of quantitation (LOQ) were 0.02 and 0.10 ppm in peanuts and peanut hay, respectively, and the limits of detection (LOD) were 0.004 and 0.011 ppm, respectively.

Residues of triazole, TA and TAA in/on peanut and peanut hay sample from the field trials were also determined using an LC/MS/MS method (Morse Method Meth-160) that was adequately validated in conjunction with the analysis of the field trial samples. The validated LOQs were 0.01 ppm for triazole and TAA in nutmeats and hay and TA in hay, and 0.05 ppm for TA in nutmeats. The data were reported as triazole residues and total conjugated residues (TA + TAA), expressed in TA equivalents.

To support the proposed label amendment, Bayer submitted three side-by-side field trials in which prothioconazole (4 lb/gal FlC) was applied as either (i) four broadcast foliar applications at rates totaling 0.69-0.73 lb ai/A (1x maximum seasonal rate) or (ii) a combination of a seed treatment at 0.010-0.012 lb ai/A, an in-furrow application at planting at 0.172-0.178 lb ai/A, and four broadcast foliar applications at 0.086-0.094 lb ai/A, for a total of 0.54-0.55 lb ai/A (~0.8x maximum seasonal use rate).

At 8-14 days after the last treatment (DAT), combined prothioconazole residues were non-detectable (<0.004 ppm) in/on all samples of peanut nutmeats, regardless of the type of treatment (foliar only vs. in-furrow + foliar). For peanut hay, combined prothioconazole residues were consistently lower for the combined soil and foliar treatment (0.71-2.58 ppm) than from the foliar only applications (2.33-6.44 ppm). Although the combination application had foliar rates and a seasonal rate that were <1x, the peanut field trial data are adequate for the purposes for which they were intended. Given that residues were <0.004 ppm in/on all nutmeat samples from both types of applications, the data indicate that inclusion of an early-season soil application will not result in over-tolerance residues in nutmeats. The current tolerance for peanut hay should be revoked as the result of a label change.

An adequate peanut processing study is available indicating that separate tolerances are not required for peanut meal or oil.

Adequate confined and field rotational crop trials are available supporting the 30-day plant-back interval specified on the labels for rotational crops without registered uses. The data indicate that prothioconazole tolerances are not required for rotational crops.

Regulatory Recommendations and Residue Chemistry Deficiencies

Although the combined in-furrow and foliar applications used only ~0.8x (0.76x) the maximum seasonal rates (vs. 1x rate for the foliar only application), the available field trial data were adequate because the combined prothioconazole residues were non-detectable (<0.004 ppm) in nutmeats from both application regimes. The field trial data support the established tolerance on peanut (0.02 ppm), and based on the label restrictions on the grazing or feeding of peanut hay, the current tolerance on peanut hay (6.0 ppm) can be deleted. As no increases in tolerances are required for this label amendment, a new human health risk assessment for prothioconazole is not required. However, pending resolution of the deficiencies noted in the previous petitions (e.g., PP#6F7134, PP6F7073 and PP#4F6830) the registration for prothioconazole remains conditional.

Background

Prothioconazole is a systemic demethylation inhibitor fungicide which belongs to the triazolinthione class of fungicides (Group 3). Prothioconazole has demonstrated protective, curative, and eradicative action against plant diseases caused by ascomycetes, basidiomycetes, and deuteromycetes fungi in many crops.

The chemical structure, nomenclature and physicochemical properties of prothioconazole and its regulated plant metabolite are presented in Tables 1 and 2.

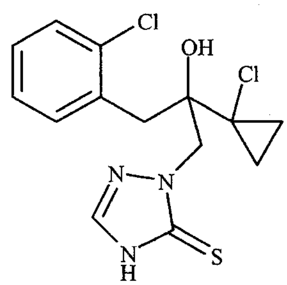
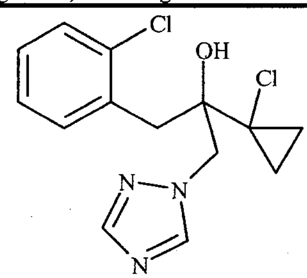
Table 1.	**Nomenclature of Prothioconazole and its Regulated Metabolite.**
Parent Compound	
Common name	Prothioconazole
Company experimental names	JAU6476
IUPAC name	2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole-3-thione
CAS Name	2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole-3-thione
CAS #	178928-70-6
End-use products/EP	Proline™ 480 SC (4 lb/gal FlC; EPA Reg. No. 264-825)
Regulated Metabolite	
Common name	Prothioconazole-desthio
Company Code	JAU6476-desthio
IUPAC name	2-(1-chlorocyclopropyl)-1-(2-chlorophenyl)-3-(1H-1,2,4-triazol-1-yl)propan-2-ol
CAS Name	α-(1-chlorocyclopropyl)-α-(2-chlorophenyl)methyl-1H-1,2,4-triazole-1-ethanol
CAS #	120983-64-4

Table 2. Physicochemical Properties of Prothioconazole Technical Grade Test Compound.

Parameter	Value	Reference (MRID)
Melting point	139.1 to 144.5 EC	46246003
pH	5.8 (1% solution)	46246002
Density	1.36 g/mL at 20 EC	46246003
Water solubility (mg/L at 20 EC)	pH 4 5 pH 8 300 pH 92000	46246001, 46246003
Solvent solubility (g/L at 20 EC)	Acetone >250 Acetonitrile 69 Dichloromethane 88 Dimethylsulfoxide 126 Ethyl acetate >250 n-Heptane <0.1 1-Octanol 58 Polyethylene glycol >250 2-Propanol 87 Xylene 8	46246001
Vapor pressure (at 20 or 25 EC)	<<4 x 10^{-7} Pa (calculated from determinations at 70 EC)	46246001, 46246003
Dissociation constant, pK_a	6.9 (calculated from K_{OW})	46246001, 46246003
Octanol/water partition coefficient (at 20 EC) [Log Kow]	unbuffered water 4.05 pH 4 4.16 pH 7 3.82 pH 92.00	46246001
UV/visible absorption	Peak maxima at 257 nm	46246003

860.1200 Directions for use

The current use of PROLINE™ 480 SC Fungicide (a 4 lb/gal FlC containing only prothioconazole, EPA Reg. No. 264-825) on peanuts allows for up to four broadcast foliar applications at up to 0.178 lb ai/A/application with a minimum RTI of 14 days, for a total of 0.713 lb ai/A/season. A 14-day preharvest interval is specified, and the use of peanut hay or threshings for livestock feed is prohibited. Bayer is requesting a label amendment for the use directions on peanuts to allow for either an in-furrow application at planting or a banded soil application at emergence at the rate of 0.178 lb ai/A. Bayer has provided a draft label containing the proposed use directions, which are summarized in Table 3.

Table 3. Summary of Proposed Directions for use of Prothioconazole.						
Application Timing, Type and Equipment	Formulation [EPA Reg. No.]	Single rate (lb ai/A)	Max. # of Appl. per Season	Max. Seasonal Appl. Rate (lb ai/A)	PHI (Days)	Use Directions and Limitations [1,2]
Peanuts						
In-furrow application at planting or banded soil application at or near emergence, ground equipment	4 lb/gal FlC [264-825]	0.178	4	0.713	14	A minimum RTI of 14 days is specified. Do not feed hay or threshings or allow livestock to graze in treated areas
Broadcast foliar applications, ground and aerial equipment		0.156-0.178				

1 Foliar applications may include use of a non-ionic surfactant. Ground and aerial applications should be applied in a minimum volume of 10 and 5 gal/A, respectively

2 The label allows immediate replanting of any crops listed on the label, and specifies a 30-day plant-back interval for crops not listed on the label.

