Data Evaluation Report on the aquatic field dissipation of prothioconazole

PMRA Submission Number N/A EPA MRID Number 46246522

Data Requirement:
PMRA Data Code: 8.3.2.2
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
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Date: October 3, 2005

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

CITATION: Wyatt, D.R. 2004. Aquatic field dissipation of JAU6476 in a California rice field, 2000. Unpublished study performed by A & L Great Lakes Laboratories, Inc., Fort Wayne, IN, Bayer Corporation, Stilwell, KS and Agricultural Advisors, Live Oak, CA and submitted by Bayer CropScience, Research Triangle Park, NC. Submitting Laboratory Study No. J6022401. Bayer Report No. 200060. Experiment initiation June 30, 2000, and completion July 13, 2001 (field phase; p. 13). Final report issued March 17, 2004.

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Primary Reviewer: Dan Hunt Dynamac Corporation	**Signature:** Dan Hunt **Date:** 10-27-2004
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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 twice (14 days apart) at a target application rate of 220.7 g a.i./ha onto a flooded plot of Oswald clay soil planted with rice in California. 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 after the second application, at which time the paddy water was allowed to evaporate from the plots, and sediment/soil samples were collected through 364 days after the second application.

Prothioconazole dissipated in the **paddy water** with a reviewer-calculated half-life value of 1.7 days ($r^2 = 0.97$) following the second application, using linear regression analysis. Prothioconazole was detected in the paddy water at a mean concentration of 219 µg/L following the first application, and decreased to 73.9 µg/L by 1 day and 0.8 µg/L by 13 days. Following the second application, prothioconazole was detected in the water at a mean concentration of 84.6 µg/L, decreased to 16.3 µg/L by 3 days, and was last detected at 0.42 µg/L (single replicate) at 14 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 initially detected in the water at a mean concentration of 42.5 µg/L immediately following the first application, and decreased to 11.4 µg/L by one day prior to the second application. Following the second application, JAU6476-desthio was detected at a maximum concentration of 50.3 µg/L at 3 days, and decreased to 14.4 µg/L by 14 days and 0.64 µg/L by 60 days. 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 above the LOQ at a mean concentration of 0.46 µg/L at 3 days after the first application, was a maximum of 1.04 µg/L at 3 days after the second application, and was detected below the LOQ at 28 and 60 days posttreatment. The transformation product **1,2,4-triazole (1-H-1,2,4-triazole)** was detected at a maximum concentration of 0.13 µg/L at 7 days after the second application and **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.

Prothioconazole dissipated in the **sediment/soil** with a reviewer-calculated half-life value of 203.9 days ($r^2 = 0.40$) following the second application, using linear regression analysis. Prothioconazole was detected in the 0- to 3-inch depth of the sediment/soil at a mean concentration of 26.1-31.9 µg/kg from 0-13 days following the first application, was a maximum of 57.1 µg/kg immediately following the second application, and ranged from 17.5-39.0 µg/kg from 3 to 28 days and from 10.3 to 18.8 µg/kg from 60 to 273 days posttreatment. The transformation product **JAU6476-desthio** was initially detected in the sediment/soil at a mean concentration above the LOQ at 17.0 µg/kg at 7 days following the first application, increased to

a maximum of 32.7 µg/kg by 14 days after the second application, and decreased to 20.4 µg/kg by 364 days posttreatment. The transformation product **JAU6476-S-methyl** was only detected in the sediment/soil once at a mean concentration above the LOQ, at 10.2 µg/kg at 122 days after the second application. The transformation product **1,2,4-triazole** was detected at levels below the LOQ throughout the study period following the second application while the transformation product **JAU6476 thiazocine** was not detected above the LOQ at any sampling interval. Prothioconazole and its transformation products were not detected above the LOQ in soil below the 0-3 inch depth at any sampling intervals.

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 of the analytes 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 (298 x 14 ft; Figure 4, p. 67) planted to rice in Sutter County, California (pp. 12-14; Figures 2-3, pp. 65-66). The soil at the test site was a Oswald clay loam and was classified as a clay loam from 0-6 inches (29.6% sand, 34.0% silt, 36.4% clay, pH 6.3, 3.02% organic matter, CEC 20.10 meq/100 g, bulk density 1.24 g/cm^3), clay from 6-18 inches, clay loam from 18-24 inches, silt loam from 24-30 inches, and loam from 30-36 inches (Table 3, p. 36). The treated plot was divided into five equal-sized sections for sampling, and each section was further divided into 17 rows with three subsections (p. 15). A control plot (dimensions not reported) was also established at the test site and planted with rice; the control plot was located 238 ft from the treated plot. A three-year plot history indicated that Ordram, Londax, Roundup, 2,4-D, and Fury were recently applied to the test plot (Table 2, p. 35). The test area was disked and leveled approximately six weeks prior to treatment, and water was added 16 days prior to treatment (Table 5, p. 38). Characteristics of the paddy water were as follows: total suspended solids 22 mg/L, pH 7.5, hardness 60 mg $CaCO_3$/L, total dissolved solids 77 mg/L, total organic carbon 6.36 mg/L (Table 4, p. 37). The test plot was maintained under 2.5-4.5 inches of water until 60 days posttreatment of the second application, when the flood water was allowed to evaporate (pp. 14 and 28; Table 6, p. 40). Details regarding the rice crop (variety, date of planting, harvest, etc.) were not provided.

