Data Evaluation Report on the aquatic field dissipation of prothioconazole

PMRA Submission Number N/A EPA MRID Number 46246524

Data Requirement:
PMRA Data Code:
EPA DP Barcode: D303488
OECD Data Point:
EPA Guideline: 164-2

Test material: JAU6476

End Use Product name: JAU6476 480 SC **Concentration of a.i.:** 41.4%
Formulation type: Soluble concentrate

Active ingredient

Common name:	Prothioconazole.
Chemical name:	
IUPAC:	(RS)-2-[2-(1-Chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-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 No:	178928-70-6.
Synonyms:	JAU6476.
SMILES string:	ClC1(C(Cc2ccccc2Cl)(CN2N=CNC2=S)O)CC1.

Primary Reviewer: Dan Hunt
Dynamac Corporation
Signature:
Date:

QC Reviewer: Joan Harlin
Dynamac Corporation
Signature:
Date:

Secondary Reviewer: Roxolana Kashuba
EPA/OPP/EFED/ERB4
Signature: 10/12/05
Date: October 12, 2005

Company Code:
Active Code:
Use Site Category:
EPA PC Code: 113961

CITATION: Wyatt, D.R. 2004. Aquatic field dissipation of JAU6476 in a cropped Arkansas rice field, 2000. Unpublished study performed by Bayer CropScience, Stilwell, KS, Schoffner Farm Research, Newport, AR, A & L Great Lakes Laboratories, Inc., Fort Wayne, IN, and Battelle, Columbus, OH and submitted by Bayer CropScience, Research Triangle Park, NC. Submitting Laboratory Study No. J6022403. Bayer Report No. 200078. Experiment initiation July 25, 2000, and completion October 23, 2000 (field phase; p. 12). Final report issued March 17, 2004.

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Primary Reviewer: Dan Hunt
Dynamac Corporation
Signature: Dan Hunt
Date: 10-27-2004

QC Reviewer: Joan Harlin
Dynamac Corporation
Signature: Joan Harlin
Date: 10/29/04

Secondary Reviewer: John Ravenscroft
EPA
Signature:
Date:

Company Code:
Active Code:
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EPA PC Code: 113961

CITATION: Wyatt, D.R. 2004. Aquatic field dissipation of JAU6476 in a cropped Arkansas rice field, 2000. Unpublished study performed by Bayer CropScience, Stilwell, KS, Schoffner Farm Research, Newport, AR, A & L Great Lakes Laboratories, Inc., Fort Wayne, IN, and Battelle, Columbus, OH and submitted by Bayer CropScience, Research Triangle Park, NC. Submitting Laboratory Study No. J6022403. Bayer Report No. 200078. Experiment initiation July 25, 2000, and completion October 23, 2000 (field phase; p. 12). Final report issued March 17, 2004.

EXECUTIVE SUMMARY

Prothioconazole ((RS)-2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-3H-1,2,4-triazole-3-thione; JAU6476; formulated as JAU6476 480 SC, containing 41.1% prothioconazole) was applied once at target application rate of 287.0 g a.i./ha onto a flooded plot of loam soil (Foley Calhoun complex) planted with rice in Arkansas. Following application, water and soil/sediment samples were collected for analysis of prothioconazole and four transformation products: JAU6476-desthio (2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole); JAU6476-S-methyl (alpha-1(1-chlorocyclopropyl)-alpha-[(2-chlorophenyl)methyl]-3-(methylthio)-1H-1,2,4-triazole-1-ethanol); JAU6476 thiazocine (6-(1-chlorocyclopropyl)-6,7-dihydro-triazole-5H-[1,2,4]triazolo[5,1-b][1,3]benzothiazon-6-ol); and 1,2,4-triazole (1-H-1,2,4-triazole). Water samples were collected through 60 days posttreatment, at which time the paddy water was allowed to evaporate from the plots, and sediment/soil samples were collected through 90 days posttreatment. Crop samples were collected at the same time as water samples, and rice grain and straw were collected at 90 days posttreatment. All crop samples were analyzed for prothioconazole and JAU6476-desthio only.

Prothioconazole dissipated in the **paddy water** with a reviewer-calculated half-life value of 0.6 days ($r^2 = 0.84$), using linear regression analysis. Prothioconazole was detected in the **paddy water** at a mean concentration of 27.1 μg/L following the application, decreased to 2.2 μg/L by 1 day, and was last detected at 0.7 μg/L at 3 days posttreatment. The transformation product **JAU6476-desthio (2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole)** was detected in the water at a maximum concentration of 87.2 μg/L at 1 day, decreased to 47.5 μg/L by 3 days and 6.4 μg/L by 7 days, and was 0.3 μg/L at 60 days posttreatment. The transformation product **JAU6476-S-methyl (alpha-1(1-chlorocyclopropyl)-alpha-[(2-chlorophenyl)methyl]-3-(methylthio)-1H-1,2,4-triazole-1-ethanol)** was detected in the water at a maximum concentration of 3.0 μg/L at 1 day, and was detected below the MDL by 7 and 14 days posttreatment. The transformation product **1,2,4-triazole (1-H-1,2,4-triazole)** was only detected in the water above the LOQ twice, at a mean concentration of 0.3-0.5 μg/L at 1 day and 3 days posttreatment. The transformation product **JAU6476 thiazocine (6-(1-chlorocyclopropyl)-6,7-dihydro-triazole-5H-[1,2,4]triazolo[5,1-b][1,3]benzothiazon-6-ol)** was not detected above the LOQ at any sampling interval.

A half-life of prothioconazole in **sediment/soil** could not be determined due to too few detections. Prothioconazole was not detected in the **sediment/soil** at a concentration above the LOQ in any replicate sample or at any sampling interval, but was detected sporadically at levels below the LOQ. The transformation product **JAU6476-desthio** was detected in the 0-3 inch depth sediment/soil at a mean concentration of 28.8-28.9 μg/kg at 3 and 14 days, then decreased to 18.0 μg/kg by 60 days and 15.4 μg/kg by 90 days posttreatment. JAU6476-desthio was not detected above the LOQ in soil below the 0-3 inch depth. The reviewer-calculated half-life of JAU6476-desthio in sediment/soil was 90.0 days ($r^2 = 0.38$). The transformation product **JAU6476-S-methyl** was detected in the sediment/soil at mean concentrations below the LOQ (0-

3 and 3-6 inch depths) throughout the study period. T and the transformation products **1,2,4-triazole** and **JAU6476 thiazocine** were not detected at any sampling intervals.