Conclusion. The proposed use directions are adequate and indicate that inclusion of either an in-furrow or banded application at up to 0.178 lb ai/A will not result in combined prothioconazole residues exceeding the current 0.02 ppm tolerance. Although the side-by side field trial data reflected a slightly lower total use rate (~0.8x) for the combined in-furrow and foliar applications and a significantly lower rate for the foliar portion of the combined application as compared to the foliar only (50%), residues were non-detectable (<0.004 ppm) in/on nutmeats.

860.1300 Nature of the Residue – Plants

The qualitative nature of prothioconazole residues in plants is adequately understood based the available wheat, peanut, and sugar beet metabolism studies (DP #D303508, S. Funk 8/21/2006). For purposes of both tolerance enforcement and risk assessment, the residues of concern are the sum of prothioconazole and its prothioconazole-desthio, expressed as parent. The contribution of triazole derivatives (triazole, TA, and TAA) from prothioconazole to the aggregate exposure for human-health risk assessment has been considered to be below HED's level of concern (DP# 322215, M. Doherty, 2/07/2006).

860.1300 Nature of the Residue – Animals

The qualitative nature of prothioconazole residues in livestock commodities is adequately understood based the goat and hen metabolism studies (DP #D303508, S. Funk 8/21/2006). For purposes of tolerance enforcement, the residue of concern in livestock commodities consists of the sum of prothioconazole, the prothioconazole desthio metabolite, and conjugates that can be converted to either of these two compounds by acid hydrolysis, calculated as prothioconazole. For purposes of risk assessment, the residue of concern consists of prothioconazole, the prothioconazole desthio metabolite, the 4-hydroxy prothioconazole metabolite, and conjugates that can be converted to any of these three compounds by acid hydrolysis. Additionally, contribution of triazole derivatives (in poultry commodities) from the use of prothioconazole to the aggregate exposure for human-health risk assessment has been considered to be below HED's level of concern (DP# 322215, M. Doherty, 2/07/2006).

860.1340 Residue Analytical Methods

Adequate analytical methods are available for enforcing prothioconazole tolerances in plant an animal commodities (DP# D303508, S. Funk, 8/21/2006). These methods include a LC/MS/MS method for enforcement of tolerances for residues of prothioconazole and the desthio metabolite in plant commodities (Bayer Method RPA JA/03/01), and a LC/MS/MS method (Bayer Report No. 200537) for the enforcement of tolerances for residues in milk and cattle tissues.

In the current peanut field trials, samples of nutmeats and hay were analyzed for residues of prothioconazole and prothioconazole-desthio using the LC/MS/MS enforcement method, Bayer Method RPA JA/03/01. Residues were extracted at 65°C for 2 hours with a mixture of methanol, 30% hydrogen peroxide, and 5% aqueous sodium bicarbonate, which converts prothioconazole to its sulfonic acid derivative while the desthio metabolite remains unchanged. Isotopically labeled internal standards were added, and the residues were cleaned up by C_{18} solid-phase extraction (SPE) and diluted with 1% acetic acid for analysis by LC-MS/MS, using internal standards. The results for prothioconazole sulfonic acid and prothioconazole desthio were reported in prothioconazole equivalents and then totaled to yield "total prothioconazole derived residues." For nutmeats, the LOQ and LOD for the individual analytes were 0.01 and 0.002 ppm, respectively, and the LOQ and LOD for combined residues in nutmeats were 0.02 and 0.004 ppm. For peanut hay, the LOQ was 0.05 ppm for each analyte, for a combined LOQ of 0.10 ppm, and the LODs were 0.004 ppm for the desthio-metabolite and 0.007 ppm for the sulfonic acid of prothioconazole, for a combined LOD of 0.011 ppm.

Residues of triazole, TA and TAA were also determined in nutmeat and hay samples using the same LC/MS/MS method (Morse Method Meth-160; MRID 46492901) that was also used in earlier peanut field trials (DP# D303508, S. Funk, 8/21/2006). For this method, samples were extracted with methanol/water (80/20), and isotopically labeled internal standard were added for each analyte. Aliquots were then taken for the separate analysis of triazole, TA and TAA. For triazole, an aliquot was mixed with dansyl chloride to form the dansyl derivative of triazole, which was partitioned into ethyl acetate and then redissolved in acetonitrile (ACN)/water for LC/MS/MS analysis. For TA, an aliquot was cleaned up using a Certify II SPE cartridge, derivatized to the butyl ester using butanolic HCl, and then further derivatized using heptafluorobutyric anhydride. The mixture was then redissolved in ACN/water for LC/MS/MS analysis. For determination of TAA, the aliquot was cleaned up by C_{18} SPE, derivatized to the butyl ester using butanolic HCl, and then redissolved in ACN/water for LC/MS/MS analysis. Residue levels were quantified using reference standards of dansyl-1,2,4-triazole, TA butyl ester HFBA, and TAA butyl ester. The validated LOQs were 0.01 ppm for triazole and TAA in nutmeats and hay, and TA in hay, and 0.05 ppm for TA in nutmeats. The LODs were also calculated for each analyte in each matrix; however, due to the presence of endogenous triazole-related residues in controls, the calculated LOD were higher than the validated LOQs. Therefore, only the LOQs were used. The data were reported as triazole residues and total conjugated residues (TA + TAA), expressed in TA equivalents.

Both of the above LC/MS/MS methods were validated in conjunction with the analysis of field trial samples using control samples of each commodity fortified with the appropriate analytes at levels bracketing the residues found in the treated samples.

Conclusions. The LC/MS/MS method, Bayer Method RPA JA/03/01, is adequate for collecting data on residues of prothioconazole and prothioconazole-desthio in/on peanut nutmeats and hay, and the LC/MS/MS method, Morse Method Meth-160, is adequate for collecting data on residues of triazole, TA and TAA in/on peanut nutmeats and hay,

860.1360 Multiresidue Methods

Acceptable multiresidue method testing data were submitted for prothioconazole, metabolites prothioconazole-desthio and prothioconazole-4-hydroxy, and the triazole-related compounds triazole, TA, and TAA. These data were forwarded to the FDA for further evaluation (DP# D303508, S. Funk, 8/21/2006). Based on the results of the testing, the multiresidue methods are not appropriate for determining prothioconazole residues of concern, or for determining residues of triazole, TA, or TAA.

860.1380 Storage Stability

Adequate storage stability data are available indicating that prothioconazole-derived residues are stable at ≤-15 °C for approximately 36 months in wheat forage, wheat hay, wheat grain, and canola seed (DP# 303508, S. Funk, 8/21/06). Data are also available indicating that conjugate triazole residues (TA and TAA) are relatively stable in frozen canola seed and wheat forage and straw for up to 24 months. However, the data also indicate that triazole is not stable in frozen canola seeds and declines by ~24% per year in frozen wheat forage.

The storage intervals incurred in the current peanut field trial and processing study are presented in Table 4.

Table 4. Summary of Freezer Storage Conditions for Peanut Nutmeat and Hay.