Precipitation was recorded on-site and air and soil temperatures, relative humidity, wind speed, solar radiation, and evapotranspiration data were collected from a weather station located 16 miles east of the test site (p. 16). Total precipitation during the study period was 14.95 inches, compared to a historical average of 22.23 inches; air and soil temperatures were approximately equal to historical averages (Table 7, p. 41).

Prothioconazole was broadcast twice, on June 30, 2000 and July 14, 2000, at a target application rate of 220.7 g a.i./ha (3.15 oz a.i./A) onto the flooded plot (p. 14). The target application rate was 110% of the proposed label rate. The application was made using a boom equipped with 10 flat fan nozzles spaced 20 inches apart and 18 inches above the water. Meteorological conditions during each application were as follows: wind speed 0 mph, air temperature 65-68°F, relative humidity 61-78% (p. 14). The test site was maintained weed-free during the study period with Liberty® (one application) and Touchdown® (four applications; Table 5, pp. 38-39).

The application rate was verified for both applications using solvent saturation pads and water pans (pp. 14-15). Two solvent saturation pads (13.7 x 22 cm) were placed on stands in each of the five sections of the test plot immediately prior to each application (10 pads total for each application). Following each 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. 17-18 and Appendix 3, pp. 134-136). 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 (27 x 21 cm^2 or 31 x 21 cm^2) containing approximately 500 mL of control water were also placed on stands in each section of the test plot prior to each application (5 pans total for each application; p. 15). Water from each pan was collected and poured into a plastic bag after each 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. 144-146).

Water samples were collected from the treated plot one day prior to the first application, at each application, at 1, 3, 7, and 13 days after the first application and at 3, 7, 14, 28, and 60 days following the second application (p. 15; Table 5, pp. 38-39). Three 500-mL water samples were collected at each sampling interval; samples were taken from the top two inches of the water column and consisted of five 100-mL aliquots (one from each of the five sections of the treated plot; p. 16). Water samples were stored frozen for 679-761 days prior to analysis (Table 11, pp. 45-48).

Sediment samples were collected from the treated plot one day prior to the first application, at each application, at 1, 3, 7, and 13 days after the first application, and at 3, 7, 14, 28, 60, and 90 days following the second application (p. 15; Table 5, pp. 38-39). Soil samples were collected at 121, 182, 273, and 364 days after the second application. 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 sampled only once during the study, and only one acceptable core was taken from each subsection. Sediment samples were collected to a depth of 6 inches using a 2-inch diameter liner. Soil cores were taken in two segments, 0-6 inches and 6-12 inches, using a hand-driven corer with 1- or 2-inch diameter liners. Sediment/soil cores were stored frozen at the field facility before being shipped frozen to the processing laboratory (p. 16). 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. 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 374-740 days prior to analysis (Tables 12-16, pp. 49-58).

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; p. 20; Figure 1, pp. 61-64).

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. 61-64 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, 165-169). 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. 26).

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 (pp. 24-25; Appendix 8, 172-174). 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 µm) 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. 26).

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. 151-152). 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. 26).

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 (pp. 21-22; Appendix 6, pp. 157-160). 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. 26).

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. 26). Soil samples were fortified with each analyte at 10 µg/kg and 100 µg/kg.

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

Analyte	**Percent Recovery**			
	Water		**Soil**	
	0.3 µg/L	**3 µg/L**	**10 µg/kg**	**100 µg/kg**
Prothioconazole (JAU6476)	101.2 ± 8.5	102.9 ± 4.1	91.7 ± 10.2	95.0 ± 6.4

Analyte	Percent Recovery			
	Water		Soil	
	0.3 µg/L	3 µg/L	10 µg/kg	100 µg/kg
JAU6476-desthio	104.1 ± 11.6	98.2 ± 1.7	109.1 ± 1.5	102.0 ± 1.9
JAU6476-S-methyl	101.5 ± 1.7	98.6 ± 1.1	113.9 ± 2.7	103.8 ± 1.2
JAU6476 thiazocine	102.0 ± 2.0	100.1 ± 1.7	107.6 ± 4.8	103.4 ± 1.5
	0.1 µg/L	**1 µg/L**		
1,2,4-triazole	106.8 ± 4.4	100.0 ± 4.8	95.6 ± 3.1	82.5 ± 2.0

Means were obtained from Tables 9-10, pp. 43-44 of the study report.