Prothioconazole was detected in the rice forage at a maximum concentration of 1.85 μg/g at day 0 and decreased to 0.20 μg/g by 60 days posttreatment. JAU6476-desthio was detected in the rice forage at a maximum concentration of 1.04 μg/g at 1 day, and decreased to 0.08 μg/g by 60 days. Following rice harvest at 90 days posttreatment, prothioconazole was detected in the straw at a mean concentration of 0.30 μg/g, and JAU6476-desthio was detected at 0.16 μg/g; neither analyte was detected in the grain.

Study Acceptability: This study is classified **supplemental** and does not satisfy the USEPA Subdivision N Guideline §164-2 for aquatic field dissipation because prothioconazole was not stable in frozen storage, and the laboratory storage stability study was inadequate to demonstrate stability of any of the analytes during storage because samples were not analyzed at time 0 and sampling intervals were inadequate to determine stability over time.

MATERIALS AND METHODS

The aquatic field dissipation of prothioconazole ((RS)-2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-3H-1,2,4-triazole-3-thione; JAU6476), formulated as JAU6476 480 SC (containing 41.1% prothioconazole), was conducted on a flooded plot (420 x 24 ft; Figure 5, p. 64) planted to rice in Jackson County, Arkansas (pp. 12-13; Figures 2-3, pp. 61-62). The soil at the test site was a Foley Calhoun complex and was classified as a loam from 0-18 inches (0-6 inches: 37.2% sand, 44.0% silt, 18.8% clay, pH 5.3, 0.99% organic matter, CEC 6.01 meq/100 g, bulk density 1.42 g/cm^3; Table 3, p. 37). The treated plot was divided into five equal-sized sections for sampling, and each section was further divided into 15 rows with three subsections (p. 14). A control plot (dimensions not reported) was located 100 ft from the treated plot and planted with rice. A five-year plot history indicated that Propanil, Facet, Basagran, Reflex, Assure, Atrazine, Dual, Treflan, and Prowl were recently applied to the test plot (Table 2, p. 36). The test area was disked, landplaned, and cultivated approximately 2-3 months prior to treatment (Table 5, p. 39). Rice (var. Jefferson C-43) was planted on May 18, 2000 and emerged on May 26; the plot was flooded approximately six weeks prior to treatment. Characteristics of the paddy water were as follows: total suspended solids 64 mg/L, pH 8.0, hardness 136 mg $CaCO_3$/L, total dissolved solids 196 mg/L, total organic carbon 8.83 mg/L (Table 4, p. 38). The test plot was maintained under 2-5 inches of water until 60 days posttreatment, when the flood water was allowed to evaporate (p. 13; Table 6, p. 40).

Meteorological data were recorded on-site (p. 15). After the 60-day sampling interval when the plot was allowed to dry, total precipitation for the last 30 days of the study period was 3.35 inches or 89% of the 30-year average for the same time period; air temperatures were typical for the site (p. 29; Table 7, p. 41).

Prothioconazole was broadcast once, on July 25, 2000, at a target application rate of 287.0 g a.i./ha (4.1 oz a.i./A), onto the flooded plot (p. 13). The target application rate was 143% of the proposed label rate. The application was made using a boom equipped with 13 flat fan nozzles spaced 20 inches apart and 16 inches above the water. Meteorological conditions during application were as follows: wind speed 0 mph, air temperature 68°F, relative humidity 88%. The test site was maintained weed-free during the study period with two applications of Facet® (June 2 and 10, 2000; 0.25 lb a.i./A/application) and one application of Roundup Ultra® (August 9, 2000; 2 pt/A; Table 5, p. 39).

The application rate was verified using solvent saturation pads and water pans that were placed in a separate bareground test plot that was treated at the same time in a companion study (pp. 13-14). Two solvent saturation pads (13.7 x 22 cm) were placed in trays in each of the five sections of the bare companion study plot prior to application (10 pads total). Following application, the two pads from each section of the plot were collected and placed together in a plastic bag (one bag for each section). The pads were extracted three times by shaking for 30 minutes, once with 100 mL of 0.01% L-cysteine hydrochloride and 100 mL of acetonitrile and twice with 160 mL of acetonitrile:water (1:1, v:v; pp. 16-17 and Appendix 3, pp. 102-104). The extracts were combined and brought to volume with acetonitrile:water (1:1, v:v), and an aliquot was filtered (0.45-µm Acrodisc filter) and analyzed for prothioconazole and JAU6476-desthio by HPLC-UV (Phenomenex Luna C-18(2) column, 150 mm x 2.0 mm, 5-µm; mobile phase of 0.1% phosphoric acid:acetonitrile, 55:45, v:v).

Metal pans (231 cm^2) containing approximately 225 mL of control water were also floated in each section of the bare companion study plot prior to the test application (5 pans total; p. 14). Water from each pan was collected and poured into a plastic bag after application. Samples of water (2 mL) from the water pans were diluted to 100 mL with acetonitrile:50-60 mg/L cysteine hydrochloride in water (2:8), filtered (0.45 µm nylon Acrodisc®), and analyzed for prothioconazole and JAU6476-desthio by HPLC-UV (Betasil C_{18} column, 100 x 2 mm, 5-µm) using a mobile phase of A: 0.1% formic acid in water, B: 0.1% formic acid in acetonitrile, A:B, 80:20 to 10:90 to 80:20 (v:v; pp. 18-19; Appendix 4, pp. 108-112).

Water and crop samples were collected from the treated plot at 0, 1, 3, 7, 14, 28, and 60 days posttreatment, and rice straw and grain samples were collected at 90 days posttreatment (pp. 14-15; Table 5, p. 39). Three 500-mL water samples were collected at each sampling interval by combining five 100-mL aliquots (one from each of the five sections of the treated plot). Water samples were stored frozen for 677-750 days prior to analysis (Table 12, pp. 46-47). Rice samples were collected by pulling the plants and cutting off the roots, and straw and grain samples were taken at harvest using a small plot combine. Rice forage and straw samples were macerated using a food chopper with dry ice, and grain samples were milled without dry ice (p. 16). Rice forage samples were stored frozen for 194-269 days prior to analysis, and rice grain and straw samples were stored for 154 days prior to analysis (Table 18, pp. 53-54).