Analyte	Storage Temp. (°C)	Maximum Actual Storage Duration (days)
Prothioconazole	<-15	414
Prothioconazole-desthio		
1,2,4-Triazole	<-15	431-439
TA		
TAA		

Conclusions. As the main purpose of these peanut field trials is to compare residues resulting from the two use patterns, the instability in triazole residues would have the same impact on residues from both treatment types. Therefore, the instability of triazole in peanut nutmeat and hay is not considered to be a substantial deficiency for this study, and no additional storage stability data are required to support these peanut field trials.

860.1480 Meat, Milk, Poultry, and Eggs

The effect of prothioconazole use on peanuts on the dietary exposure of livestock was considered previously in the original petition for use on peanuts (D303508, S. Funk 8/21/2006). In fact, the potential dietary exposure of livestock from residues in/on peanut commodities is lower than considered in the original petition, as Bayer has now included a prohibition against the feeding of treated hay on its labels. Because the requested label amendment will not result in increased tolerances on peanut commodities, a reanalysis of residues in livestock is not required for this request.

860.1500 Crop Field Trials

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To support the use of prothioconazole (4 lb/gal FlC) as either an in-furrow application or a banded application at emergence to peanuts at up to 0.178 lb ai/A, in addition to the currently allowed broadcast foliar applications, Bayer has submitted side-by-side field trials comparing the use of only foliar applications to a combination of an in-furrow application with foliar applications. The field trial data from these side-by-side field trials are discussed below and the residue data are summarized in Table 5. Although Bayer is not presently requesting a seed treatment use, the combination treatment also included a seed treatment with prothioconazole.

Table 5. Summary of Side-by-side Field Trial Residue Data for Prothioconazole (FlC). [1]

Matrix	Appl. Types	Total Rate (lb ai/A)	PHI (days)	Residues (ppm)						
				n	Min.	Max.	HAFT [2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Peanut (Proposed Use = 0.71 lb ai/A total application rate, 14-day PHI)										
Total Prothioconazole-Derived Residues [3]										
Nutmeat	seed trt + in-furrow + broadcast foliar	0.54-0.55	8-14	6	<0.02	<0.02	<0.02	0.02	0.02	0.00
Hay				6	0.71	2.58	2.39	1.12	1.41	0.78
Nutmeat	broadcast foliar	0.69-0.73	8-14	6	<0.02	<0.02	<0.02	0.02	0.02	0.00
Hay				6	2.33	6.44	6.09	3.63	4.03	1.71
Total Triazole Conjugated Residues [4]										
Nutmeat	seed trt + in-furrow + broadcast foliar	0.54-0.55	8-14	6	0.30	0.92	0.87	0.69	0.63	0.25
Hay				3	0.08	0.16	0.16	0.09	0.11	0.04
Nutmeat	broadcast foliar	0.69-0.73	8-14	6	0.40	1.44	1.34	0.65	0.80	0.44
Hay				3	0.12	0.20	0.20	0.16	0.16	0.04

1 Triazole residues were not included in the summary table as they were <LOQ in/on all nutmeat and hay samples.
2 HAFT = highest average field trial residues.
3 The total prothioconazole-derived residues included residues of prothioconazole, determined as its sulfonic acid, and prothioconazole-desthio. The LOQ for the combined residues is 0.02 ppm in nutmeats and 0.10 ppm in hay.
4 Total triazole conjugates are the sum of TA and TAA, reported in TA equivalents. The validated LOQs are 0.01 ppm for TA triazole and TAA in each matrix and TA in hay, and 0.05 ppm for TAA in nutmeats.

In three side-by-side field trials conducted in 2005 on peanuts grown in Zones 2 and 3, prothioconazole (4 lb/gal FlC) was applied as either (i) only broadcast foliar applications or (ii) a combination of a seed treatment, an in-furrow application at planting, and broadcast foliar applications. For the foliar only treatment, prothioconazole was applied as four broadcast foliar applications at 0.170-0.183 lb ai/A beginning around flowering or pegging, at RTIs of 13-14 days, for a total seasonal rate of 0.69-0.73 lb ai/A (1x maximum seasonal rate). For the combination treatment, prothioconazole was first applied to peanut seed at 10 g ai/100 kg seed, which was equivalent to 0.010-0.012 lb ai/A based on the seeding rate. An in-furrow soil application was then made at planting at 0.172-0.178 lb ai/A, followed 56-64 days later by four broadcast foliar applications at 0.086-0.094 lb ai/A at RTIs of 13-14 days, for a total seasonal rate of 0.543-0.547 lb ai/A (0.77x the maximum seasonal use rate). The peanut plants were dug and the hay was cut at either 8 DAT (1 trials) or at 14 DAT (2 trials), and peanut and hay samples were allowed to dry for 3-6 days prior to collecting a single control and duplicate treated samples of each commodity from each test.

Residues of prothioconazole and its desthio metabolite were determined using an LC/MS/MS method (Bayer Report No. RPA JA/03/01), which was adequately validated in conjunction with the analysis of field trial samples. The validated LOQs for total prothioconazole residues were 0.02 ppm for nutmeats and 0.10 ppm for hay, and the LODs for combined residues were 0.004 ppm for nutmeats and 0.011 ppm for hay.

For analysis of triazole, TA and TAA residues, samples were analyzed using an LC/MS/MS method (Morse Method Meth-160), which was adequately validated in conjunction with the analysis of field trial samples. The validated LOQs were 0.01 ppm for triazole and TAA in nutmeats and hay and TA in hay, and 0.05 ppm for TA in nutmeats. The data were reported as triazole residues and total conjugated residues (TA + TAA), expressed in TA equivalents.

Total prothioconazole residues were non-detectable (<0.004 ppm) in/on all samples of peanut nutmeats, regardless of the type of treatment (foliar only vs. in-furrow + foliar). For peanut hay, total prothioconazole residues were 0.71-2.58 ppm (average 1.41 ppm) for the combined in-furrow and foliar applications and were 2.33-6.44 ppm (average 4.03 ppm) for the foliar only treatment.

Residues of triazole were <LOQ ppm for all samples of peanut nutmeat and hay, regardless of treatment. The total conjugated triazole residues in/on nutmeats were 0.30-0.92 ppm (average 0.63 ppm) for the combined in-furrow and foliar applications and were 0.40-1.44 ppm (average 0.80 ppm) for the foliar only treatment. The total conjugated triazole residues in/on peanut hay were 0.08-0.16 ppm (average 0.11 ppm) for the combined in-furrow and foliar applications and 0.12-0.20 ppm (average 0.16 ppm) for the foliar only treatment.

Conclusions. Although the combined in-furrow and foliar application was conducted at ~0.8x the maximum seasonal rate, the available side-by-side peanut field trial data are adequate to support the petition to allow the use of an in-furrow application of prothioconazole to peanuts at planting or a banded application at emergence at up to 0.71 lb ai/A/season (1x rate). At the 0.8x rate, the combined prothioconazole residues were non-detectable (<0.004 ppm) in/on nutmeats. These residue levels are 5x lower than the current tolerance on peanut at 0.02 ppm.

The residue data on peanut hay are no longer required for risk assessment as the requested label amendment now prohibits the grazing or feeding of treated peanut hay.