Field spikes were prepared in duplicate for JAU6476-desthio, JAU6476-S-methyl, and 1,2,4-triazole using control soil (p. 16; Table 18, p. 60). Soil samples were fortified with each analyte at 50 µg/kg, frozen, and taken to the field during sampling. The field spikes were kept under the same conditions as the field cores until analysis. Field spikes were analyzed following 914 days (JAU6476-desthio and JAU6476-S-methyl) or 1161 days (1,2,4-triazole) of storage, which exceeded the longest storage interval for the field samples. Field spikes were not prepared for prothioconazole and JAU6476 thiazocine in soil, and no field spikes were prepared in water.

To determine the frozen storage stability of prothioconazole and JAU6476 thiazocine in soil and water and JAU6476-desthio, JAU6476-S-methyl, and 1,2,4-triazole in water, soil samples were fortified with each analyte at 100 µg/kg, and water samples were fortified with each analyte at 20 µg/kg (p. 27; Table 18, p. 60). Soil samples were analyzed for prothioconazole and JAU6476 thiazocine following 650 days of storage. Water samples were analyzed for prothioconazole and JAU6476-desthio following 667 days of storage, and for JAU6476-S-methyl, JAU6476 thiazocine, and 1,2,4-triazole following 822 days of storage. Samples were not analyzed 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 twice (14 days apart) at a target application rate of 220.7 g a.i./ha onto a flooded plot of Oswald clay soil planted with rice, dissipated in the paddy water with a reviewer-calculated half-life value of 1.7 days ($r^2 = 0.97$), and in sediment/soil with a reviewer-calculated half-life of 203.9 days ($r^2 = 0.40$). Half-lives are based on detections following the second application, and were 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 from the saturation pads were 92.9% and 92.8% of the label rate (2.86 oz a.i./A) for the first and second applications, respectively, and corresponding recoveries from the water pans were 78.8% and 74.1% of the label rate, respectively (p. 28; Table 8, p. 42).

Prothioconazole was detected in the **paddy water** at a mean concentration of 219 μg/L following the first application, and decreased to 73.9 μg/L by 1 day and 0.8 μg/L by 13 days (Table 11, p. 45). Following the second application, prothioconazole was detected in the water at a mean concentration of 84.6 μg/L, decreased to 16.3 μg/L by 3 days, and was last detected at 0.42 μg/L (single replicate) at 14 days posttreatment (Table 11, p. 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 42.5 μg/L immediately following the first application, and decreased to 11.4 μg/L by one day prior to the second application. Following the second application, JAU6476-desthio was detected at a maximum concentration of 50.3 μg/L at 3 days, and decreased to 14.4 μg/L by 14 days and 0.64 μg/L by 60 days. 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 above the LOQ at a mean concentration of 0.46 μg/L at 3 days after the first application, was a maximum of 1.04 μg/L at 3 days after the second application, and was detected below the LOQ at 28 and 60 days posttreatment. The transformation product **1,2,4-triazole (1-H-1,2,4-triazole)** was detected at a maximum concentration of 0.13 μg/L at 7 days after the second application, and **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 in paddy water.

