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DATA EVALUATION RECORD

STUDY 5

CHEM 125620 Triticonazole §162-1

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STUDY ID 448021-25

Ayliffe, J. M., and P. J. Godward. 1993. Fungicides: RPA 400727-<sup>14</sup>C: Rate of degradation in four soils. RPA Study No. P91/411. Unpublished study performed and submitted by Rhône-Poulenc Agriculture Limited, Ongar, Essex, England.

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CONCLUSION:

Metabolism - Aerobic Soil

1. This study is *acceptable*, provides useful information on the aerobic soil metabolism of triticonazole, and *partially satisfies* EPA Subdivision N Guidelines data requirements on aerobic soil metabolism. Three separate soil sets were utilized in the determination of the degradation kinetics at 10 °C of the parent compound and examine patterns of formation and decline of the degradates. One soil was also examined at 22 °C.



2. Phenyl ring-labeled [ $^{14}\text{C}$ ]triticonazole, (1RS-(E)-5-((4-chlorophenyl)methylene)-2,2-dimethyl-1-(1H-1,2,4-triazol-1-ylmethyl)-cyclopentan-1-ol), in soil maintained at 75% of 0.33 bar and incubated in the dark at 10 °C for 363 days, degraded with mean calculated first order **half-lives of 359 days** (334 to 388 days at the 90 % confidence interval) in the sandy loam soil, **224 days** (206 to 245 days at the 90 % confidence interval) in the clay loam soil, and **691 days** (591 to 832 days at the 90 % confidence interval) in loamy sand soil. Additionally, [ $^{14}\text{C}$ ]triticonazole, applied to the same loamy sand soil maintained at 75% of 0.33 bar and incubated in the dark at 22 °C for 363 days, degraded with mean calculated first-order **half-life of 344 days** (306 to 376 days at the 90 % confidence interval). Data was also submitted for Speyer 2.2 artificial loamy sand soil, but has not been considered in this review.
3. Aerobic degradation produced chemical species through hydroxylation of the unfragmented parent molecule, triticonazole. However, unidentified bound residues could possibly include residues of toxicological concern. **Three or four identified and eight, nine or ten unknown metabolites** were monitored in each test system during this study. Without additional data, accurate half-life estimations for these aerobic metabolism products can not be calculated. Data for these metabolites, non-extractable residues, and [ $^{14}\text{C}$ ]organic volatiles, have been tabulated below. Degradates of potential concern are: triazole, triazole lactic acid, triazole acetic acid, and triazole alanine.

### Measured Residues

Metabolite	Maximum (mean of two values)							
	Sandy Loam Soil at 10°C		Clay Loam Soil at 10°C		Loamy Sand Soil at 22°C		Loamy Sand Soil at 10°C	
	% App.	Day	% App.	Day	% App.	Day	% App.	Day
RPA 406341	10.5	363	16.1	306	14.8	56	9.2	363
RPA 406780	≤7.4	7-363	13.9	28	8.4	56	8.2	56
RPA 404886	≤2.1	7-363	≤6.06	56-363	≤6.2	56-363	≤6.5	56-363
RPA 407922	10.5	363	11.1	363	--	--	--	--
eight, nine, ten unidentified degradates*	≤4.2	56-363	≤6.06	56-363	≤6.2	56-363	≤6.5	56-363
Non-Extractable [ $^{14}\text{C}$ ]Residues	7.7	245	8.9	363	12.7	363	6.0	363
[ $^{14}\text{C}$ ]volatiles	3.14	363	4.1	363	11.0	363	1.7	363

\* maximum value for each unidentified degradate

## ABSTRACT

### Metabolism - Aerobic Soil

Phenyl ring-labeled [ $^{14}\text{C}$ ]triconazole (1RS-(E)-5-((4-chlorophenyl)methylene)-2,2-dimethyl-1-(1H-1,2,4-triazol-1-ylmethyl)-cyclopentan-1-ol; radiochemical purity >98%), at a nominal concentration of 1.6 ppm, was applied to sandy loam, clay loam, and loamy sand soils from the UK. The soils were adjusted to 75% of 0.33 bar moisture content and incubated in the dark at approximately 10°C for 363 days. The loamy sand soil was also treated at 2.6 ppm, moistened, and incubated at 22°C. Calculated, first-order half-lives for the soils incubated at 10°C ranged from 224 days in the clay loam soil to 691 days in the loamy sand soil. The calculated, first-order half-life for the UK loamy sand soil incubated at 22°C was 349 days. Aerobic degradation produced chemical species through hydroxylation of the unfragmented parent molecule, triconazole. However, unidentified bound residues could possibly include residues of toxicological concern.

**Sandy loam (10°C).** Phenyl ring-labeled [ $^{14}\text{C}$ ]triconazole (radiochemical purity >98%), at a nominal application rate of 1.64 ppm, degraded with a calculated mean half-life of 359 days ( $r^2 = 0.93$ ; 334 to 388 days at the 90 % confidence interval) in sandy loam soil adjusted to 75% of 0.33 bar moisture content and incubated in the dark at  $10 \pm 2^\circ\text{C}$  for up to 363 days. The triconazole was an average of 97.5-101.0% of the applied radiation at 0-1 day posttreatment, and decreased to 44.76% at 363 days. The degradate RPA 406341 (E-2-(4-chlorobenziliden)trans-1,3-dihydroxy-5,5-dimethyl-1-(1,2,4-triazol-1-ylmethyl)cyclopentan) was a maximum average of 10.5% at 306-363 days posttreatment. The degradate tentatively identified as RPA 407922 (Metabolite 6; (1RS)-E-2-(4-chloro-3-hydroxybenzilidene)-5,5-dimethyl-1-(1,2,4-triazol-1-yl-methyl)pentan-1-ol), was a maximum of 10.5% at 363 days. The degradates RPA 406780 (2-(4-chlorobenzilidene)-1,4-dihydroxy-5,5-dimethyl-1-(1,2,4-triazol-1-ylmethyl)cyclopentane) and RPA 404886 (erythro-2-(4-chlorobenzilidene)-5-methyl-5-hydroxymethyl-1-(1H-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol), were  $\leq 7.4\%$  and  $2.1\%$  of the applied radiation, respectively. Nine unidentified degradates (designated Metabolites 1, 2, and 7-13) were each  $\leq 4.7\%$  of the applied radiation.