860.1520 Processed Food and Feed

An adequate peanut processing study is available (DP# D303508, S. Funk, 2/21/2006) indicating that separate tolerances are not required for prothioconazole residues in peanut oil or meal.

860.1650 Submittal of Analytical Reference Standards

Analytical standards for prothioconazole and its regulated metabolites are currently available in the EPA National Pesticide Standards Repository (personal communication with Theresa Cole, ACB, 4/09/2007).

860.1850/1900 Confined and Field Accumulation in Rotational Crops

Adequate confined and field rotational crop studies are available for prothioconazole reflecting seasonal application rates of 0.52-0.73 lb ai/A (DP# D303508, S. Funk, 2/21/2006). The residues of concern in rotational crops are the same as in primary crops, parent and the desthio metabolite. The available data indicate that the label-specified PBI of 30 days is adequate and that rotational crop tolerances are not required for prothioconazole. However, finite residues of triazole and triazole derivatives are found at the 30-day PBI. Triazole and triazole derivatives in rotational crops have been considered as part of the aggregate exposure issue (DP# 322215, M. Doherty, 2/07/2006).

860.1550 Proposed Tolerances

The Agency has determined that the residues of concern in plant commodities include prothioconazole and its desthio metabolite (DP# D303508, S. Funk, 8/21/2006). Permanent tolerances are establishment for the combined residues of prothioconazole and prothioconazole-desthio, calculated as parent, in/on various plant commodities at levels ranging from 0.02-17 ppm, including tolerances at 0.02 ppm for peanut and 6.0 ppm for peanut hay (Table 6).

The new peanut field trial data, which include the use of an in-furrow application at planting, indicate that the current tolerance on peanut (0.02 ppm) is adequate. However, total prothioconazole residues were found at 6.44 ppm in one hay sample from a test conducted at a 1x rate. Although over tolerance residues were found in hay, no increase in the hay tolerance is necessary as the use directions for peanuts have been amended to prohibit the feeding of treated peanut hay. Therefore, the current tolerance for peanut hay should be revoked.

Table 6.	**Tolerance Summary for Prothioconazole.**		
Crop Commodity	Current Tolerance (ppm)	Recommended Tolerance (ppm)	Comments (*Correct Commodity Definition)*
Peanut	0.02	0.02	The new peanut data support the current tolerance.
Peanut, Hay	6.0	Delete	Use directions for peanuts now prohibit the grazing or feeding of treated peanut hay or threshing.

References

DP Number: D322215
Subject: 1,2,4-Triazole, Triazole Alanine, Triazole Acetic Acid: Human Health Aggregate Risk Assessment in Support of Reregistration and Registration Actions for Triazole-derivative Fungicide Compounds
From: M. Doherty, et. al.
To: T. Gibson, C. Giles-Parker, M. Goodis, and S. Lewis
Date: 2/07/2006
MRID(s): None

DP Numbers: D303508 and D314517
Subject: Prothioconazole. Petition for Establishment of Tolerances for Use on Barley, Oilseed (Except Sunflower and Safflower) Crop Group, Dried Shelled Pea and Bean (Except Soybean) Crop Subgroup, Peanut, Rice, and Wheat. Summary of Analytical Chemistry and Residue Data. PP#4F6830
From: S. Funk
To: L. Coppolino
Date: 8/21/2006
MRID(s): 46246139, 46246141-46246150, 46246201-46246211, 46246213-46246227, 46477701-46477704

DP Numbers: D331663, 335154 & 340239
Subject: Prothioconazole. Petition for Establishment of Tolerances for Use on Sugar Beet (PP#6F7134) and Soybean (PP#6F7073). Summary of Analytical Chemistry and Residue Data.
From: S. Funk
To: B. O'Keefe
Date: 1/31/2008
MRID(s): 46841001, 46841002, 46974608, 46974609 and 47107801

Primary Evaluator [signature] Date: 5/5/2008
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In the absence of signatures, this document is considered to be a draft with deliberative material for internal use only.

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B; Durham, NC 27713; submitted 4/03/08). The DER has been reviewed by the HED and revised to reflect current OPP policies.

STUDY REPORT:

47214701 Duah, F. and Harbin, A. (2007) JAU6476 480 SC– Magnitude of the Residue in/on Peanuts. Project Number: RAJAY035, 0504011, N106806A. Unpublished study prepared by Bayer Crop., Gustafson Seed Technology Center and Battelle. 271 p.

EXECUTIVE SUMMARY:

Bayer CropScience has submitted three side-by-side field trials conducted in 2005 on peanuts grown in Zones 2 and 3, comparing prothioconazole residues in/on peanuts and peanut hay resulting from applications of prothioconazole (4 lb/gal FlC) as either (i) only broadcast foliar applications or (ii) a combination of a seed treatment, an in-furrow application at planting, and broadcast foliar applications. For the foliar only applications, prothioconazole was applied as four broadcast foliar applications at 0.170-0.183 lb ai/A beginning around flowering or pegging, at retreatment intervals (RTIs) of 13-14 days, for a total seasonal rate of 0.69-0.73 lb ai/A. For the combination treatment, prothioconazole was first applied to peanut seed at 10 g ai/100 kg seed, which was equivalent to 0.010-0.012 lb ai/A based on the seeding rate. An in-furrow soil application was then made at planting at 0.172-0.178 lb ai/A, followed 56-64 days later by four broadcast foliar applications at 0.086-0.094 lb ai/A at RTIs of 13-14 days, for a total seasonal rate of 0.543-0.547 lb ai/A. The peanut plants were dug and the hay was cut at either 8 or 14 days after the last foliar application (DAT), and peanut and hay samples were allowed to dry for 3-6 days prior to collecting a single control and duplicate treated samples of each commodity from each test.

Samples were stored frozen for up to ~14 months prior to analysis. The available storage stability data support this storage interval for the prothioconazole-related residues and for

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residues of triazolylalanine (TA) and triazolylacetic acid (TAA). However, the data indicate that residues of 1,2,4-triazole are not likely to be stable for this interval in either peanut nutmeats or hay. However, the instability of triazole residues is not considered a major deficiency for this study, because any instability in triazole residues would affect residues from both treatments similarly, and the main purpose of these field trials was to compare residues between the two treatments.

Residues of prothioconazole and its desthio metabolite were determined using an LC/MS/MS method (Bayer Report No. RPA JA/03/01), which was adequately validated in conjunction with the analysis of field trial samples. Residues were extracted for 2 hours at 65°C with a mixture of methanol, 30% hydrogen peroxide, and 5% aqueous sodium bicarbonate, which converts prothioconazole to its sulfonic acid derivative but does not change the desthio metabolite. Residues were then cleaned up using a C_{18} solid-phase extraction (SPE) cartridge and analyzed by LC-MS/MS, using internal standards. Residues of prothioconazole sulfonic acid and prothioconazole-desthio are reported in parent equivalents and then summed to yield "total prothioconazole derived residues." For nutmeats, the limits of quantitation (LOQ) and detection (LOD) for each analyte were 0.01 and 0.002 ppm, respectively, for a combined LOQ of 0.02 ppm and a combined LOD of 0.004 ppm. For peanut hay, the LOQ was 0.05 ppm for each analyte, for a combined LOQ of 0.10 ppm, and the LODs were 0.004 ppm for the desthio-metabolite and 0.007 ppm for the sulfonic acid of prothioconazole, for a combined LOD of 0.011 ppm.