	Days posttreatment of the last application										
	App 1 (-14)	(-13)	(-11)	(-7)	(-1)	App 2 (0)	3	7	14	28	60
Prothioconazole	**158.70 279.00 221.74**	**62.70 86.44 72.48**	**34.48 52.90 22.50**	**5.29 6.21 10.00**	**0.67 1.09 0.73**	**87.20 83.90 82.60**	**18.70 17.80 12.40**	**2.52 2.04 2.59**	**(0.18) 0.42 (0.19)**	<MDL <MDL <MDL	<MDL <MDL <MDL
JAU6476-desthio	**46.9 45.2 35.6**	**28.3 28.2 25.8**	**30.7 36.8 26.9**	**26.7 24.8 51.1**	**11.6 10.4 12.1**	**44.49 45.99 40.88**	**58.34 51.50 41.04**	**38.61 34.77 40.28**	**13.40 15.48 14.43**	**4.41 4.03 4.56**	**0.53 0.69 0.69**
JAU6476-S-methyl	(0.06) <MDL <MDL	(0.26) (0.24) (0.26)	**0.45 0.46 0.48**	**0.52 0.50 1.05**	(0.28) (0.28) (0.28)	**0.39 0.43 0.39**	**1.02 1.06 1.03**	**0.72 0.73 0.75**	**0.37 0.35 0.32**	(0.20) (0.19) (0.20)	(0.03) (0.03) (0.03)
JAU6476 thiazocine	<MDL <MDL <MDL	(0.07) (0.08) (0.07)	(0.13) (0.14) (0.13)	(0.09) (0.08) (0.19)	(0.05) (0.05) (0.05)	(0.05) (0.05) (0.06)	(0.17) (0.16) (0.16)	(0.12) (0.11) (0.12)	(0.05) (0.05) (0.06)	(0.02) (0.03) (0.03)	<MDL <MDL <MDL
1,2,4-triazole	<MDL <MDL <MDL	(0.04) (0.03) (0.03)	(0.05) (0.05) (0.05)	(0.06) (0.06) (0.05)	(0.06) (0.05) (0.05)	(0.03) (0.05) (0.04)	**0.11 0.12 0.12**	**0.11 0.14 0.13**	(0.07) (0.06) (0.06)	(0.05) (0.05) (0.05)	(0.02) <MDL (0.02)

Data were obtained from Table 11, pp. 45-48 of the study report. Values in parenthesis are below the LOQ and above the Method Detection Limit.
MDL: Prothioconazole: 0.09 ug/L, JAU6476-desthio: 0.12 ug/L, JAU6476-S-methyl: 0.02 ug/L, JAU6476 thiazocone: 0.02 ug/L, 1,2,4-triazole: 0.02ug/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 detected in the 0- to 3-inch (0- to 7.5 -cm) **sediment/soil** at a mean concentration of 26.1-31.9 µg/kg from 0-13 days following the first application, was a maximum of 57.1 µg/kg immediately following the second application, and ranged from 17.5-39.0 µg/kg from 3 to 28 days and from 10.3 to 18.8 µg/kg from 60 to 273 days posttreatment (Table 12, pp. 49-50). The transformation product **JAU6476-desthio** was initially detected in the sediment/soil at a mean concentration above the LOQ at 17.0 µg/kg at 7 days following the first application, increased to a maximum of 32.7 µg/kg by 14 days after the second application, and decreased to 20.4 µg/kg by 364 days posttreatment (Table 13, pp. 51-52). The transformation product **JAU6476-S-methyl** was detected in the sediment/soil only once at a mean concentration above the LOQ, at 10.2 µg/kg at 122 days after the second application (Table 14, pp. 53-54). The transformation product **1,2,4-triazole** was detected at levels below the LOQ throughout the study period following the second application, whereas the transformation product **JAU6476 thiazocine** was not detected above the LOQ at any sampling interval (Tables 15-16, pp. 55-58). Prothioconazole and its transformation products were not detected above the LOQ in soil below the 0-3 inch depth at any sampling intervals.

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

		Days posttreatment of the last application															
	Depth (in)	App1 (-14)	(-13)	(-11)	(-7)	(-1)	App2 (0)	3	7	14	28	60	90	122	182	273	364
Prothioconazole	0-3	**30.8** **29.8** **19.0**	**27.0** **37.3** **28.5**	**25.1** **29.5** **25.7**	**32.9** **36.9** **25.9**	**40.4** **24.6** **13.4**	**73.2** **45.4** **52.6**	**(9.0)** **23.8** **19.7**	**39.3** **38.9** **26.7**	**44.7** **30.5** **41.8**	**37.0** **48.0** **31.5**	**24.0** **18.0** **14.3**	**12.5** **11.1** **(7.3)**	**25.1** **14.6** **16.7**	**22.2** **11.0** **12.8**	**20.1** **15.2** **12.4**	**14.8** **(5.1)** **(9.9)**
	3-6	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL (4.9) <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL
JAU6476-desthio	0-3	(2.0) (2.0) (0.9)	(5.3) (6.3) (5.5)	**(8.1)** **10.2** **10.7**	**17.0** **17.6** **16.4**	**19.7** **15.9** **13.4**	**24.1** **21.2** **21.3**	**13.3** **21.4** **20.6**	**30.6** **37.4** **26.5**	**37.4** **27.6** **33.2**	**25.3** **29.5** **26.1**	**28.9** **21.7** **15.3**	**29.4** **25.1** **28.4**	**29.4** **25.8** **21.9**	**21.3** **(9.7)** **13.3**	**24.6** **19.8** **20.7**	**27.2** **17.3** **16.7**
	3-6	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL (1.1) <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	(0.6) <MDL <MDL
JAU6476-S-methyl	0-3	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	(1.1) (1.2) (0.9)	(1.9) (1.4) (1.1)	(2.2) (1.5) (1.9)`	(1.0) (1.8) (1.7)	(3.0) (4.1) (2.3)	(6.9) (4.5) (3.6)	(6.0) (7.9) (6.3)	(9.0) (8.1) (4.9)	(8.4) (9.0) (8.9)	**12.3** **11.4** **(6.8)**	(7.8) (3.6) (5.2)	(9.4) (6.9) (6.5)	(7.9) (3.8) (4.2)
	3-6	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL
JAU6476 thiazocine	0-3	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL
	3-6	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL
1,2,4-triazole	0-3	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	<MDL <MDL <MDL	(1.0) <MDL <MDL	<MDL (1.1) (1.0)	(1.0) (1.6) (1.2)	(1.5) (1.1) (1.4)	(1.5) (2.0) (1.6)	(2.2) (1.8) (1.4)	(2.9) (2.4) (2.1)	(2.3) (2.5) (2.6)	(3.0) (2.2) (1.7)	(3.9) (3.1) (2.9)	(4.4) (2.5) (3.0)
	3-6	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL	<MDL