**Clay loam (10°C).** Phenyl ring-labeled [ $^{14}\text{C}$ ]triconazole (radiochemical purity >98%), at a nominal application rate of 1.64 ppm, degraded with a calculated mean half-life of 224 days ( $r^2 = 0.91$ ; 206 to 245 days at the 90 % confidence interval) in clay loam soil adjusted to 75% of 0.33 bar moisture content and incubated in the dark at  $10 \pm 2^\circ\text{C}$  for up to 363 days. The triconazole was an average of 97.1% of the applied radiation immediately posttreatment, and decreased to 25.1% at 363 days. RPA 406341 was a maximum average of 16.1% at 306 days. RPA 406780 was a maximum of 13.9% at 28 days. RPA 407922 was a maximum of 11.1% at 363 days. RPA 404886 and nine uncharacterized degradates (Metabolites 1, 2, 7-13), were each  $\leq 6.1\%$  of the applied radiation.

**Loamy Sand (10°C).** Phenyl ring-labeled [U-<sup>14</sup>C]triconazole (radiochemical purity >98%), at a nominal application rate of 2.46 ppm, degraded with a calculated mean half-life of 691 days ( $r^2 = 0.72$ ; 591 to 832 days at the 90 % confidence interval) in loamy sand soil adjusted to 75% of 0.33 bar moisture content and incubated in the dark at  $10 \pm 2^\circ\text{C}$  for up to 363 days posttreatment. Triconazole was an average of 96.5-100.7% of the applied radiation at 0-1 day posttreatment, and was 62.2% at 363 days posttreatment. RPA 406341 and RPA 406780 were maximum averages of 9.2% and 8.2%, respectively, at 56 days. RPA 404886 and ten uncharacterized degradates (Metabolites 1, 2, and 6-13) were each at  $\leq 6.5\%$  of the applied radiation.

**Loamy Sand (22°C).** Phenyl ring-labeled [U-<sup>14</sup>C]triconazole (radiochemical purity >98%), at a nominal application rate of 2.46 ppm, degraded with a calculated mean half-life of 344 days ( $r^2 = 0.82$ ; 306 to 376 days at the 90 % confidence interval) in loamy sand soil adjusted to 75% of 0.33 bar moisture content and incubated in the dark at  $22 \pm 2^\circ\text{C}$  for up to 363 days posttreatment. Triconazole was an average of 91.5-96.3% of the applied radiation at 0-7 days posttreatment, and decreased to 42.9% at 363 days posttreatment. RPA 406341 and RPA 406780 were maximum averages of 14.8% of the applied radiation at 56 days posttreatment and 8.4% at 28 days, respectively. RPA 404886 and nine uncharacterized degradates (Metabolites 1 and 6-13), were each  $\leq 6.2\%$  of the applied radiation.

Unextracted [<sup>14</sup>C]residues were maximums of 5.0-8.9% and 11.33-12.68% of the applied radiation at 245-363 days posttreatment in soils incubated at 10°C and 22°C, respectively. Volatile radioactivity was 0.03-0.04% of the applied radiation at 1 day posttreatment and maximums of 1.43-4.06% and 11.03% at 363 days for the soils incubated at 10°C and 22°C, respectively.

## MATERIALS AND METHODS

Subsamples of moist, sieved (2 mm) UK sandy loam (73% sand, 13.5% silt, 13.5% clay, 1.43% organic matter content, pH 6.30, CEC 5.99 meq/100 g; Table 1, p.9); UK clay loam (47% sand, 32% silt, 21% clay, 5.65% organic matter content, pH 6.08, CEC 28.50 meq/100 g); and UK loamy sand (79% sand, 11.5% silt, 9.5% clay, 32.24% organic matter content, pH 6.24, CEC 51.12 meq/100 g) soils were weighed (75 g; 50 g for loamy sand) into glass dishes, moistened to 75% of 0.33 bar, and treated with phenyl ring-labeled [U-<sup>14</sup>C]triconazole (1RS-(E)-5-((4-chlorophenyl) methylene)-2,2-dimethyl-1-(1H-1,2,4-triazol-1-ylmethyl)-cyclopentan-1-ol; radiochemical purity >98%, specific activity 32 mCi/mMol, Commissariat a l'Energie Atomique, France; pp.8-9) plus non-radiolabeled triconazole (99.3% purity, p.8), dissolved in methanol, at a nominal application rate of 1.64 ppm (2.46 ppm for loamy sand; p.10). The dishes of treated soil were placed in closed glass chambers fitted with inlet and outlet ports. Humidified, carbon dioxide-free air was drawn through the chambers, then sequentially through trapping solutions of

ethylene glycol to collect organic volatiles and through 4 M potassium hydroxide to collect  $^{14}\text{CO}_2$  (p.10; diagram not presented). The samples were maintained in the dark at  $10 \pm 2^\circ\text{C}$  and  $22 \pm 2^\circ\text{C}$  (loamy sand only), and were weighed at regular intervals and remoistened as necessary to maintain 75% of 0.33 bar. Duplicate samples of each treated soil type were collected for analysis at 0, 1, 7, 14, 28, 56, 84, 112, 140, 168, 245, 306 and 363 days posttreatment; storage intervals and conditions were not specified. Volatile traps were collected for analysis and replaced at each sampling interval.