For analysis of triazole, TA and TAA residues, samples were analyzed using an LC/MS/MS method (Morse Method Meth-160), which was adequately validated in conjunction with the analysis of field trial samples. Residue were extracted with methanol/water and then separately cleaned up and derivatized for analysis by LC/MS/MS. The validated LOQs were 0.01 ppm for triazole and TAA in nutmeats and hay, and TA in hay, and 0.05 ppm for TA in nutmeats. The data were reported as triazole residues and total conjugated residues (TA + TAA), expressed in TA equivalents.

Total prothioconazole residues were non-detectable (<0.004 ppm) in/on all samples of peanut nutmeats, regardless of the type of treatment (foliar only vs. in-furrow + foliar). For peanut hay, total prothioconazole residues were 0.71-2.58 ppm (average 1.41 ppm) for the combined in-furrow and foliar applications and were 2.33-6.44 ppm (average 4.03 ppm) for the foliar only treatment.

Residues of triazole were <LOQ ppm for all samples of peanut nutmeat and hay, regardless of treatment. The total conjugated triazole residues in/on nutmeats were 0.30-0.92 ppm (average 0.63 ppm) for the combined in-furrow and foliar applications and were 0.40-1.44 ppm (average 0.80 ppm) for the foliar only treatment. The total conjugated triazole residues in/on peanut hay were 0.08-0.16 ppm (average 0.11 ppm) for the combined in-furrow and foliar applications and 0.12-0.20 ppm (average 0.16 ppm) for the foliar only treatment.

The data suggest that use of an in-furrow (or seed treatment) at planting will not result in higher residues in/on peanut nutmeats and hay than from use of only foliar applications.

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However, these finding are equivocal as the two treatments had different seasonal application rates. The seasonal use rate for the combined applications was ~0.8x compared to the seasonal rate for the foliar only applications.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Although there are questions about the stability of triazole residues in peanut nutmeats and hay during frozen storage, the peanut field trials are classified as scientifically acceptable for the purposes for which they were intended. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Chemistry Summary Document, DP Number 347039.

COMPLIANCE:

Signed and dated GLP, quality assurance, and data confidentiality statements were provided. No deviations from regulatory requirements were noted that would impact the study results or their interpretation.

A. BACKGROUND INFORMATION

Prothioconazole is a systemic demethylation inhibitor fungicide which belongs to the triazolinthione class of fungicides (Group 3). In the U.S., a 4 lb/gal FlC formulation of prothioconazole (Proline™ 480 SC; EPA Reg. No. 264-825) is registered to Bayer CorpScience for use on canola, rapeseed, ckickpeas, lentils, dried shelled peas and beans (except soybean), peanuts, barley, and wheat. The current use on peanuts allows for up to four broadcast foliar applications at 0.178 lb ai/A/application at a minimum RTI of 14 days, for a total of 0.713 lb ai/A/season. A 14-day preharvest interval is specified, and the use of peanut hay or threshings for livestock feed is prohibited.

Bayer has requested an amendment to the label directions on peanuts to allow for inclusion of either an in-furrow application at planting or a pre-emergence banded application at 0.178 lb ai/A. To support this request, Bayer has submitted side-by-side field trials comparing the use of only foliar applications to a combination of an in-furrow and foliar applications.

TABLE A.1. Nomenclature of Prothioconazole and its Regulated Metabolite.

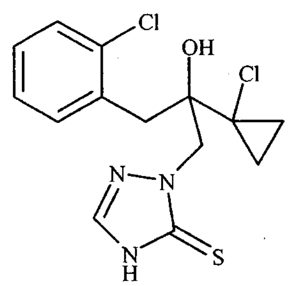
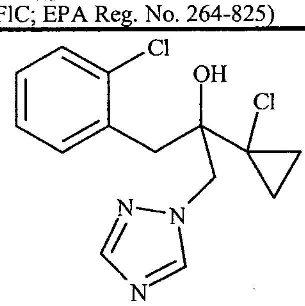
Parent Compound	
Common name	Prothioconazole
Company experimental names	JAU6476
IUPAC name	2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole-3-thione
CAS name	2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole-3-thione
CAS #	178928-70-6
End-use products/EP	Proline™ 480 SC (4 lb/gal FlC; EPA Reg. No. 264-825)
Regulated Metabolite	
Common name	Prothioconazole-desthio
Company Code	JAU6476-desthio
IUPAC name	2-(1-chlorocyclopropyl)-1-(2-chlorophenyl)-3-(1H-1,2,4-triazol-1-yl)propan-2-ol
CAS name	∀-(1-chlorocyclopropyl)-∀-(2-chlorophenyl)methyl-1H-1,2,4-triazole-1-ethanol
CAS #	120983-64-4

TABLE A.2. Physicochemical Properties of Prothioconazole Technical Grade Test Compound.

Parameter	Value	Reference (MRID)
Melting point	139.1 to 144.5 EC	46246003
pH	5.8 (1% solution)	46246002
Density	1.36 g/mL at 20 EC	46246003
Water solubility (mg/L at 20 EC)	pH 4 5 pH 8 300 pH 9 2000	46246001, 46246003
Solvent solubility (g/L at 20 EC)	Acetone >250 Acetonitrile 69 Dichloromethane 88 Dimethylsulfoxide 126 Ethyl acetate >250 n-Heptane <0.1 1-Octanol 58 Polyethylene glycol >250 2-Propanol 87 Xylene 8	46246001
Vapor pressure (at 20 or 25 EC)	<<4 x 10^{-7} Pa (calculated from determinations at 70 EC)	46246001, 46246003
Dissociation constant, pK_a	6.9 (calculated from K_{OW})	46246001, 46246003
Octanol/water partition coefficient (at 20 EC) [Log Kow]	unbuffered water 4.05 pH 4 4.16 pH 7 3.82 pH 9 2.00	46246001
UV/visible absorption	Peak maxima at 257 nm	46246003

B. EXPERIMENTAL DESIGN

Three side-by-side field trials were conducted in Zones 2 and 3 during 2005 comparing the use of prothioconazole (4 lb/gal FlC) on peanuts as ~~either~~ (i) only broadcast foliar applications with ~~or~~ (ii) a combination of a seed treatment, an in-furrow application at planting, and broadcast foliar applications (Table B.1.2). For the treatment using only foliar applications, prothioconazole was applied as four broadcast foliar applications at 0.170-0.183 lb ai/A/application beginning around flowering or pegging, at RTIs of 13-14 days, for a total of 0.691-0.726 lb ai/A. For the combination treatment, prothioconazole was first applied to peanut seed at 10 g ai/100 kg of seed, which was equivalent to 0.010-0.012 lb ai/A based on the seeding rate. An in-furrow soil application was then made at planting at 0.172-0.178 lb ai/A, followed 56-64 days later by four broadcast foliar applications at 0.086-0.094 lb ai/A and RTIs of 13-14 days. The total seasonal rate for the combined applications was 0.543-0.547 lb ai/A.

The seed treatment was made using an aqueous dilution of the 4 lb/gal FlC formulation and a Hege 22 Seed Treater. All the field applications were made with ground equipment using 5-10 gal/A for the in-furrow application and 12-18 gal/A for the foliar applications. None of the applications included the use of an adjuvant.

B.1. Study Site Information

TABLE B.1.1. Trial Site Conditions for Peanuts.