Sediment samples were collected from the treated plot at 3, 14, and 60 days posttreatment, and soil samples were collected at 90 days posttreatment (pp. 14-15; Table 5, p. 39). For each sampling event, one row from each of the five sections of the treated plot was randomly selected and one core was collected from each of the three subsections from each row. Each subsection was only sampled once during the study, and only one core was taken from each subsection.

Sediment samples were collected to a depth of 6 inches using a 2¼-inch diameter liner. Soil cores were taken in two segments, 0-6 inches and 6-12 inches, using a 2-stage hand soil probe; 0-6 inch depth cores were taken with a 2¼-inch diameter soil probe and 6-12 inch depth cores were taken with a 1½-inch diameter soil probe. Sediment/soil cores were stored frozen at the field facility before being shipped frozen to the processing laboratory. Cores were sectioned into 3-inch segments and combined to produce three composite samples (by combining one core from each of the five sections of the treated plot) per segment and sampling event. Composite samples were homogenized by mixing with dry ice and then run through a hammermill equipped with a 2-mm sieve (p. 16). The milled soil was mixed in a bucket mixer and transferred to a freezer for dry ice sublimation. The samples were split into analytical and long-term samples and placed back into frozen storage until analysis. Sediment/soil samples were stored frozen for 674-746 days prior to analysis (Tables 13-17, pp. 48-52).

Water, soil, and sediment samples were analyzed for prothioconazole and the transformation products JAU6476-desthio (2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole); JAU6476-S-methyl (alpha-1(1-chlorocyclopropyl)-alpha-[(2-chlorophenyl)methyl]-3-(methylthio)-1H-1,2,4-triazole-1-ethanol); JAU6476 thiazocine (6-(1-chlorocyclopropyl)-6,7-dihydro-triazole-5H-[1,2,4]triazolo[5,1-b][1,3]benzothiazon-6-ol); and 1,2,4-triazole (1-H-1,2,4-triazole), and rice samples were analyzed for prothioconazole and JAU6476-desthio (pp. 19-26; Figure 1, pp. 57-59).

Complete chemical names for prothioconazole and its transformation products.

Applicant's Code Name	**Chemical Name**	**Molecular Weight**
Prothioconazole (JAU6476)	2-[2-(1-Chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole-3-thione	344.3
JAU6476-desthio	2-[2-(1-Chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole	312.2
JAU6476-S-methyl	Alpha-1(1-chlorocyclopropyl)-alpha-[(2-chlorophenyl)methyl]-3-(methylthio)-1H-1,2,4-triazole-1-ethanol	358.0
JAU6476 thiazocine	6-(1-Chlorocyclopropyl)-6,7-dihydro-triazole-5H-[1,2,4]triazolo[5,1-b][1,3]benzothiazon-6-ol	307.8
1,2,4-triazole	1-H-1,2,4-triazole	69.1

Chemical names and molecular weights were obtained from Figure 1, pp. 57-59 of the study report.

Analytical method for prothioconazole, JAU6476-desthio, JAU6476-S-methyl, and JAU6476 thiazocine in water. Water samples (50 mL) were fortified with a mixed internal standard of prothioconazole, JAU6476-desthio, JAU6476-S-methyl, and JAU6476 thiazocine, and passed through a C_{18} SPE cartridge (p. 23; Appendix 7, 132-134). Residues were eluted from the cartridge with acetonitrile:water (9:1) and analyzed by HPLC (Luna C18 column, 100 x 4.6 mm, 5 µ) using MS/MS detection. The mobile phase conditions for the separation consisted of mobile phase A (0.1% formic acid in water) and B (0.1% formic acid in acetonitrile) under the following gradient conditions: A:B, 55:45 to 5:95 to 55:45. Retention times were 3.5 minutes for JAU6476 thiazocine, 4.8 minutes for JAU6476-desthio, 5.4 minutes for prothioconazole, and 6.7 minutes for JAU6476-S-methyl. The LOQ was 0.3 µg/L for each analyte in water (p. 27).

Analytical method for 1,2,4-triazole in water. Water samples (50 mL) were fortified with a triazole internal standard, and the sample was derivatized with dansyl chloride to form a dansyl triazole derivative (p. 24; Appendix 8, 139-142). The extracts were partitioned twice with ethyl acetate and the extracts were combined, concentrated to dryness, and redissolved in water:acetonitrile (1:1, v:v). Extracts were analyzed by HPLC (Luna C18 column, 100 x 4.6 mm, 5 µ) using MS/MS detection. The mobile phase conditions for the separation consisted of mobile phase A (0.1% formic acid in water) and B (0.1% formic acid in acetonitrile) under the following gradient conditions: A:B, 50:50 to 30:70 to 10:90 to 50:50. The approximate retention time of dansyl 1,2,4-triazole was 5.4 minutes. The LOQ was 0.1 µg/L for 1,2,4-triazole in water (p. 27).

Analytical method for prothioconazole, JAU6476-desthio, JAU6476-S-methyl, and JAU6476 thiazocine in soil/sediment. Soil/sediment samples (15 g) were extracted by shaking for one hour with acetonitrile:water:cysteine hydrochloride (800:200:0.5, v:v:w), and the slurry was centrifuged for 10 minutes (p. 20; Appendix 5, pp. 116-118). Following extraction, a mixed internal standard of prothioconazole, JAU6476-desthio, JAU6476-S-methyl, and JAU6476 thiazocine was added to an aliquot of the extract, and a 700-µL aliquot was diluted with 300 µL of water. The extracts were analyzed by LC/MS/MS as previously described for the water samples. The LOQ was 10 µg/kg for each analyte in soil (p. 27).