At each sampling interval, samples were Soxhlet-extracted with acetonitrile:water (4:1, v/v) for 3 hours, cooled, and measured or adjusted to volume (p.11). Aliquots of the extracts were analyzed for total radioactivity using LSC; the limit of quantitation was not reported. The remaining extracts were concentrated and analyzed by HPLC using the following operating conditions (pp.12):

Column	Partisil ODS3; 25 cm x 4.6 mm
Injection volume	Not specified
Detector	UV at 263 nm; radioactive flow monitor
Mobile phase	Acetonitrile:water:acetic acid (40:60:2, v/v/v) containing 0.1 M ammonium acetate
Flow rate	1.0 mL/minute

The samples were chromatographed and compared with reference standards of triticonazole, RPA 406780, RPA 404766, RPA 404886, and RPA 406341 (pp.12, 15; Figure AIII.1, p. 45). The extracted soil was air-dried, and triplicate subsamples were analyzed for total radioactivity by LSC following combustion (p.11). No further analyses were conducted on post-extracted solids. To confirm the identification of isolated compounds, [ $^{14}\text{C}$ ]residues in select soil sample extracts (not specified) were analyzed by LC/MS under the following operating conditions (pp.12, 64):

Positive ion thermospray mass spectroscopy	
Column	Spherisorb ODS 2; 25 cm x 4.6 mm
Injection volume	100 $\mu\text{L}$
Detector	UV at 263 nm
Mobile phase	Acetonitrile:water:acetic acid (50:50:2, v/v/v) containing 0.1 M ammonium acetate
Flow rate	1.0 mL/minute

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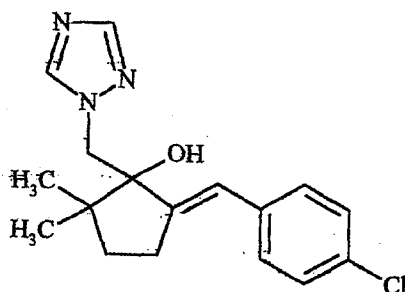
Aliquots of the ethylene glycol and 4 M potassium hydroxide trapping solutions were analyzed for total radioactivity by LSC (p.12).

Soils were analyzed (methods unspecified) prior to and after the study to confirm microbial viability (Table 1, p.9).

## RESULTS/DISCUSSION

Aerobic degradation produced chemical species through hydroxylation of the unfragmented parent molecule, triticonazole. However, unidentified bound residues could possibly include residues of toxicological concern. Degradates of potential concern are: triazole, triazole lactic acid, triazole acetic acid, and triazole alanine.

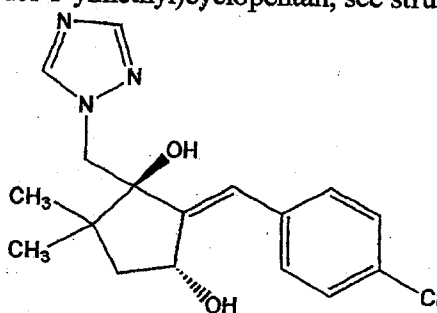
**Sandy loam soil (10°C).** Phenyl ring-labeled [U-<sup>14</sup>C]triticonazole ((1R,3E)-5-((4-chlorophenyl)methylene)-2,2-dimethyl-1-(1H-1,2,4-triazol-1-ylmethyl)-cyclopentan-1-ol; radiochemical purity >98%; see structure below), at a nominal application rate of



**Triticonazole**

1.64 ppm, degraded with a calculated mean half-life of 359 days ( $r^2 = 0.93$ ; 334 to 388 days at the 90 % confidence interval) in sandy loam soil adjusted to 75% of 0.33 bar moisture content and incubated in the dark at  $10 \pm 2^\circ\text{C}$  for up to 363 days (p.21; Figure AIV.7, p.57). Based on HPLC analysis, triticonazole was an average 97.51-100.99% of the applied radiation at 0 and 1 days posttreatment, and decreased to an average 44.76% at 363 days posttreatment (Table 7, p. 16).

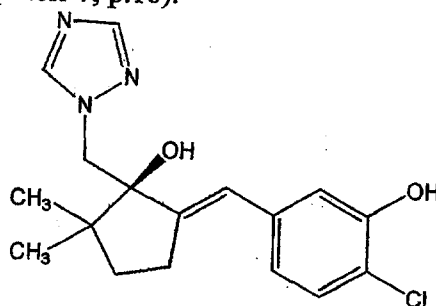
The degradate, **RPA 406341** (Metabolite 5; E-2-(4-chlorobenziliden)trans-1,3-dihydroxy-5,5-dimethyl-1-(1,2,4-triazol-1-ylmethyl)cyclopentan; see structure below), was initially



**RPA 406341**

detected (day 14) at an average 2.63% of the applied radiation, and increased to an average of 10.48-10.53% at 306 and 363 days posttreatment (Table 7, p.16).

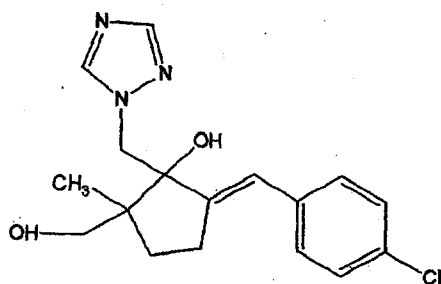
The degradate Metabolite 6, (tentatively identified as **RPA 407922**; (1R)-E-2-(4-chloro-3-hydroxybenzilidene)-5,5-dimethyl-1-(1,2,4-triazol-1-yl-methyl)pentan-1-ol; see structure below), was initially (day 56) detected at an average of 1.35% (0.02 ppm, reviewer calculated) of the applied radiation, and increased to a maximum of 10.49% (0.17 ppm) at 363 days posttreatment (Table 7, p.16).