Trial Identification (City, State, Year)	Soil characteristics			
	Type	%OM	pH	CEC
Seven Springs, NC 2005	Sandy Loam	0.9	5.8	25.1
Tifton, GA 2005	Sandy Loam	0.95	5.9	3.9
Molino FL 2005	Sandy Loam	2.2	6.3	7.7

The peanuts were grown and maintained at each test site using typical agricultural practices for the respective geographical regions (Table B.1.1). Detailed temperature and precipitation data were reported for all sites, and fell within historical averages for the regions. Detailed information was also provided on maintenance chemicals and other pesticides used at each site.

TABLE B.1.2. Study Use Pattern on Peanuts.

Location (City, State), Year	Application Information [1]							
	End-use Product	Trt#	Method [2]; Timing	Volume (gal/A)	Single Rates (lb ai/A)	No. of App.	RTI [3] (days)	Total Rate (lb ai/A)
Seven Springs, NC 2005	4 lb/gal FlC	Trt# 1	Seed treatment	NA	0.011	1	NA	0.543
			In-furrow soil application at planting	10	0.177	1	NA	
			Broadcast foliar applications from pegging to 70% crop maturity (BBCH 66-87)	13-15	0.087-0.091	4	67; 13	
		Trt# 2	Broadcast foliar applications from pegging to 70% crop maturity (BBCH 66-87)	14-15	0.179-0.183	4	13	0.726
Tifton, GA 2005	4 lb/gal FlC	Trt# 1	Seed treatment	NA	0.012	1	NA	0.547
			In-furrow soil application at planting	5.3	0.178	1	NA	
			Broadcast foliar applications from beginning of flowering to maturity (BBCH 61-89)	17-18	0.089	4	56; 14	
		Trt# 2	Broadcast foliar applications from beginning of flowering to maturity (BBCH 61-89)	17-18	0.178-0.179	4	14	0.714
Molino FL 2005	4 lb/gal FlC	Trt# 1	Seed treatment	NA	0.010	1	NA	0.546
			In-furrow soil application at planting	5.2	0.172	1	NA	
			Broadcast foliar applications from pegging to crop maturity (BBCH 66-89)	13-16	0.086-0.094	4	64; 13-14	
		Trt# 2	Broadcast foliar applications from pegging to crop maturity (BBCH 66-89)	12-16	0.170-0.176	4	13-14	0.691

1 None of the field applications included the use of any adjuvants.
2 Seed treatments were made using a Hege 11 Seed Treater, and all field applications were made using ground equipment.
3 The RTI between the in-furrow application and the first foliar application was 56-67 days, and the RTI for all foliar applications was 13-14 days.

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Region [1]	Peanut		
	Submitted	Requested [2]	
		Canada	US
1	--	NA	--
2	2	NA	--
3	1	NA	--
4	--	NA	--
5	--	NA	--
6	--	NA	--
7	--	NA	--
8	--	NA	--
9	--	NA	--
10	--	NA	--
11	--	NA	--
12	--	NA	--
13		NA	--
Total	3	NA	NS

[1] Regions 14-21 and 1A, 5A, 5B, and 7A were not included as the use on peanuts is in the U.S. only.
[2] A specific number of side-by-side tests were not required.
NA = not applicable

B.2. Sample Handling and Preparation

Single control and duplicate treated samples of peanuts (≥1 kg/sample) and peanut hay (≥500 g/sample) were harvested at commercial maturity (BBCH 89). The plants were dug and the hay was cut at either 8 (1 test) or 14 (2 tests) days after treatment (DAT). As per standard commercial practices, the peanuts and hay were allowed to dry in the field or under shelter until attaining commercial dryness (3-6 days), after which composite samples were placed in labeled cloth bags and placed in frozen storage (<-15°C) for 138-141 days until shipment via freezer truck to Bayer Research Park (BRP), Stilwell, KS, where the samples were stored at ≤-15°C. All samples were later shipped via freezer truck to Battelle Agri-Food, Columbus, OH. At Battelle, the frozen peanuts were shelled and the nutmeat and hay samples were ground with dry ice and stored at ≤-20°C until analysis for residues of prothioconazole and its metabolite prothioconazole-desthio. Frozen subsamples of homogenized nutmeats and hay were also shipped back to BRP, and then shipped to Pyxant Labs, Colorado Springs, CO, for analysis of triazole-related residues. Samples were stored at ≤-20°C at Pyxant Labs until analysis.

B.3. Analytical Methodology

Samples of peanut nutmeat and hay were analyzed for residues of prothioconazole and its desthio metabolite using an LC/MS/MS method (Bayer Report No. RPA JA/03/01), which is the current tolerance enforcement method for plant commodities. The method was slightly modified to use a different solvent for preparation of the fortification solutions and to use slightly different m/z values for the quantitation.

For this method, residues are extracted with a mixture of methanol, 30% hydrogen peroxide, and 5% aqueous sodium bicarbonate at 65°C for 2 hours. This oxidative extraction procedure converts prothioconazole to its sulfonic acid derivative, while the desthio metabolite remains unchanged. The cooled extract is spiked with isotopically labeled internal standards, cleaned up by C_{18} solid-phase extraction (SPE), and diluted with 1% acetic acid for analysis by LC-MS/MS, using internal standards. The results for prothioconazole sulfonic acid and prothioconazole desthio are reported in prothioconazole equivalents and then totaled to yield "total prothioconazole derived residues." For nutmeats, the LOQ and LOD for each analyte were 0.01 and 0.002 ppm, respectively, and the LOQ and LOD for combined residues in nutmeats were 0.02 and 0.004 ppm. For peanut hay, the LOQ was 0.05 ppm for each analyte, for a combined LOQ of 0.10 ppm, and the LODs were 0.004 ppm for the desthio-metabolite and 0.007 ppm for the sulfonic acid of prothioconazole, for a combined LOD of 0.011 ppm.

For analysis of triazole, TA and TAA residues, samples were analyzed using an LC/MS/MS method (Morse Method Meth-160; MRID 46492901), which was also used in the analysis of peanut samples from earlier field trials (DP# D303508, S. Funk, 8/21/2006). For this method, homogenized samples of peanut nutmeats and hay were extracted with methanol/water (80/20), and isotopically labeled internal standards were added for each analyte. Aliquots were then taken for the separate analysis of triazole, TA and TAA. For triazole, an aliquot was mixed with dansyl chloride to form the dansyl derivative of triazole, which was partitioned into ethyl acetate and then redissolved in acetonitrile (ACN)/water for LC/MS/MS analysis. For TA, an aliquot was cleaned up using a Certify II SPE cartridge, derivatized to the butyl ester using butanolic HCl, and then further derivatized using heptafluorobutyric anhydride (HFBA). The mixture was then redissolved in ACN/water for LC/MS/MS analysis. For determination of TAA, the aliquot was cleaned up by C_{18} SPE, derivatized to the butyl ester using butanolic HCl, and then redissolved in ACN/water for LC/MS/MS analysis. Residue levels were quantified using reference standards of dansyl-1,2,4-triazole, triazolylalanine butyl ester HFBA, and triazolylacetic acid butyl ester. The method was modified to use different calibration standards and gradient for HPLC. The validated LOQs were 0.01 ppm for triazole and TAA in nutmeats and hay, and TA in hay, and 0.05 ppm for TA in nutmeats. LODs were also calculated for each analyte in each matrix; however, due to the presence of endogenous triazole-related residues in controls, the calculated LOD were higher than the validated LOQs. Therefore, only the LOQs were used. The data were reported as triazole residues and total conjugated residues (TA + TAA), expressed in TA equivalents.