Data were obtained from Tables 12-16, pp. 49-58 of the study report. Values in parenthesis are below the LOQ and above the Method Detection Limit.
MDL: Prothioconazole: 3.2 ug/kg, JAU6476-desthio: 0.5 ug/kg, JAU6476-S-methyl: 0.9 ug/kg, JAU6476 thiazocone: 1.5 ug/kg, 1,2,4-triazole: 1.0 ug/kg.
LOQ: Prothioconazole, JAU6476-desthio, JA6476-S-methyl JAU6476 thiazocone, and 1,2,4-triazole: 10 ug/kg.

Recoveries from field spikes prepared for JAU6476-desthio, JAU6476-S-methyl, and 1,2,4-triazole at 50 µg/kg soil were 94.80%, 90.80%, and 50.80%, respectively, following 914 days, 914 days, and 1161 days of storage, respectively (Table 18, p. 60). Field spikes were not prepared for prothioconazole and JAU6476 thiazocine.

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 18, p. 60). Recovery of prothioconazole from soil was 32.20% following 650 days, and recovery from water was 39.00% following 667 days. Recovery of JAU6476 thiazocine from soil was 91.50% following 650 days and recovery from water was 80.50% following 822 days. Recovery of JAU6476-desthio from water was 87.00% following 667 days. Recoveries of JAU6476-S-methyl, and 1,2,4-triazole were 68.00-70.50% following 822 days. The stability of JAU6476-desthio, JAU6476-S-methyl, and 1,2,4-triazole in soil was not determined.

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 650 and 822 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 32.20% in soil following 650 days of storage, and a recovery of 39.00% in water following 667 days of storage (Table 18, p. 60). 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 23% of the applied radioactivity was bound to the soil (pp. 27 and 32). The author stated that in a similar study described in another study report, only 41% of prothioconazole could be recovered one hour after fortification (p. 32).

   The stability of the transformation products JAU6476-desthio and JAU6476-S-methyl in soil was shown to be >90% based on recoveries from field spikes that were fortified in the laboratory, then sent to the field site and kept under the same conditions as the field samples (Table 18, p. 60). The field spikes were analyzed following 914 days of storage, which exceeded the longest storage interval for the field samples. However, 1,2,4-triazole was not stable in frozen storage, with a recovery of 50.80% from soil following 1161 days of storage. Field spikes were not prepared for prothioconazole or JAU6476 thiazocine.

REVIEWER'S COMMENTS

1. The registrant-calculated DT_{50} values for prothioconazole in paddy water were 1.8 days and 1.74 days, respectively, for the first and second application, and the registrant-calculated DT_{50} value for sediment/soil was 77 days following the second application (Figures 24-26, pp. 115-117). The registrant-calculated DT_{50} values for JAU6476-desthio in paddy water were 8.3 days and 9.09 days, respectively, for the first and second application, and the registrant-calculated DT_{50} value for sediment/soil was 83 days following the second application. Half-life calculations were performed using linear regression and GraphPad Prism software (p. 31).

2. Recoveries from duplicate water samples that were fortified with prothioconazole and transformation products at 1.5 µg/L and analyzed concurrently with the test samples were 99-110% for prothioconazole, 95-100% for JAU6476-desthio, 99-101% for JAU6476-S-methyl, 103% for JAU6476 thiazocine, and 103% for 1,2,4-triazole (p. 30). Recoveries from duplicate soil samples that were fortified with prothioconazole and transformation products at 0.05 µg/g and analyzed concurrently with the test samples were 81-103% for prothioconazole, 95-110% for JAU6476-desthio, 95-106% for JAU6476-S-methyl, 96-112% for JAU6476 thiazocine, and 76-85% for 1,2,4-triazole.