**RPA 407922**

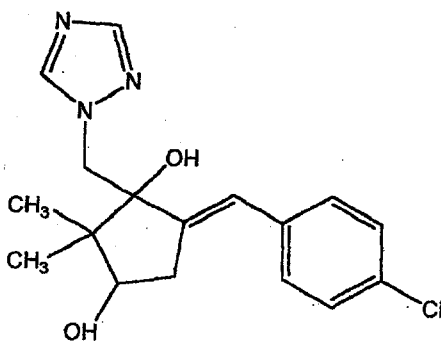
The degradates, **RPA 406780** (Metabolite 3; 2-(4-chlorobenzilidene)-1,4-dihydroxy-5,5-dimethyl-1-(1,2,4-triazol-1-ylmethyl)cyclopentane; see structure below) was present at an average of  $\leq 7.39\%$  of the applied radiation from 7 to 363 days posttreatment and





RPA 406780

RPA 404886 (Metabolite 4; erythro-2-(4-chlorobenzylidene)-5-methyl-5-hydroxymethyl-1-(1H-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol; see structure below), was present at an average of  $\leq 2.07\%$  of the applied radiation from 7 to 363 days posttreatment. Nine unidentified degradates (Metabolites 1, 2, and 7-13) each were an average  $\leq 4.71\%$  of the applied radiation (0.08 ppm) at 56-363 days posttreatment.



RPA 404886

Unextracted [ $^{14}\text{C}$ ]residues accounted for a maximum average of 7.74% of the applied radiation at 245 days posttreatment (Table 2, p.13), and were not further analyzed. Volatile radioactivity was an average of 0.04% of the applied radiation at 1 day posttreatment and a maximum of 3.14% at 363 days (Table 2, p.13). Material balances (based on LSC analysis of individual replicates) were 90.86-102.39% (mean 96.34%) of the applied radiation during the 363-day study (p.22).

**Clay loam (10°C).** Phenyl ring-labeled [ $^{14}\text{C}$ ]triticonazole (see structure above; radiochemical purity >98%), at a nominal application rate of 1.64 ppm, degraded with a calculated mean half-life of 224 days ( $r^2 = 0.91$ ; 206 to 245 days at the 90% confidence interval) in clay loam soil adjusted to 75% of 0.33 bar moisture content and incubated in the dark at  $10 \pm 2^\circ\text{C}$  for up to 363 days (p.21; Figure AIV.8, p.56). Based on HPLC analysis, triticonazole was an average of 97.06% of the applied radiation immediately

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posttreatment, 50.41% at 112 days and 25.13% at 363 days posttreatment (Table 8, p. 17).

The degradate, RPA 406341 (see structure above) was initially an average of 3.34% of the applied radiation at 7 days posttreatment, 8.65-13.42% at 28-245 days, a maximum of 16.13% at 306 days, and 12.94% at 363 days.

RPA 406780 (see structure above) was initially an average 2.36% of the applied radiation at 7 days posttreatment, a maximum of 13.94% at 28 days, and was 6.56-13.50% at 56-363 days with no pattern of decline (Table 8, p.17).

Metabolite 6, tentatively identified as RPA 407922, (see structure above) was initially an average 0.56% of the applied radiation at 84 days,  $\leq 3.72\%$  at 112-306 days, and was a maximum of 11.09% (0.18 ppm) at 363 days posttreatment (Table 8, p.17).

RPA 404886 (see structure above) and nine unidentified degradates (Metabolites 1, 2, 7-13), each accounted for an average  $\leq 6.06\%$  ( $\leq 0.10$  ppm) of the applied radiation at 56-363 days.

Unextracted [ $^{14}\text{C}$ ]residues were 7.65-8.86% (0.13-0.15 ppm) of the applied radiation at 168-363 days, and were not further analyzed (Table 3, p.13). Volatile radioactivity was an average 0.04% of the applied radiation at 1 day posttreatment and a maximum of 4.06% (0.07 ppm) at 363 days (Table 3, p.13). Material balances (based on LSC analysis of individual replicates) were 84.98-100.20% (mean 93.09%) of the applied radiation during the 363-day study (p.22).

**Loamy Sand (10°C).** Phenyl ring-labeled [ $^{14}\text{C}$ ]triticonazole (see structure above; radiochemical purity >98%), at a nominal application rate of 2.46 ppm, degraded with a calculated mean half-life of 691 days ( $r^2 = 0.72$ ; 591 to 832 days at the 90 % confidence interval) in loamy sand soil adjusted to 75% of 0.33 bar moisture content and incubated in the dark at  $10 \pm 2^\circ\text{C}$  for up to 363 days (p.21; Figure AIV.9, p.59). However, the half-life may be of questionable validity because it was calculated beyond the scope of the observed data. Based on HPLC analysis, triticonazole was an average 96.47-100.68% of the applied radiation at 0 and 1 day posttreatment, and 62.18% at 363 days (Table 9, p. 18).

The degradate, RPA 406341 (see structure above) was initially detected at 1.26% of the applied radiation at 7 days posttreatment, and was an average 3.66-9.15% at 28-363 days with no pattern of decline (Table 9, p.18).

**RPA 406780** (see structure above) was initially detected at 1.05% of the applied radiation at 7 days posttreatment, a maximum average of 8.20% at 56 days, and an average 2.57-5.66% at 168-363 days posttreatment.

**RPA 404886** (see structure above) and ten unidentified degradates (designated Metabolites 1, 2, and 6-13) were each present at  $\leq 6.49\%$  ( $\leq 0.16$  ppm) of the applied radiation at 56-363 days.

Unextracted [ $^{14}\text{C}$ ]residues were a maximum average of 5.97% (0.15 ppm) of the applied radiation at 363 days posttreatment (Table 4, p.14), and were not further analyzed. Volatile radioactivity was an average 0.03% of the applied radiation at 1 day posttreatment and a maximum of 1.67% (0.04 ppm) at 363 days (Table 4, p.14). Material balances (based on LSC analysis of individual replicates) were 88.95-101.64% (mean 95.77%) of the applied radiation during the 363-day study (p.22).

**Loamy Sand (22°C).** Phenyl ring-labeled [ $\text{U-}^{14}\text{C}$ ]triconazole (see structure above; radiochemical purity  $>98\%$ ), at a nominal application rate of 2.46 ppm, degraded with a calculated mean half-life of 344 days ( $r^2 = 0.82$ ; 306 to 376 days at the 90 % confidence interval) in loamy sand soil adjusted to 75% of 0.33 bar moisture content and incubated in the dark at  $22 \pm 2^\circ\text{C}$  for up to 363 days (p.21; Figure AIV.11, p.61). Based on HPLC analysis, triconazole was an average 91.50-96.26% of the applied radiation at 0-7 days posttreatment, and decreased to 42.91% (1.06 ppm) at 363 days (Table 11, p. 20).