Analytical method for 1,2,4-triazole in soil/sediment. Soil samples (15 g) were sonicated for one hour at 65°C with acetonitrile:water (6:4, v:v) and sediment samples were sonicated with 1.0% sodium hydroxide:acetonitrile (6:4, v:v); the slurry was centrifuged for 10 minutes (p. 21; Appendix 6, pp. 124-128). Following extraction, a triazole internal standard was added to a 1-mL aliquot of the extract, and 4 mL of 10 mM dansyl chloride and 4 mL of 0.25 M sodium bicarbonate were added to form a dansyl triazole derivative. After sonication for 30 minutes, 1 mL of 0.5 M ammonium hydroxide was added and the derivative was partitioned with 6 mL of ethyl acetate. The ethyl acetate layer was dried through anhydrous sodium sulfate, evaporated to dryness and reconstituted in 1 mL of water:acetonitrile (1:1, v:v), then filtered through a 0.45-µm nylon Acrodisc. The extracts were analyzed by LC/MS/MS as previously described for the water samples. The LOQ was 10 µg/kg for 1,2,4-triazole in soil (p. 27).

Analytical method for prothioconazole and JAU6476-desthio in rice. Samples (5 g) were extracted with 50 mL of acetonitrile:water (8:2, v:v) and 4 mL of cysteine-hydrochloride solution, and the extracts were filtered and partitioned with n-hexane (p. 25). The acetonitrile phase was partitioned twice with dichloromethane and the dichloromethane fraction was concentrated. After re-dissolving the residues in acetonitrile, an internal standard was added and the solution was diluted with water and analyzed by HPLC (Superspher 60 RP-select B column) using MS/MS detection. The mobile phase conditions for the separation consisted of mobile phase A (acetonitrile:water, 1:9, v:v + 0.1 mL acetic acid/L) and B (acetonitrile) under the following gradient conditions: A:B, 55:45 to 10:90 to 55:45. Approximate retention times were 4.5 minutes for JAU6476-desthio and 5.6 minutes for prothioconazole. The LOQ was 0.01 µg/g for prothioconazole and JAU6476-desthio in plant matrices (p. 27).

To determine the efficiency of the analytical methods, samples of water were fortified with prothioconazole and the transformation products JAU6476-desthio, JAU6476-S-methyl, and JAU6476 thiazocine at 0.3 µg/L and 3 µg/L, and with 1,2,4-triazole at 0.1 µg/L and 1 µg/L (p. 27). Soil samples were fortified with each analyte at 10 µg/kg and 100 µg/kg, and rice samples were fortified with prothioconazole and JAU6476-desthio at 0.01 µg/g.

Mean (± SD) method validation recoveries of prothioconazole and its transformation products from water, soil and rice.

Analyte	**Percent Recovery**						
	Water		**Soil**		**Rice* (10 µg/kg)**		
	0.3 µg/L	**3 µg/L**	**10 µg/kg**	**100 µg/kg**	**Forage**	**Grain**	**Straw**
Prothioconazole	96 ± 17	99 ± 3.9	88 ± 4.2	93 ± 2.7	97 ± 6.9	90 ± 9.0	88 ± 10.8
JAU6476-desthio	107 ± 4.6	99 ± 2.2	113 ± 3.6	105 ± 2.5	88 ± 11.7	90 ± 1.7	94 ± 7.2
JAU6476-S-methyl	104 ± 1.1	99 ± 1.1	118 ± 1.5	107 ± 2.8	–	–	–
JAU6476 thiazocine	103 ± 4.8	99 ± 1.3	115 ± 2.8	106 ± 3.3	–	–	–
	0.1 µg/L	**1 µg/L**					
1,2,4-triazole	115 ± 4.0	102 ± 1.2	104 ± 4.8	98 ± 0.9	–	–	–

Means were obtained from Tables 9-11, pp. 43-45 of the study report.
*Crop recoveries include concurrent recoveries.

To determine the frozen storage stability of prothioconazole and its transformation products in soil and water, soil samples were fortified with prothioconazole and JAU6476 thiazocine at 100 ppb, and with JAU6476-desthio, JAU6476-S-methyl, and 1,2,4-triazole at 50 ppb, and water samples were fortified with each analyte at 20 ppb (p. 28; Table 20, p. 56). Soil samples were analyzed for prothioconazole and JAU6476 thiazocine following 653 days of storage, for JAU6476-desthio and JAU6476-S-methyl following 813 days, and for 1,2,4-triazole following 1161 days. Water samples were analyzed for all analytes following 822 days of storage. Samples were not anlayzed at day 0 to determine initial recoveries.

RESULTS AND DISCUSSION

Prothioconazole ((RS)-2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-3H-1,2,4-triazole-3-thione; JAU6476; formulated as JAU6476 480 SC, containing 41.1% prothioconazole), applied once at target application rate of 287.0 g a.i./ha onto a flooded plot of loam soil (Foley Calhoun complex) planted with rice, dissipated in the paddy water with a reviewer-calculated half-life value of 0.6 days ($r^2 = 0.84$); a half-life of prothioconazole in sediment/soil could not be determined due to too few detections. The half-life in water was calculated using *linear regression analysis* performed on a plot of ln-transformed prothioconazole concentrations vs. time and the equation $t_{½} = -ln\ 2 / k$, where k is the rate constant.

Mean recoveries of prothioconazole (as prothioconazole plus JAU6476-desthio) from the saturation pads and water pans were 110% and 95% of the label rate (2.86 oz a.i./A), respectively (p. 29; Table 8, p. 42). However, the reviewer notes that the application monitors were not placed in the treated plot, but were placed in a plot from a companion study that was treated at the same time.

Prothioconazole was detected in the **paddy water** at a mean concentration of 27.1 µg/L following the application, decreased to 2.2 µg/L by 1 day, and was last detected at 0.7 µg/L at 3 days posttreatment (Table 12, pp. 46-47). The transformation product **JAU6476-desthio (2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole)** was initially detected in the water at a mean concentration of 62.4 µg/L at day 0, increased to a maximum of 87.2 µg/L by 1 day, decreased to 47.5 µg/L by 3 days and 6.4 µg/L by 7 days, and was 0.3 µg/L at 60 days posttreatment. The transformation product **JAU6476-S-methyl (alpha-1(1-chlorocyclopropyl)-alpha-[(2-chlorophenyl)methyl]-3-(methylthio)-1H-1,2,4-triazole-1-ethanol)** was initially detected in the water at a mean concentration of 1.8 µg/L at day 0, was a maximum of 3.0 µg/L at 1 day and was detected below the MDL at 7 and 14 days posttreatment. The transformation product **1,2,4-triazole (1-H-1,2,4-triazole)** was only detected in the water above the LOQ twice, at a mean concentration of 0.3-0.5 µg/L at 1 day and 3 days posttreatment. The transformation product **JAU6476 thiazocine (6-(1-chlorocyclopropyl)-6,7-dihydro-triazole-5H-[1,2,4]triazolo[5,1-b][1,3]benzothiazon-6-ol)** was not detected above the LOQ at any sampling interval.