3. Tank mix samples were collected but were not analyzed because the analyses of verification pads and pans showed that the applications were satisfactory, as stated by the study author (pp. 15 and 28).

4. The reviewer notes that two additional aquatic field dissipation studies were conducted on rice cropped plots in Arkansas (MRIDs 46246523 and 46246524).

5. 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

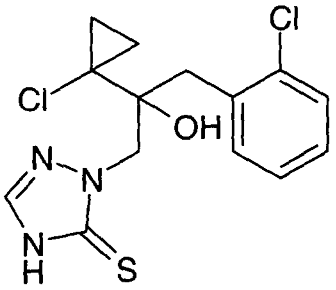
Prothioconazole [JAU6476]

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.

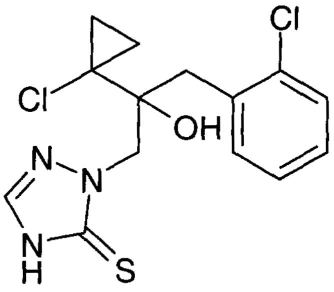


Identified Compounds

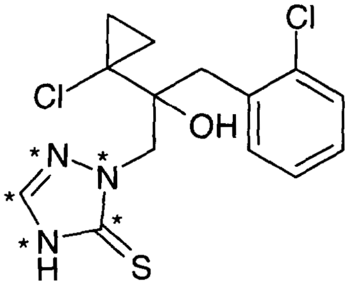
Prothioconazole [JAU6476]

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

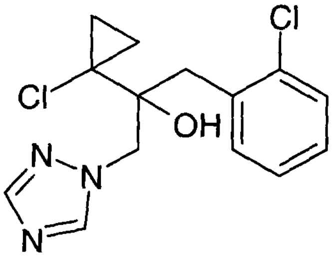


*Position of radiolabel.

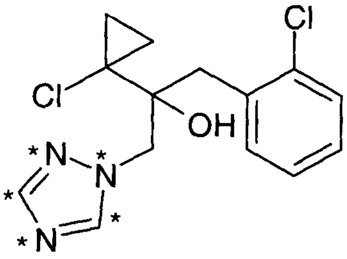
JAU6476-desthio [SXX0665]

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

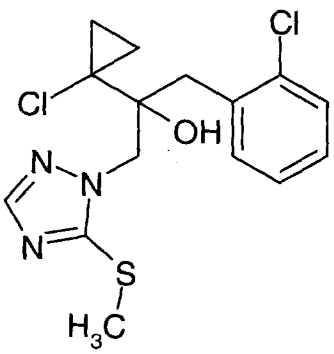


*Position of radiolabel.

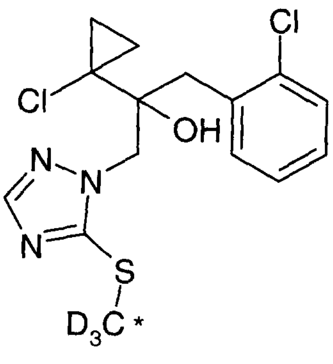
JAU6476-S-methyl or S-methyl-JAU6476 [KTS9473; WAK7681]

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

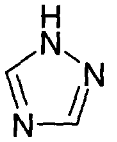


*Position of radiolabel; D = deuterium; ^{2}H.

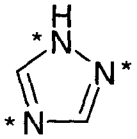
1,2,4-triazole or 1-H-1,2,4-triazole

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



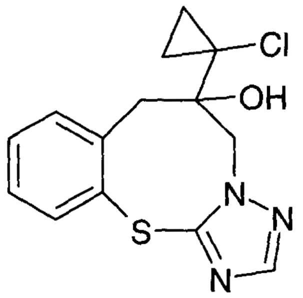
*Position of radiolabel.