The degradate, **RPA 406341** (see structure above) was initially (day 7) detected at 0.65% of the applied radiation, was a maximum average of 14.76% at 56 days, an average 8.15-8.57% at 84-168 days, and was 7.23% at 363 days (Table 11, p.20).

**RPA 406780** (see structure above) was initially (day 7) detected at 1.15% of the applied radiation, increased to an average 7.39-8.39% at 14-56 days posttreatment, 2.42-5.01% at 84-306 days, and 3.24% at 363 days.

**RPA 404886** (see structure above) and nine unidentified degradates (Metabolites 1 and 6-13) were each an average of  $\leq 6.20\%$  ( $\leq 0.15$  ppm) of the applied radiation at 56-363 days posttreatment.

Unextracted [ $^{14}\text{C}$ ]residues were an average 11.33-12.68% (0.28-0.31 ppm) of the applied radiation at 245-363 days posttreatment (Table 6, p.15), and were not further analyzed. Volatile radioactivity was an average of 0.04% of the applied radiation at 1 day posttreatment and maximum average of 11.03% (0.27 ppm) at 363 days (Table 6, p.15). Material balances (based on LSC analysis of individual replicates) were 88.72-98.55% (mean 93.80%) of the applied radiation during the 363-day study (p.22).

COMMENTS:

1. One study was conducted using the Speyer 2.2 loamy sand soil. However, artificial soils are not acceptable for meeting Subdivision N Guidelines, and the study is not reported in this study review.
2. A sample history detailing the storage intervals and conditions for soil samples was not provided. The study was conducted over 16 months based on the reported start and completion dates (2/28/92 and 6/28/93, respectively). Storage stability studies are required for samples stored longer than 30 days prior to analysis. It is preferable that a storage stability study for the maximum period samples were stored were submitted, but the absence of evidence that additional peaks were emerging along the chromatographic baselines (day 0 soil extract, p.44), would indicate that no significant degradation occur during sample storage. The registrant should be reminded that failure to provide this data could delay the acceptance of submitted studies.
3. The experimental temperature was  $10 \pm 2^\circ\text{C}$  during the incubation period for all soils except for the UK loamy sand which, in a separate experiment, was incubated at  $22 \pm 2^\circ\text{C}$ . Subdivision N Guidelines require that the experimental temperature be held constant ( $\pm 1^\circ\text{C}$ ) between  $18^\circ\text{C}$  and  $30^\circ\text{C}$ .
4. The temperature of the loamy sand test system ( $22^\circ\text{C}$  study) increased to  $30 \pm 2^\circ\text{C}$  for 4 days (posttreatment interval not specified) during the study (p.10). The study authors stated that this deviation did not affect the integrity of the study.
5. The major degradates, RPA 406341 and RPA 406780, were tentatively identified using HPLC analysis by comparison of retention times with authentic reference standards, and the chemical structure of Metabolite 6 was partially elucidated by LC/MS. Only the identity of parent compound was confirmed by HPLC and LC/MS (p.7). The study authors stated that LC/MS analyses indicated that "the majority of the metabolites are probably hydroxylated derivatives of RPA 400727 (parent) having molecular weights of 333 and 349 (p.23). Additional work on the metabolites is reported in a later study, under concurrent review by the Agency (MRID 448021-24), in which Metabolite 6 was identified as RPA 407922 ((1RS)-E-2-(4-chloro-3-hydroxybenzilidene)-5,5-dimethyl-1-(1,2,4-triazol-1-yl-methyl)pentan-1-ol).
6. The identity of the volatile components were not determined. The study authors stated that in another triticonazole aerobic soil metabolism study under concurrent review by the Agency (MRID 448021-24), the identity of the volatile was shown to be  $^{14}\text{CO}_2$  (p.22). Volatile radioactivity reached maximum averages of  $\leq 4.1\%$  ( $\leq 0.07$  ppm) and  $11.0\%$  (0.27 ppm) at 363 days for the soils incubated at  $10^\circ\text{C}$  and  $22^\circ\text{C}$ , respectively.

7. Limits of quantitation and detection were not reported for HPLC and LSC analysis. It is necessary that both limits of quantitation and detection be reported to allow the reviewer to evaluate the adequacy of the test method for the determination of the parent compound and its degradates.
8. The study authors stated that the nominal application rate was 360 g ai/ha, equivalent to a seed treatment rate of 200 g ai/100 kg seed, at a seeding rate of 180 kg/ha (p.7). The maximum label rate was not reported.
9. The soil series names were not reported. The soils tested were described as three agricultural soils (UK sandy loam, UK clay loam, and UK high O.M. loamy sand) and the "standard soil" Speyer 2.2 (p.9). Soils were not classified according to the USDA Soil Classification System.
10. The study author calculated half-lives for each of the two replicates for each soil type and presented a mean half-life. The individual half-lives for each soil type were in good agreement.
11. The degradation of parent compound was limited in the Speyer 2.2 loamy sand and UK loamy sand (10°C), for which the respective registrant-calculated mean half-lives were 799 ( $r^2 = 0.58$  and  $0.60$ ) and 707 days ( $r^2 = 0.66$  and  $0.78$ ). These half-lives may be of questionable validity because they were determined beyond the scope of the observed data (363 days). Data which appear linear may become curvilinear over time.
12. The proposed metabolic pathway for triticonazole in soil is shown in Figure 1, p.24.
13. The study was conducted according to UK Principles of Good Laboratory Practice and Food Laboratory Practice in the Testing of Chemicals (OECD, Paris). A Quality Assurance Statement and a Statement of No Data Confidentiality were provided.
14. The data presented in Tables 1-11 are averages of duplicate samples calculated by the study author. Data from the individual samples are not reported except when a degradate was detected in only one sample.
15. In MRID 448021-24, phenyl ring-labeled [U- $^{14}$ C]triticonazole, at a nominal application rate of 1.70 ppm, degraded with a calculated half-life of 302 days ( $r^2 = 0.89$ ) in sandy loam soil adjusted to 75% of 0.33 bar moisture content and incubated in the dark at  $22 \pm 2^\circ\text{C}$  for up to 363 days. Triticonazole was an average of 88.2-90.0% of the applied radiation at 0-14 days posttreatment, 46.9% at 224 days, and 44.65% at 363 days. RPA 406341 was a maximum average of 10.6% of the applied radiation at 56 days. RPA 406780, RPA 404886, RPA 407922, and six unidentified degradates (designated Metabolites 4, 5, 7, 8, 10, and 11), were each  $\leq 7.8\%$  of the applied radiation throughout the study period. At 363 days, unextracted [ $^{14}$ C]residues,  $^{14}\text{CO}_2$ , and [ $^{14}$ C]volatiles had reached maximums of 15.8%, 12.2%, and 0.4% of the applied radiation, respectively.