Mean concentration of prothioconazole residues expressed as µg/L soil, in paddy water.

	Days posttreatment						
	0	1	3	7	14	28	60
Prothioconazole	**19.5** **35.4** **26.4**	**2.4** **1.9** **2.4**	**1.0** **0.4** **0.6**	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL
JAU6476-desthio	**52.6** **68.1** **66.5**	**80.8** **76.6** **97.8**	**33.5** **45.3** **49.6**	**6.1** **6.7** **6.1**	**3.6** **3.8** **4.2**	**0.7** **0.6** **0.6**	**0.3** **0.4** **0.3**
JAU6476-S-methyl	**1.6** **1.8** **2.1**	**2.7** **2.6** **3.8**	**0.9** **1.4** **1.0**	**0.1** **0.1** **0.1**	**0.1** **0.1** **0.1**	<MDL <MDL <MDL	<MDL <MDL <MDL
JAU6476 thiazocine	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL
1,2,4-triazole	<MDL <MDL <MDL	**0.5** **0.6** **0.3**	**0.2** **0.3** **0.3**	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL

Data were obtained from Table 12, pp. 46-47 of the study report. Values in parenthesis are below the LOQ and above the Method Detection Limit.

MDL: Prothioconazole: 0.16 ug/L, JAU6476-desthio: 0.04 ug/L, JAU6476-S-methyl: 0.01 ug/L, JAU6476 thiazocone: 0.05 ug/L, 1,2,4-triazole: 0.01ug/L.

LOQ: Prothioconazole, JAU6476-desthio, JA6476-S-methyl, and JAU6476 thiazocone: 0.3 ug/L, 1,2,4-triazole: 0.1 ug/L.

Prothioconazole was not detected in the **sediment/soil** at a concentration above the LOQ in any replicate sample or at any sampling interval, but was detected sporadically at levels below the LOQ (Table 13, p. 48). The transformation product **JAU6476-desthio** was detected in the 0-3 inch depth sediment/soil at a mean concentration of 28.8-28.9 µg/kg at 3 days and 14 days, and then decreased to 18.0 µg/kg by 60 days and 15.4 µg/kg by 90 days posttreatment (Table 14, p. 49). JAU6476-desthio was not detected above the LOQ in soil below the 0-3 inch depth. The reviewer-calculated half-life of JAU6476-desthio in sediment/soil was 90.0 days ($r^2 = 0.38$). The transformation product **JAU6476-S-methyl** was detected in the sediment/soil at mean concentrations below the LOQ (0-3 and 3-6 inch depths) throughout the study period, and the transformation products **1,2,4-triazole** and **JAU6476 thiazocine** were not detected at any sampling intervals (Tables 15-17, pp. 50-52).

Mean concentration of prothioconazole residues expressed as µg/kg soil, in sediment/soil.

	Depth (in)	Days posttreatment			
		3	14	60	90
Prothioconazole	0-3	<MDL (1.5) <MDL (1.7) <MDL	<MDL (1.6) <MDL <MDL (1.4)	<MDL <MDL <MDL <MDL <MDL	<MDL <MDL <MDL (1.6) <MDL
	3-6	<MDL <MDL <MDL <MDL <MDL	<MDL <MDL <MDL <MDL <MDL	<MDL <MDL <MDL <MDL <MDL	<MDL <MDL (2.1) <MDL <MDL
JAU6476-desthio	0-3	**25.3** **24.9** **16.7** **45.0** **32.2**	**16.0** **57.2** **26.3** **18.9** **26.1**	**20.4** **18.6** **14.4** **13.3** **23.1**	**27.6** **13.7** **13.1** **13.6** **(8.9)**
	3-6	(2.4) (2.2) (2.1) (3.1) (4.6)	(2.4) (3.6) (3.4) (1.3) (1.9)	(1.3) <MDL <MDL (1.3) (1.3)	<MDL <MDL <MDL <MDL <MDL
JAU6476-S-methyl	0-3	(3.3) (3.2) (2.6) (8.9) (5.5)	**(3.2)** **15.2** **(6.6)** **(4.1)** **(5.7)**	(4.3) (3.5) (3.7) (3.1) (6.9)	(5.0) (2.6) (3.1) (3.5) (1.9)
	3-6	<MDL <MDL (0.5) (0.8) (1.0)	(0.5) (0.7) (1.0) <MDL (0.7)	<MDL <MDL <MDL (0.5) (0.7)	<MDL <MDL <MDL <MDL <MDL
JAU6476 thiazocine	0-3	<MDL	<MDL	<MDL	<MDL
	3-6	<MDL	<MDL	<MDL	<MDL
1,2,4-triazole	0-3	<MDL	<MDL	<MDL	<MDL
	3-6	<MDL	<MDL	<MDL	<MDL

Data obtained from Tables 13-17, pp. 48-52 in the study report. Values in parenthesis are below the LOQ and above the Method Detection Limit.

MDL: Prothioconazole: 1.3 ug/kg, JAU6476-desthio: 1.1 ug/kg, JAU6476-S-methyl: 0.5 ug/kg, JAU6476 thiazocone: 0.9 ug/kg, 1,2,4-triazole: 1.5 ug/kg.

LOQ: Prothioconazole, JAU6476-desthio, JA6476-S-methyl JAU6476 thiazocone, and 1,2,4-triazole: 10 ug/kg.

Prothioconazole was detected in the rice forage at a maximum concentration of 1.85 µg/g at day 0 and decreased to 0.20 µg/g by 60 days posttreatment, and JAU6476-desthio was detected in the rice forage at a maximum concentration of 1.04 µg/g at 1 day and decreased to 0.08 µg/g by 60 days (Table 18, p. 53). Following rice harvest at 90 days posttreatment, prothioconazole was detected in the straw at a mean concentration of 0.30 µg/g and JAU6476-desthio was detected in the straw at 0.16 µg/g (Table 18, p. 54); neither analyte was detected in the grain.

Mean concentration of prothioconazole and JAU6476-desthio expressed as µg/g, in rice forage samples.