Unidentified reference compounds

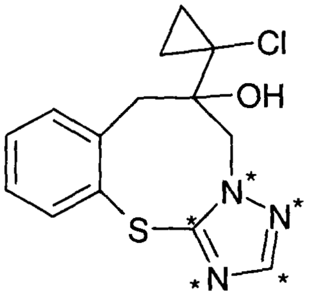
JAU6476-thiazocine

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	46246522
Guideline No.	164-2

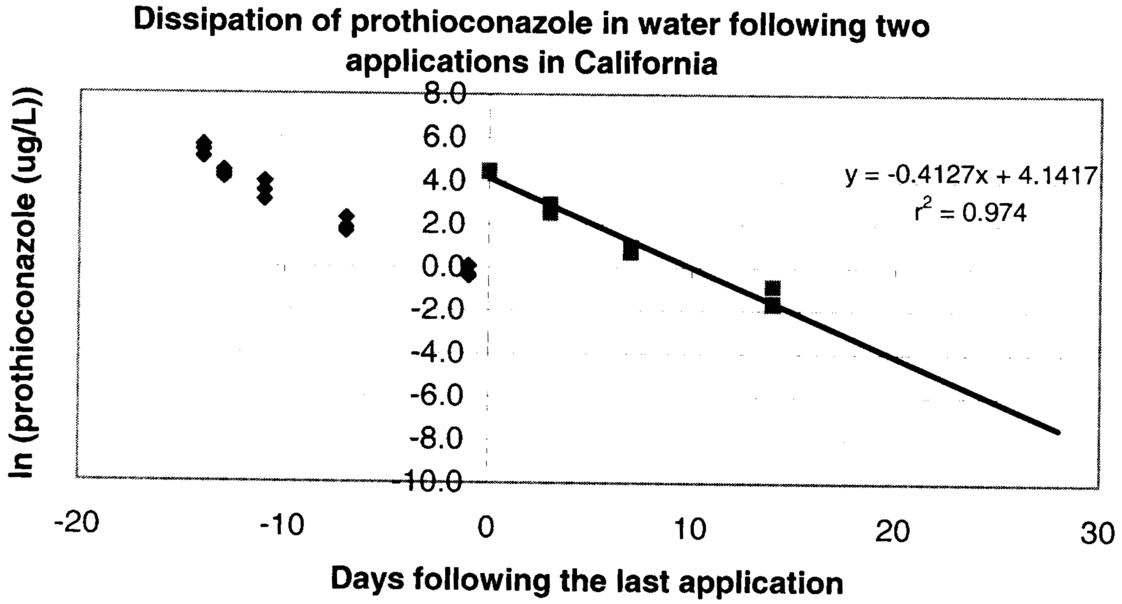
California field site

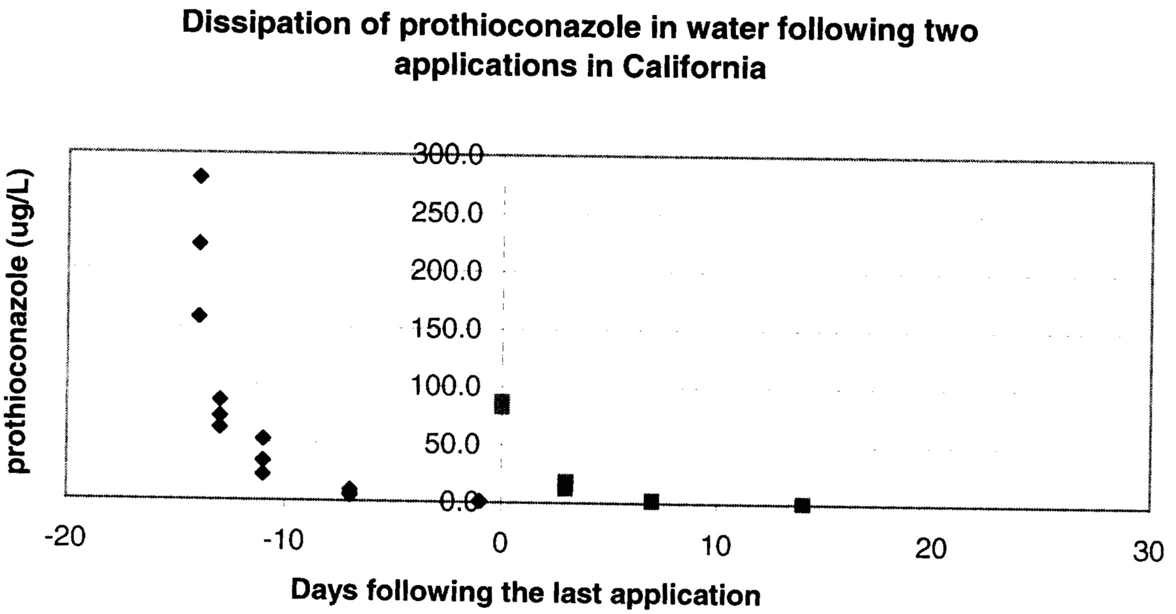
Half-life in water (days) = **1.7**

Days posttreatment of the last application	Prothioconazole (μg/L)	Ln (Prothioconazole)
-14	158.70	5.067
-14	279.00	5.631
-14	221.74	5.402
-13	62.70	4.138
-13	86.44	4.459
-13	72.48	4.283
-11	34.48	3.540
-11	52.90	3.968
-11	22.50	3.114
-7	5.29	1.666
-7	6.21	1.826
-7	10.00	2.303
-1	0.67	-0.400
-1	1.09	0.086
-1	0.73	-0.315
0	87.20	4.468
0	83.90	4.430
0	82.60	4.414
3	18.70	2.929
3	17.80	2.879
3	12.40	2.518
7	2.52	0.924
7	2.04	0.713
7	2.59	0.952
14	0.18	-1.715
14	0.42	-0.868
14	0.19	-1.661
28	--	
28	--	
28	--	

Data obtained from Table 11, pp. 45 and 47 of the study report.

Chemical Name	Prothioconazole
PC Code	113961
MRID	46246522
Guideline No.	164-2





Chemical Name Prothioconazole
PC Code 113961
MRID 46246522
Guideline No. 164-2

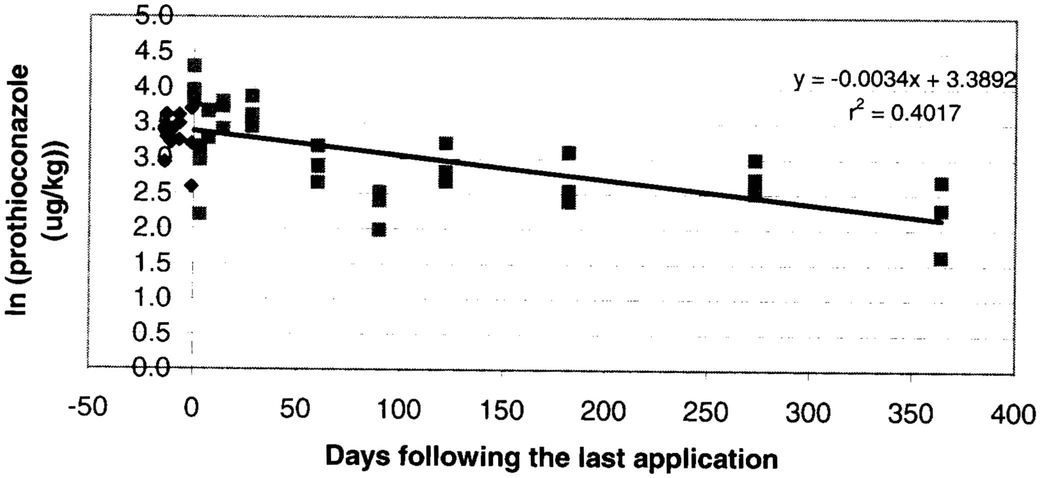
California field site
Half-life in sediment (days) = 203.9 * 0- to 7.5-cm soil depth