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ATTACHMENT 1  
Data Critical to the Study Interpretation

THE FOLLOWING ATTACHMENT IS NOT AVAILABLE ELECTRONICALLY  
SEE THE FILE COPY

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Page \_\_\_\_\_ is not included in this copy.

Pages 14 through 21 are not included in this copy.

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The material not included contains the following type of information:

- Identity of product inert ingredients.
- Identity of product impurities.
- Description of the product manufacturing process.
- Description of quality control procedures.
- Identity of the source of product ingredients.
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**ATTACHMENT 2**  
**Excel Workbook**

*Handwritten initials*

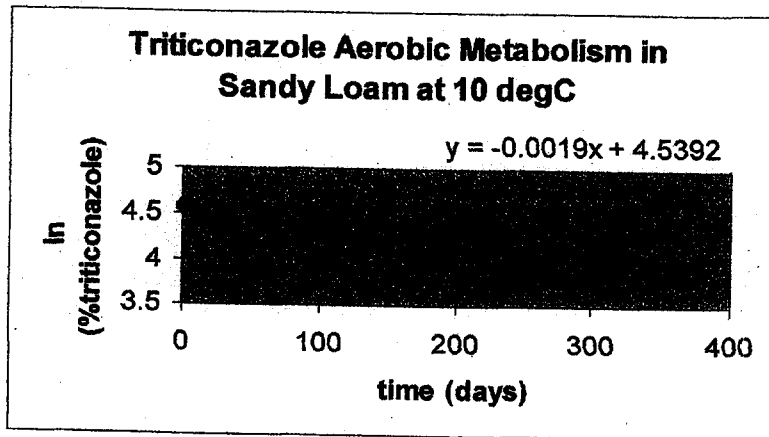


Triticonazole

in sandy loam soil under 10 degC  
aerobic conditions

% triticonazole	time (days)	ln(% triticonazole)
98.1	0	4.585997
97.01	0	4.574814
100.14	1	4.606569
101.84	1	4.623403
97.37	7	4.578518
96.32	7	4.567676
85.94	14	4.453649
91.77	14	4.519285
80.47	28	4.387884
85.05	28	4.443239
81.89	56	4.405377
80.72	56	4.390986
75.13	84	4.31922
80.05	84	4.382651
71.67	112	4.272072
68.64	112	4.228875
77.56	140	4.351052
71.43	140	4.268718
67.93	168	4.218478
66.45	168	4.19645
55.52	245	4.016743
54.54	245	3.998934
58.71	306	4.07261
58.42	306	4.067658
46.14	363	3.83168
43.38	363	3.769999

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SUMMARY OUTPUT

student's t = 1.318

<i>Regression Statistics</i>	
Multiple R	0.984267297
R Square	0.92981142
Adjusted R Square	0.926886896
Standard Error	0.064690516
Observations	26

ANOVA

	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>
Regression	1	1.330518432	1.330518	317.936	2.38264E-15
Residual	24	0.100436709	0.004185		
Total	25	1.430955141			

	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>
Intercept	4.53919586	0.017949448	252.8878	1.25E-42	4.502149827
X Variable 1	-0.001931285	0.000108312	-17.8308	2.38E-15	-0.00215483

	<i>Upper 95%</i>	<i>Lower 95.0%</i>	<i>Upper 95.0%</i>
	4.576241	4.502149827	4.57624149
	-0.00171	-0.00215483	-0.0017077

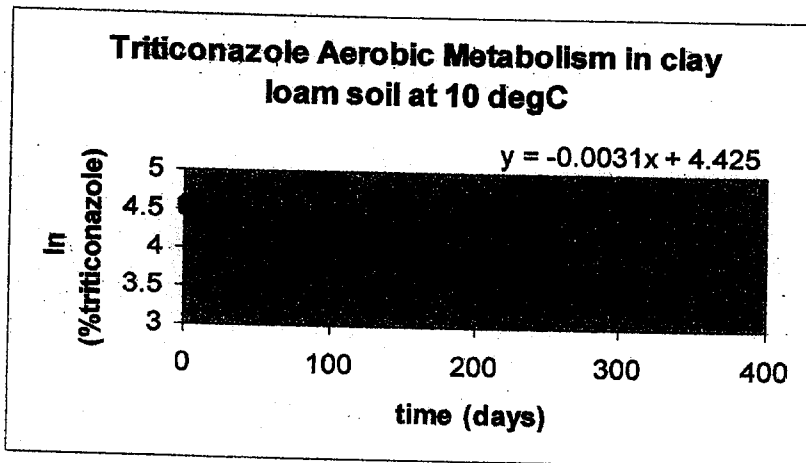
24

Triticonazole

in clay loam soil under 10 degC  
aerobic conditions

% triticonazole	time (days)	ln(% triticonazole)
94.53	0	4.548917
99.59	0	4.601062
96.1	1	4.565389
86.92	1	4.464988
88.59	7	4.464019
83.55	7	4.425445
80.14	14	4.383775
83.26	14	4.421968
64.88	28	4.172539
68.49	28	4.226688
63.1	56	4.144721
62.85	56	4.140751
66.45	84	4.19645
53.22	84	3.974434
49.22	112	3.8963
51.59	112	3.943328
56.82	140	4.039888
63.88	140	4.157006
49.89	168	3.909821
43.69	168	3.777119
46.15	245	3.831897
39	245	3.663562
38.25	306	3.644144
35.19	306	3.560762
24.5	363	3.199073
25.78	363	3.249599