	Days posttreatment						
	0	1	3	7	14	28	60
Prothioconazole	2.05 1.64	1.60 1.86	0.99 0.82	0.63 1.11	0.41 0.74	0.33 0.59	0.15 0.26
JAU6476-desthio	0.97 0.78	1.07 1.01	0.60 0.45	0.27 0.43	0.14 0.22	0.11 0.16	0.08 0.09

Data were obtained from Table 18, p. 53 of the study report.
MDL: Prothioconazole: 0.002 ug/g, JAU6476-desthio: 0.004 ug/g.
LOQ: Prothioconazole and JAU6476-desthio: 0.01 ug/g.

The laboratory storage stability study was inadequate to demonstrate stability of any of the analytes during storage because samples were not analyzed at time 0 to determine initial recoveries, and were analyzed only at one time point (Table 20, p. 56). Recovery of prothioconazole from soil was 9.90% following 653 days and recovery from water was 26.00% following 822 days. Recovery of JAU6476-desthio from soil was 85.00% following 813 days and recovery from water was 88.00% following 822 days. Recovery of JAU6476-S-methyl from soil was 87.20% following 813 days and recovery from water was 73.00% following 822 days. Recovery of JAU6476 thiazocine from soil was 90.60% following 653 days and recovery from water was 89.50% following 822 days. Recovery of 1,2,4-triazole from soil was 46.00% following 1161 days and recovery from water was 73.00% following 822 days.

STUDY DEFICIENCIES

1. The laboratory storage stability study was inadequate to demonstrate stability of any of the analytes during storage because samples were not analyzed at time 0 to determine initial recoveries, and sampling intervals were inadequate to determine stability of the analytes over time. Laboratory storage stability samples were analyzed only at one time point, between 653 and 1161 days. Laboratory storage stability samples should be analyzed at time 0 and up to at least the maximum storage interval for test samples, with a sufficient number of intervals in between, to allow the reviewer to determine stability over time.

   Of particular concern, prothioconazole was not shown to be stable in soil or water samples stored frozen for any length of time, with a recovery of 9.90% in soil following 653 days of storage and a recovery of 26.00% in water following 822 days of storage (Table 20, p. 56). It is necessary to demonstrate the stability of prothioconazole under typical storage conditions to ensure that the degradation of the parent occurred in the field and not during storage of the test samples. If the parent compound degraded during storage of the samples, then the calculated half-life value will not correctly reflect dissipation in the field. However, the study author stated that in an experiment to test the binding of ^{14}C-labeled prothioconazole to soil, control soil was fortified and immediately analyzed for the parent, and that the time zero recovery indicated that 28% of the applied radioactivity was bound to the soil (pp. 28 and 32). The author stated that in a similar study conducted in another study report, only 41% of prothioconazole could be recovered one hour after fortification (p. 32). In a similar study conducted with [^{14}C] 1,2,4-triazole, 31% of the applied radioactivity was bound to soil following 28 days in frozen storage, indicating that poor recoveries from the laboratory frozen storage stability study were due to adsorption and not degradation.

REVIEWER'S COMMENTS

1. The study author stated that the application rate was verified using solvent saturation pads and water pans that were placed in a separate bareground test plot that was treated at the same time in a companion study (pp. 13-14). The reviewer notes that the application rate should have been verified for the test plot by the same means (monitoring pads and pans) to accurately determine whether the target application rate was achieved.

2. The registrant-calculated DT_{50} values for prothioconazole and JAU6476-desthio in paddy water were 0.6 days and 2.7 days, respectively, and the DT_{50} of JAU6476-desthio in sediment/soil was 88 days (Figures 18-19, pp. 89-90); a half-life was not calculated for prothioconazole in sediment/soil.

3. Recoveries from duplicate water samples that were fortified with prothioconazole and transformation products at 1.5 μg/L or 0.5 μg/L (1,2,4-triazole) and analyzed concurrently with the test samples were 106-111% for prothioconazole, 102-111% for JAU6476-desthio, 101-104% for JAU6476-S-methyl, 101-104% for JAU6476 thiazocine, and 110-112% for 1,2,4-triazole (p. 31). Recoveries from duplicate soil samples that were fortified with prothioconazole and transformation products at 50 μg/kg and analyzed concurrently with the test samples were 81-98% for prothioconazole, 103-111% for JAU6476-desthio, 107-113% for JAU6476-S-methyl, 106-114% for JAU6476 thiazocine, and 95-100% for 1,2,4-triazole. Mean recoveries from crop samples that were fortified with prothioconazole and JAU6476-desthio at 0.01 μg/g ranged from 89-106% for prothioconazole and 84-88% for JAU6476-desthio.

4. The study author stated that field spikes were prepared for the parent and transformation products in soil (p. 15). However, recoveries were not reported and results were not discussed.

5. Tank mix samples were collected before and after the test application, and recoveries of the parent from the tank mix ranged from 100.86-118.7% of theoretical (pp. 14; Table 8, p. 42).

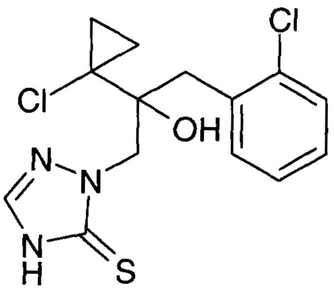
6. The reviewer notes that two additional aquatic field dissipation studies were conducted on rice cropped plots in California (MRID 46246522) and Arkansas (MRID 46246523).

7. Signed and dated Good Laboratory Practice, Quality Assurance, Certification of Authenticity, and Data Confidentiality statements were provided with the study (pp. 2-5).

ATTACHMENT:
Structures of Parent and Transformation Products

Prothioconazole [JAU6476]

IUPAC name: (RS)-2-[2-(1-Chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-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 No: 178928-70-6.
SMILES string: ClC1(C(Cc2ccccc2Cl)(CN2N=CNC2=S)O)CC1.