The above LC/MS/MS methods were validated in conjunction with the analysis of the field trial samples using control samples of nutmeat and hay fortified separately with prothioconazole and prothioconazole-desthio at 0.01-0.20 ppm, and triazole, TA, and TAA at 0.01-7.4 ppm.

C. RESULTS AND DISCUSSION

The number and geographic representation of the peanut field trials are adequate as a side-by-side comparison between the two application method (foliar application only vs. combined seed treatment, in-furrow, and foliar applications).

The LC/MS/MS methods used to determine prothioconazole derived residues and residues of triazole, TA and TAA in/on peanut nutmeat and hay were adequately validated in conjunction with the analysis of field trial samples. For the prothioconazole derived residues, the average concurrent recoveries (±S.D.) for prothioconazole were 84 ± 20% for nutmeats and 84 ± 9% for hay. For the triazole-related residues, average concurrent recoveries were 90-109% from nutmeats with standard deviations of 6-10%, and 81-91% from hay with standard deviations of 6-12%. The validated LOQ for prothioconazole and desthio-prothioconazole were each 0.01 ppm in nutmeats and 0.05 ppm in hay, for combined LOQs of 0.02 and 0.10 ppm in nutmeats and hay, respectively. For the triazole-related residues, the validated LOQs were 0.01 ppm for each compound in hay and for triazole and TAA in nutmeats, and 0.05 ppm for TA in nutmeats. Apparent residues in/on control samples of nutmeats and hay were <LOQ for the prothioconazole-related residues and for triazole. However, combined residues of TA and TAA were ≥LOQ in control samples, although the levels of control residues were well below the residues in treated samples (Table C.3.2). Adequate sample calculations and example chromatograms were provided for both methods, and the fortification levels used for the concurrent recoveries bracketed the measured residue levels.

Following collection, samples were stored frozen for up to 414 days (13.6 months) prior to analysis of prothioconazole residues and for up to 439 days (14.4 months) prior to analysis of triazole residues (Table C.2). Storage stability data are available indicating that prothioconazole-derived residues are stable at ≤-15 °C for approximately 36 months in wheat forage, wheat hay, wheat grain, and canola seed (DP# 303508, S. Funk, 8/21/06). Data are also available indicating that conjugate triazole residues (TA and TAA) are relatively stable in frozen canola seed and wheat forage and straw for up to 24 months. However, the data also indicate that triazole is not stable in frozen canola seeds and declines by ~24% per year in frozen wheat forage.

As the main purpose of these field trials was to compare residues resulting from the two use patterns, the instability in triazole residues would have the same impact on residues from both treatment types. Therefore, the instability of triazole in peanut nutmeat and hay is not considered to be a substantial deficiency for this study.

TABLE C.1. Summary of Concurrent Method Recoveries of Prothioconazole-related Residues and Triazole-related Residues from Peanut Matrices.

Matrix	Analyte	Spike level (mg/kg)	Sample size (n)	Recoveries (%)	Mean Recovery ∀ SD
Peanut nutmeat	Prothioconazole (JAU6476)	0.01	3	60, 58, 71	63 ± 7
		0.05	2	95, 98	97
		0.20	2	102, 104	103
		0.01-0.20	**7**	**58-104**	**84 ± 20**
	Desthio- Prothioconazole	0.01	1	88	NA
	Triazole	0.01	4	108, 101, 83, 78	93 ± 14
		0.05	2	87, 89	88
		0.20	2	88, 87	88
		0.01-0.20	**8**	**78-108**	**90 ± 10**
	Triazolylalanine (TA)	0.05	4	116, 106, 113, 98	108 ± 8
		0.25	2	109, 112	111
		1.0	2	114, 107	111
		2.0	1	103	NA
		0.05-2.0	**9**	**98-116**	**109 ± 6**
	Triazolylacetic acid (TAA)	0.01	4	88, 88, 88, 95	90 ± 4
		0.05	2	93, 113	103
		0.20	2	106, 101	104
		0.01-0.20	**8**	**88-113**	**96 ± 9**
Peanut hay	Prothioconazole (JAU6476)	0.05	4	85, 79, 89, 100	88 ± 9
		0.25	2	90, 87	89
		0.98	2	85, 88	87
		7.4	3	73, 72, 73	73 ± 1
		0.05-7.4	**11**	**72-100**	**84 ± 9**
	Desthio- Prothioconazole	0.05	2	98, 98	98
	Triazole	0.01	3	78, 74, 109	87 ± 19
		0.05	2	89, 83	86
		0.20	2	91, 80	86
		0.01-0.20	**7**	**74-109**	**86 ± 12**
	Triazolylalanine (TA)	0.01	3	71, 82, 74	76 ± 6
		0.05	2	88, 85	87
		0.20	2	81, 84	83
		0.01-0.20	**7**	**71-88**	**81 ± 6**
	Triazolylacetic Acid (TAA)	0.01	3	83, 94, 94	90 ± 6
		0.05	2	99, 86	93
		0.20	2	93, 86	90
		0.01-0.20	**7**	**83-99**	**91 ± 6**

[1] Standard deviations are only reported for spiking levels with ≥3 values.

TABLE C.2. Summary of Freezer Storage Conditions for Peanut Nutmeat and Hay.

Analytes	Storage Temp. (°C)	Actual Storage Duration [1] (days)	Limit of Demonstrated Storage Stability (months) [2]
Prothioconazole	≤-15	414	36 [2]
Desthio-prothioconazole			
Triazole	≤-15	431-439	737-742 [3]
TA			
TAA			

[1] Sample extracts were analyzed within 9 days of extraction.
[2] Data are available indicating that combined prothioconazole residues are stable in frozen canola seed and wheat hay for up to 36 months (DP# 303508, S. Funk, 8/21/06).
[3] Data are available from an on-going storage stability study indicating that TA and TAA are relatively stable in frozen canola seeds and wheat forage and straw for up to 24 months; however, residues of triazole were not stable in canola seeds and declined by ~24% per year in wheat forage (DP#s 331663,335154 &340239,. S. Funk, 1/31/08).

Total prothioconazole-related residues were non-detectable (<0.004 ppm) in/on all samples of peanut nutmeats, regardless of the type of treatment (foliar only vs. in-furrow + foliar). For peanut hay, total prothioconazole residues were 0.71-2.58 ppm and averaged 1.41 ppm for the combined in-furrow and foliar applications and were 2.33-6.44 ppm and averaged 4.03 ppm for the foliar only treatment (Tables C.3.1 and C.4).

Residues of triazole were <0.01 ppm for all samples of peanut nutmeat and hay, regardless of treatment (Table C.3.2). The total conjugated triazole residues in/on nutmeats were 0.30-0.92 ppm and averaged 0.63 ppm for the combined in-furrow and foliar applications and were 0.40-1.44 ppm and averaged 0.80 ppm for the foliar only treatment. The total conjugated triazole residues in/on peanut hay were 0.08-0.16 ppm for the combined in-furrow and foliar applications and 0.12-0.20 ppm for the foliar only treatment.