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SUMMARY OUTPUT

student's t = 1.318

Regression Statistics	
Multiple R	0.952236294
R Square	0.906753959
Adjusted R Square	0.902868707
Standard Error	0.12091649
Observations	26

ANOVA

	df	SS	MS	F	Significance F
Regression	1	3.412254125	3.412254	233.3836	7.285E-14
Residual	24	0.350899144	0.014621		
Total	25	3.763153269			

	Coefficients	Standard Error	t Stat	P-value	Lower 95%
Intercept	4.425007807	0.033550271	131.8919	7.55E-36	4.355763466
X Variable 1	-0.003092834	0.000202452	-15.2769	7.28E-14	-0.00351067

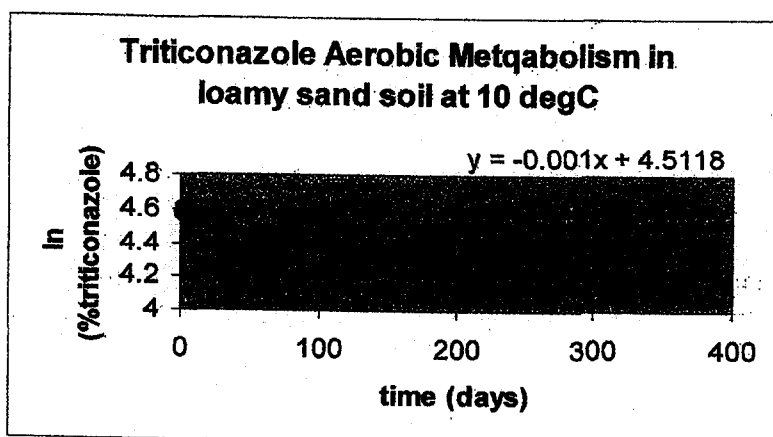
	Upper 95%	Lower 95.0%	Upper 95.0%
	4.494252	4.355763466	4.49425215
	-0.00267	-0.00351067	-0.002675

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Triticonazole

in loamy sand soil  
under 10 degC aerobic  
conditions

% triticonazole	time (days)	ln(% triticonazo le)
96.69	0	4.57151
96.26	0	4.567053
100.42	1	4.609361
100.94	1	4.614526
92.48	7	4.526992
95.92	7	4.563515
92	14	4.521789
96.81	14	4.57275
80.18	28	4.384274
83.42	28	4.423888
74.14	56	4.305955
74.65	56	4.312811
82.27	84	4.410007
83.07	84	4.419684
75.04	112	4.318021
72.94	112	4.289637
83.38	140	4.423408
82.65	140	4.414615
76.09	168	4.331917
74.13	168	4.30582
71.14	245	4.26465
70.3	245	4.252772
75.83	306	4.328494
70.8	306	4.259859
65.1	363	4.175925
59.27	363	4.082103



SUMMARY OUTPUT

student's t = 1.318

<i>Regression Statistics</i>	
Multiple R	0.846126489
R Square	0.715930035
Adjusted R Square	0.704093787
Standard Error	0.076990931
Observations	26

ANOVA

	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>
Regression	1	0.358538375	0.358538	60.48623	5.18287E-08
Residual	24	0.142262482	0.005928		
Total	25	0.500800857			

	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>
Intercept	4.511811221	0.021362401	211.2034	9.43E-41	4.467721402
X Variable 1	-0.001002545	0.000128907	-7.77729	5.18E-08	-0.00126859

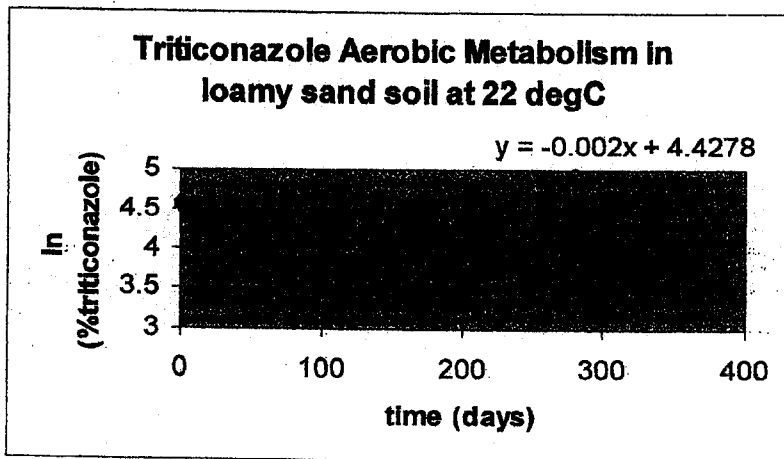
	<i>Upper 95%</i>	<i>Lower 95.0%</i>	<i>Upper 95.0%</i>
	4.555901	4.467721402	4.55590104
	-0.00074	-0.00126859	-0.0007365

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Triticonazole

in loamy sand soil under 22 degC  
aerobic conditions

% triticonazole	time (days)	ln(% triticonazole)
98.07	0	4.585682
94.44	0	4.547965
93.16	1	4.534318
96.54	1	4.569957
90.94	7	4.5102
92.07	7	4.522549
82.44	14	4.412071
76.71	14	4.340032
70.87	28	4.260847
72.21	28	4.279579
63.95	56	4.158102
67.43	56	4.21109
67.13	84	4.206631
65.15	84	4.176892
61.64	112	4.121311
58.54	112	4.06971
65.63	140	4.184033
69.22	140	4.23729
56.54	168	4.034948
55.49	168	4.016203
46.06	245	3.829945
44.81	245	3.802431
57.51	306	4.051959
44.92	306	3.804883
45.94	363	3.827336
39.88	363	3.685875