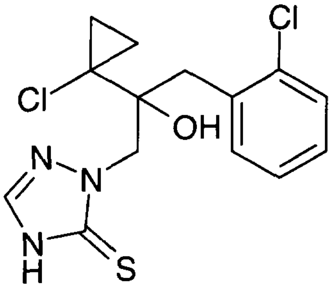


Identified Compounds

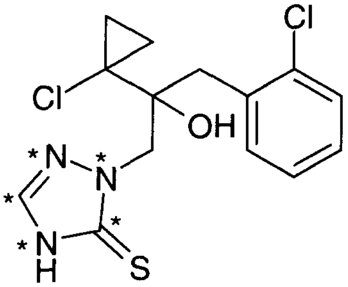
Prothioconazole [JAU6476]

IUPAC name: (RS)-2-[2-(1-Chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-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 No: 178928-70-6.
SMILES string: ClC1(C(Cc2ccccc2Cl)(CN2N=CNC2=S)O)CC1.

Unlabeled



[Triazole-1,2,4-^{15}N,3,5-^{13}C]JAU6476

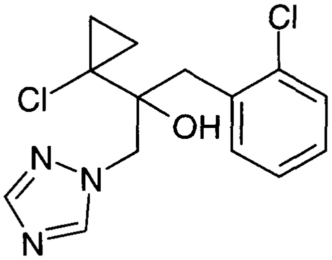


*Position of radiolabel.

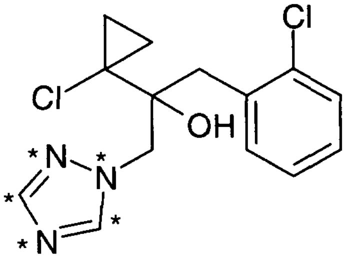
JAU6476-desthio [SXX0665]

IUPAC name: Not reported.
CAS name: 2-[2-(1-Chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole.
CAS No.: Not reported.

Unlabeled



[1,2,4-$^{15}N_3$,3,5-$^{13}C_2$]JAU6476-desthio

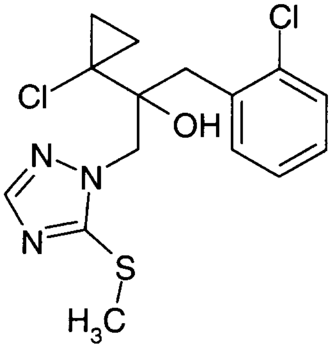


*Position of radiolabel.

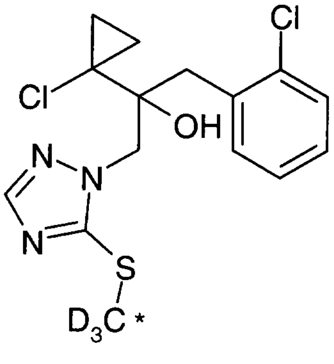
JAU6476-S-methyl or S-methyl-JAU6476 [KTS9473; WAK7681]

IUPAC name: Not reported.
CAS name: alpha-1(1-Chlorocyclopropyl)-alpha-[(2-chlorophenyl)methyl]-3-(methylthio)-1H-1,2,4-triazole-1-ethanol.
CAS No.: Not reported.

Unlabeled



[Methyl-d_3-^{13}C]JAU6476-S-methyl or [Methyl-d_3-^{13}C]S-methyl-JAU6476

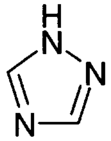


*Position of radiolabel; D = deuterium; ^{2}H.

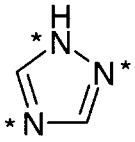
1,2,4-triazole or 1-H-1,2,4-triazole

IUPAC name: Not reported.
CAS name: 1-H-1,2,4-triazole.
CAS No.: Not reported.

Unlabeled



[1,2,4-$^{15}N_3$]1,2,4-triazole or [1,2,4-$^{15}N_3$]1-H-1,2,4-triazole



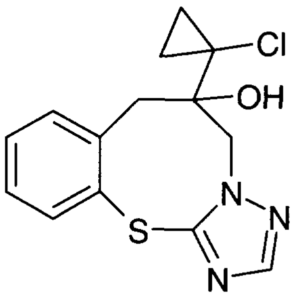
*Position of radiolabel.

Unidentified reference compounds

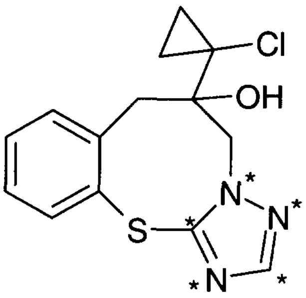
JAU6476-thiazocine

IUPAC name: Not reported.
CAS name: 6-(1-Chlorocyclopropyl)-6,7-dihydro-triazole-5H-[1,2,4]triazolo[5,1-b][1,3]benzothiazon-6-ol.
CAS No.: Not reported.

Unlabeled



[Thiazocine-$^{15}N_3$-$^{13}C_2$]JAU6476-thiazocine



*Position of radiolabel.

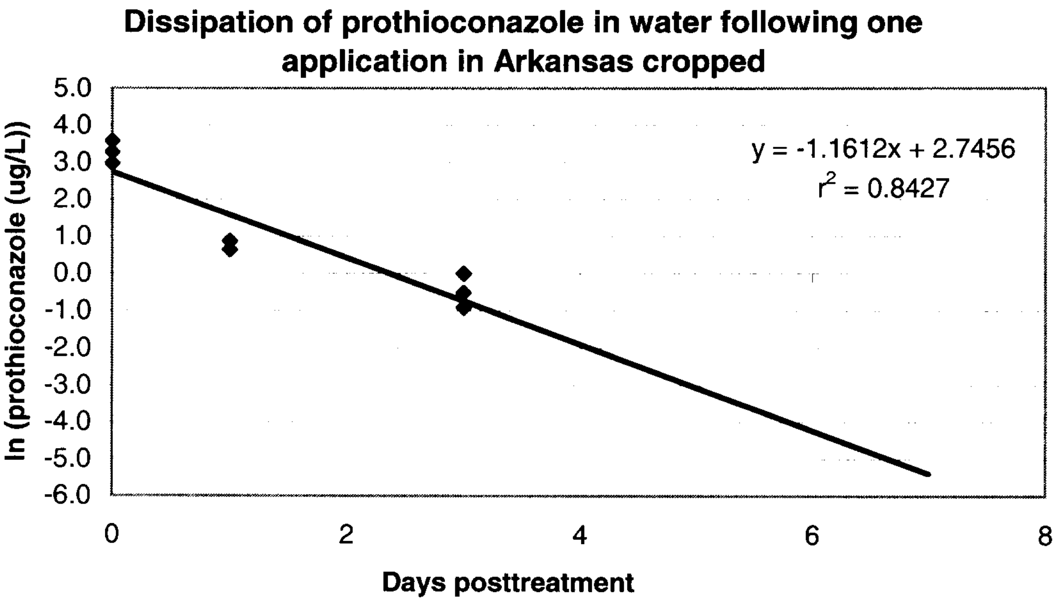
Chemical Name	Prothioconazole
PC Code	113961
MRID	46246524
Guideline No.	164-2