Days posttreatment of the last application	Prothioconazole (µg/kg)	Ln (Prothioconazole)
-14	30.8	3.428
-14	29.8	3.395
-14	19.0	2.944
-13	27.0	3.296
-13	37.3	3.619
-13	28.5	3.350
-11	25.1	3.223
-11	29.5	3.384
-11	25.7	3.246
-7	32.9	3.493
-7	36.9	3.608
-7	25.9	3.254
-1	40.4	3.699
-1	24.6	3.203
-1	13.4	2.595
0	73.2	4.293
0	45.4	3.816
0	52.6	3.963
3	9.0	2.197
3	23.8	3.170
3	19.7	2.981
7	39.3	3.671
7	38.9	3.661
7	26.7	3.285
14	44.7	3.800
14	30.5	3.418
14	41.8	3.733
28	37.0	3.611
28	48.0	3.871
28	31.5	3.450
60	24.0	3.178
60	18.0	2.890
60	14.3	2.660
90	12.5	2.526
90	11.1	2.407
90	7.3	1.988
122	25.1	3.223
122	14.6	2.681
122	16.7	2.815
182	22.2	3.100
182	11.0	2.398
182	12.8	2.549
273	20.1	3.001
273	15.2	2.721
273	12.4	2.518
364	14.8	2.695
364	5.1	1.629
364	9.9	2.293

Data obtained from Table 12, pp. 49-50 in the study report.

Chemical Name	Prothioconazole
PC Code	113961
MRID	46246522
Guideline No.	164-2

Dissipation of prothioconazole in sediment/soil following two applications in California (0- to 7.5-cm soil depth)



Dissipation of prothioconazole in sediment/soil following two applications in California (0- to 7.5-cm soil depth)