SUMMARY OUTPUT

student's t = 1.318

<i>Regression Statistics</i>	
Multiple R	0.908108604
R Square	0.824661237
Adjusted R Square	0.817355455
Standard Error	0.113266683
Observations	26

ANOVA

	<i>df</i>	<i>SS</i>	<i>MS</i>	<i>F</i>	<i>Significance F</i>
Regression	1	1.448148999	1.448149	112.8779	1.4867E-10
Residual	24	0.307904196	0.012829		
Total	25	1.756053194			

	<i>Coefficients</i>	<i>Standard Error</i>	<i>t Stat</i>	<i>P-value</i>	<i>Lower 95%</i>
Intercept	4.427803816	0.031427706	140.8885	1.55E-36	4.362940233
X Variable 1	-0.002014849	0.000189644	-10.6244	1.49E-10	-0.00240625

	<i>Upper 95%</i>	<i>Lower 95.0%</i>	<i>Upper 95.0%</i>
	4.492667	4.362940233	4.4926674
	-0.00162	-0.00240625	-0.0016234



Triticonazole Degradates in sandy loam soil under 10 degC aerobic conditions

time (days)	RPA 406341 % parent	RPA 406780 % parent	RPA 404886 % parent	RPA 407922 % parent	Met #1	Met #2	Met #7	Met #8	Met #9	Met #10	Met #11	Met #12	Non-Extract. % parent	volatiles % parent
0													0.4	0
1													0.54	0.04
7		0.53											0.8	0.11
14	2.63	2.49											1.23	0.19
28	6.04	4.4											1.65	0.34
56	4.16	2.55	1.16	1.35			0.57	0.56			2.85		2.56	0.55
84	4.23	2.39	1.42				1.52				1.52	1.32	2.72	0.81
112	6.27	2.78	1.33			2.45	2.23	1.19			1.84	1.45	3.53	1.07
140	7.36	5.74		1.22									3.91	1.52
168	6.19	3.75	2.07	1.88		2.72	1.54	1.71		0.47	2.82		5.68	1.93
245	8.62	7.39		1.99		6.93		2.93		2.24			7.74	2.26
306	10.53	6.94		2.87		4.71	1.98						7.36	2.68
363	10.48	7.06		10.49	3.71	1.14	4.21			3.22		0.52	7	3.14

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Triticonazole Degradates in clay loam soil under 10 degC aerobic conditions

time (days)	RPA 406341 %parent	RPA 406780 %parent	RPA 404886 %parent	RPA 407922 %parent	Met #1	Met #2	Met #7	Met #8	Met #9	Met #10	Met #11	Met #12	Met #13	Non-Extract. % parent	volatiles % parent
0														0.61	0
1														1.41	0.04
7	3.34	2.36												1.08	0.11
14	6.78	6.87												1.08	0.22
28	13.02	13.94												1.76	0.4
56	12.24	13.5												1.82	0.69
84	8.65	6.58			0.78	0.56					2.7			5.41	1.08
112	10.33	8.54			1.67	1.8	1.96	1.73	2.4		1.14	0.98		4.11	1.41
140	13.25	11.41					0.82	2.34	2.86			2.46	0.24	5.49	1.84
168	13.23	8.57				1.91	1.08	5.01	3.36			1.4		8.26	2.26
245	13.42	9.94				3.72		3	2.09	4.4				8.86	2.69
306	16.13	12.57				2.2		5.28	2.23					7.66	3.88
363	12.94	8.1				11.09	2.26	3.63	6.06	1.68	1.18			8.83	4.06

23

Triticonazole Degradates in loamy sand soil under 10 degC aerobic conditions

time (days)	RPA 406341 %parent	RPA 406780 %parent	RPA 404886 %parent	RPA 407922 %parent	Met #1	Met #2	Met #7	Met #8	Met #9	Met #10	Met #11	Met #12	Non-Extract. %parent	volatiles %parent
0													0.49	0
1													0.62	0.08
7	1.26	1.05											1.17	0.08
14			6.64										0.89	0.15
28	6.44	8.2											1.29	0.24
56	9.15	2.51		0.3									1.49	0.39
84	4.12	2.8		0.75			0.9					1.97	2.39	0.52
112	4.51	0.88				0.57	0.19	1.28				3.26	2.79	0.69
140	5.06	2.57											3.31	0.88
168	3.66	3.58		3.09		2.06	0.64			1.08			4.54	1.01
245	7.09	3.88				2.33		1.46		1.52		1.33	5.16	1.28
306	8.44	5.66				1.45	0.88						4.98	1.48
363	9.09				0.71	6.49	1.88	1.21	2.53	2.45	0.44		5.97	1.67

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Triticonazole Degradates in loamy sand soil under 22 degC aerobic conditions

time (days)	RPA 406341 %parent	RPA 406780 %parent	RPA 404886 %parent	RPA 407922 %parent	Met #1	Met #7	Met #8	Met #9	Met #10	Met #11	Met #12	Met #13	Non-Extract. %parent	volatiles %parent
0													0.49	0.
1													0.78	0.04
7	0.65	1.15											1.09	0.15
14	6.8	7.39											1.58	0.25
28	9.45	8.39											2.13	0.47
56	14.78	7.83			1.22								3.67	1.05
84	8.57	3.12	1.49		1.52	0.3	2.11	1.48	0.1		3.01		4.56	2.25
112	8.42	2.88	1.55		1.25	1.32	2.98	1.38		1.71	1.77		5.62	3.41
140	8.15	5.01											7.26	4.5
168	8.43	2.67	0.73		3.17	1.15	3.21		1.66		2.21	0.82	9.4	5.64
245	4.91	3.51			4.25	4.04	5.31	4.31					12.68	7.85
306	7.77	2.42			2.4	4.83	0.75						11.63	9.4
363	7.23	3.24	0.68		3.54	6.2	3.93		0.53		1.08		11.33	11.03

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