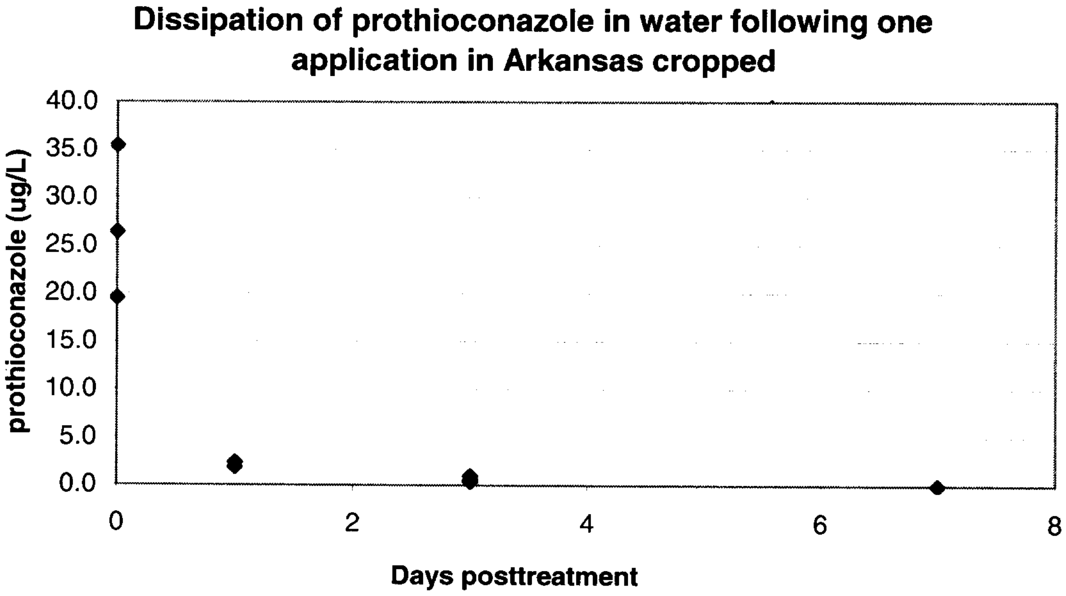
Arkansas cropped field site
Half-life in water (days) = 0.6

Days posttreatment	Prothioconazole (µg/L)	Ln (Prothioconazole)
0	19.5	2.970
0	35.4	3.567
0	26.4	3.273
1	2.4	0.875
1	1.9	0.642
1	2.4	0.875
3	1.0	0.000
3	0.4	-0.916
3	0.6	-0.511
7	<MDL	
7	<MDL	
7	<MDL	

Data obtained from Table 12, p. 46 of the study report.

Chemical Name	Prothioconazole
PC Code	113961
MRID	46246524
Guideline No.	164-2


Dissipation of prothioconazole in water following one application in Arkansas cropped


Dissipation of prothioconazole in water following one application in Arkansas cropped

Chemical Name	Prothioconazole
PC Code	113961
MRID	46246524
Guideline No.	164-2

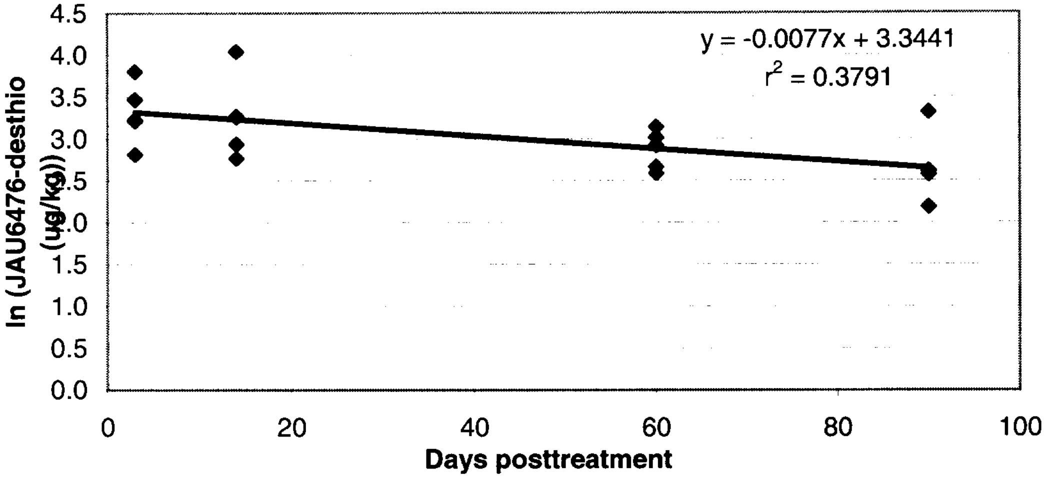
Arkansas cropped field site (JAU6476-desthio)
Half-life in sediment (days) = 90.0 *** 0- to 7.5-cm soil depth**

Days posttreatment	JAU6476-desthio (µg/kg)	Ln (JAU6476-desthio)
3	25.3	3.231
3	24.9	3.215
3	16.7	2.815
3	45.0	3.807
3	32.2	3.472
14	16.0	2.773
14	57.2	4.047
14	26.3	3.270
14	18.9	2.939
14	26.1	3.262
60	20.4	3.016
60	18.6	2.923
60	14.4	2.667
60	13.3	2.588
60	23.1	3.140
90	27.6	3.318
90	13.7	2.617
90	13.1	2.573
90	13.6	2.610
90	8.9	2.186

Data obtained from Table 14, p. 49 of the study report.

Chemical Name	Prothioconazole
PC Code	113961
MRID	46246524
Guideline No.	164-2

Dissipation of JAU6476-desthio in sediment/soil following one application in Arkansas cropped (0- to 7.5-cm soil depth)



Dissipation of JAU6476-desthio in sediment/soil following one application in Arkansas cropped (0- to 7.5-cm soil depth)