Although both the prothioconazole and triazole residue data indicate that higher residues are likely to result from the use of only the foliar applications vs. the in-furrow plus foliar applications, the total seasonal use rate was not equivalent for the two use patterns (i.e., total rate = 0.71 lb/A vs. 0.54 lb/A). A more appropriate comparison would have utilized an in-furrow application at 0.178 lb ai/A followed by three foliar applications, each at 0.178 lb ai/A, for a total seasonal rate of 0.71 lb ai/A.

Common cultural practices were used to maintain plants, and the weather conditions and the maintenance chemicals and fertilizer used in the study did not have a notable impact on the residue data.

TABLE C.3.1. Prothioconazole Residue Data from Peanut Field Trials with Prothioconazole (4 lb/gal FlC).

Trial ID (City, State, Year)	EPA Region	Variety	Application types	Total Rate (lb ai/A)	Commodity	PHI (days)	Residues (ppm)[2] Total Prothioconazole-Derived	
Seven Springs, NC 2005	2	NC11	seed trt + in-furrow + broadcast foliar	0.543	Nutmeat	14	ND	ND
					Hay		0.71	0.75
			broadcast foliar	0.726	Nutmeat	14	ND	ND
					Hay		2.33	2.40
Tifton, GA 2005	2	C99R	seed trt + in-furrow + broadcast foliar	0.547	Nutmeat	8	ND	ND
					Hay		1.12	1.12
			broadcast foliar	0.714	Nutmeat	8	ND	ND
					Hay		3.40	3.86
Molino FL 2005	3	Georgia Greens	seed trt + in-furrow + broadcast foliar	0.546	Nutmeat	14	ND	ND
					Hay		2.58	2.19
			broadcast foliar	0.691	Nutmeat	14	ND	ND
					Hay		6.44	5.73

[1] The total prothioconazole-derived residues included residues of prothioconazole, determined as its sulfonic acid, and prothioconazole-desthio. The LOQ and LOD for the combined residues were respectively 0.02 and 0.004 ppm in nutmeats, and 0.10 and 0.011 ppm in hay.

TABLE C.3.2. Triazole Residue Data from Peanut Field Trials with Prothioconazole (4 lb/gal FlC).

Trial ID (City, State, Year)	EPA Region	Variety	Application types	Total Rate (lb ai/A)	Commodity	PHI (days)	Residues (ppm)[1] Triazole		Total Triazole Conjugates[2]	
Seven Springs, NC 2005	2	NC11	seed trt + in-furrow + broadcast foliar	0.543	Nutmeat	14	<0.01	<0.01	0.82	0.92
					Hay		<0.01		0.08	
			broadcast foliar	0.726	Nutmeat	14	<0.01	<0.01	1.44	1.23
					Hay		<0.01		0.16	
			control	NA	Nutmeat	14	<0.01		0.404	
					Hay		<0.01		0.033	
Tifton, GA 2005	2	C99R	seed trt + in-furrow + broadcast foliar	0.547	Nutmeat	8	<0.01	<0.01	0.69	0.68
					Hay		<0.01		0.16	
			broadcast foliar	0.714	Nutmeat	8	<0.01	<0.01	0.60	0.70
					Hay		<0.01		0.20	
			control	NA	Nutmeat	8	<0.01		0.178	
					Hay		<0.01		0.036	
Molino FL 2005	3	Georgia Greens	seed trt + in-furrow + broadcast foliar	0.546	Nutmeat	14	<0.01	<0.01	0.36	0.30
					Hay		<0.01		0.09	
			broadcast foliar	0.691	Nutmeat	14	<0.01	<0.01	0.40	0.41
					Hay		<0.01		0.12	
			control	NA	Nutmeat	14	<0.01		0.05	
					Hay		<0.01		0.01	

[1] The validated LOQs are 0.01 ppm for triazole and TAA in each matrix and TA in hay, and 0.05 ppm for TA in nutmeats.
[2] Total triazole conjugates are the sum of TA and TAA, reported in TA equivalents.

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TABLE C.4. Summary of Side-by-side Trial Field Residue Data for Prothioconazole (FIC). [1]

Matrix	Appl. Types	Total Rate (lb ai/A)	PHI (days)	Residues (ppm)						
				n	Min.	Max.	HAFT [2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Total Prothioconazole-Derived Residues [3]										
Nutmeat	seed trt + in-furrow + broadcast foliar	0.54-0.55	8-14	6	<0.02	<0.02	<0.02	0.02	0.02	0.00
Hay				6	0.71	2.58	2.39	1.12	1.41	0.78
Nutmeat	broadcast foliar	0.69-0.73	8-14	6	<0.02	<0.02	<0.02	0.02	0.02	0.00
Hay				6	2.33	6.44	6.09	3.63	4.03	1.71
Total Triazole Conjugated Residues [4]										
Nutmeat	seed trt + in-furrow + broadcast foliar	0.54-0.55	8-14	6	0.30	0.92	0.87	0.69	0.63	0.25
Hay				3	0.08	0.16	0.16	0.09	0.11	0.04
Nutmeat	broadcast foliar	0.69-0.73	8-14	6	0.40	1.44	1.34	0.65	0.80	0.44
Hay				3	0.12	0.20	0.20	0.16	0.16	0.04

1 Triazole residues were not included in the summary table as they were <LOQ in/on all nutmeat and hay samples.
2 HAFT = highest average field trial residues.
3 The total prothioconazole-derived residues included residues of prothioconazole, determined as its sulfonic acid, and prothioconazole-desthio. The LOQ for the combined residues is 0.02 ppm in nutmeats and 0.10 ppm in hay.
4 Total triazole conjugates are the sum of TA and TAA, reported in TA equivalents. The validated LOQs are 0.01 ppm for TA triazole and TAA in each matrix and TA in hay, and 0.05 ppm for TAA in nutmeats.

D. CONCLUSION

Prothioconazole-related residues and residues of TA and TAA in/on peanut nutmeats and hay following four foliar application totaling ~0.71 lb ai/A were greater or equal to the same residues in/on nutmeat and hay following a combination of a seed treatment, in-furrow, and foliar applications at rates totaling ~0.55 lb ai/A. A more appropriate comparison should have utilized the same total application rate of 0.71 lb ai/A for both the foliar application only and the combination treatment of in-furrow application and foliar applications. However, the peanut field trial data are adequate for purposes of comparing the two use patterns at the rates applied.

E. REFERENCES

DP Numbers: D303508 and D314517
Subject: Prothioconazole. Petition for Establishment of Tolerances for Use on Barley, Oilseed (Except Sunflower and Safflower) Crop Group, Dried Shelled Pea and Bean (Except Soybean) Crop Subgroup, Peanut, Rice, and Wheat. Summary of Analytical Chemistry and Residue Data. PP#4F6830
From: S. Funk
To: L. Coppolino
Date: 8/21/2006
MRID(s): 46246139, 46246141-46246150, 46246201-46246211, 46246213-46246227, 46477701-46477704

DP Numbers: D331663, 335154 & 340239
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From: S. Funk
To: B. O'Keefe
Date: 1/31/2008
MRID(s): 46841001, 46841002, 46974608, 46974609 and 47107801.

F. DOCUMENT TRACKING

RDI: A. M. Acierto (05/08/08); S. Funk (5/08/08).
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