(1-18-07)

Data Evaluation Report on the aerobic biotransformation of tetraconazole in soil

PMRA Submission Number {.....} EPA MRID Number 45851801

Data Requirement: PMRA Data Code:
EPA DP Barcode: D288649
OECD Data Point:
EPA Guideline: 162-1

Test material:
Common name: Tetraconazole.
Chemical name
IUPAC: (RS)-2-(2,4-Dichlorophenyl)-3-(1H-1,2,4-triazol-1-yl)propyl 1,1,2,2-tetrafluoroethyl ether (Reviewer's Comment No. 8).
CAS name: 1-[2-(2,4-Dichlorophenyl)-3-(1,1,2,2-tetrafluoroethoxy)propyl]-1H-1,2,4-triazole.
CAS No: 112281-77-3 (Reviewer's Comment No. 8).
Synonyms: (±)-2-(2,4-Dichlorophenyl)-3-(1H-1,2,4-triazol-1-yl)propyl 1,1,2,2-tetrafluoroethyl ether (Appendix A, p. 72; Reviewer's Comment No. 9.i).
SMILES string:

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Company Code:
Active Code:
Use Site Category:
EPA PC Code: 120603

CITATION: Scacchi, A. and G. Pizzingrilli. 1995. Aerobic soil degradation of ^{14}C-tetraconazole in three German standard soils. Unpublished study performed by Isagro Ricerca, Novara, Italy; sponsored by Isagro S.p.A., Milano, Italy; and submitted by Sipcam Agro USA, Inc., Roswell, Georgia (pp. 1, 3). Isagro Ricerca Report No.: R/ABT.95.01. Experiment initiation February 13, 1995, and completion June 16, 1995 (p. 8). Final report issued June 26, 1995.

EXECUTIVE SUMMARY:

The biotransformation of [triazole-U-^{14}C]-labeled (±)-2-(2,4-dichlorophenyl)-3-(1H-1,2,4-triazol-1-yl)propyl 1,1,2,2-tetrafluoroethyl ether (tetraconazole) was studied in sand (Speyer 2.1; pH 5.9, organic carbon 0.62%), loamy sand (Speyer 2.2; pH 5.6, organic carbon 2.32%) and sandy loam (Speyer 2.3; pH 6.4, organic carbon 1.22%) soils from Germany for 100 days under aerobic conditions in darkness at 20 ± 2°C and a soil moisture of 40% of maximum holding capacity. [^{14}C]Tetraconazole was applied at an application rate of 1.30 mg a.i./kg soil dry wt. (equivalent to 1.47 kg a.i./ha). This experiment was conducted in accordance with BBA Guidelines for the Official Testing of Plant Protectants (Part IV, 4-1, 1986) and in compliance with Italian Principles of GLP (1992). The test system consisted of 250-mL Erlenmeyer flasks containing treated moist soil (50 g dry wt.), with each flask sealed with an air-permeable stopper. Traps for the collection of CO_2 and volatile organics were not used. Duplicate flasks were collected after 0, 7, 15, 30, 50, 70 and 100 days of incubation. Soil samples were sequentially extracted with acetone, methanol:water (1:1, v:v) and methanol:0.1N HCl (1:1, v:v). Soil extracts and extracted soil were analyzed for total radioactivity using LSC. Extracts were combined, concentrated and analyzed for [^{14}C]tetraconazole by normal-phase TLC; [^{14}C]tetraconazole in the soil extracts was identified by comparison to labeled reference standard. Identification of parent test substance was confirmed using reverse-phase HPLC.

Test conditions specified in the study protocol and methods were reportedly maintained throughout the incubations; however, no supporting data were provided.

Overall recovery of radiolabeled material in all three soils averaged 98.44 ± 1.02% (range 96.46-100.41%, n = 42) of the applied, with no significant declines in material balances for any soil type. Recoveries averaged (n = 14) 98.92 ± 1.10% (range 96.46-100.41%) of the applied in the sand soil, 98.33 ± 0.87% (range 97.09-100.03%) in the loamy sand soil, and 98.05 ± 0.85% (range 96.78-99.36%) in the sandy loam soil. Tetraconazole only slightly degraded in the three soils during incubation comprising 86.71-93.21% of the applied at study termination (100 days). Minor unidentified [^{14}C]polar products were detected in all three soil types at <2% of the applied at any sampling interval. For all three soils, extractable [^{14}C]residues remained high comprising 96.40-98.18% of the applied at day 0 and 88.07-95.22% at 70-100 days, while nonextractable residues increased from 0.26-0.64% at day 0 to 2.35-8.92% at 70-100 days.

Results Synopsis:

Soil type: Sand (Speyer 2.1) from Germany.
Half-life (observed): >100 days.
Major transformation products: None.
Minor transformation products: Unidentified [^{14}C]polar compounds.

Soil type: Loamy sand (Speyer 2.2) from Germany.
Half-life (observed): >100 days.
Major transformation products: None.
Minor transformation products: Unidentified [^{14}C]polar compounds.

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Soil type: Sandy loam (Speyer 2.3) from Germany.
Half-life (observed): >100 days.
Major transformation products: None.
Minor transformation products: Unidentified [^{14}C]polar compounds.

Study Acceptability: This study, conducted with [triazole-U-^{14}C]tetraconazole, is classified supplemental. The study is scientifically valid, but cannot be used towards fulfillment of the aerobic soil metabolism guideline, Subdivision N Guideline §162-1, data requirements for tetraconazole because the study was conducted for an insufficient length of time.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was conducted in accordance with BBA Guidelines for the Official Testing of Plant Protectants (Part IV, 4-1, 1986; pp. 8, 23). The following deviations from USEPA Subdivision N Guideline §162-1 were noted.

The study was terminated after 100 days of incubation prior to establishment of the pattern of degradation of parent tetraconazole. Subdivision N guidelines requires that aerobic soil metabolism studies be conducted until either the pattern of degradation of the parent test compound and the patterns of formation and decline of all degradates are established, or for 1 year, whichever occurs first. This does not affect the validity of the study.

The three foreign test soils were not characterized according to the USDA textural classification system and, therefore, not determined to be comparable to possible target soils found in the U.S.A. This does not affect the validity of the study.

The soil moisture was maintained at 40% of field capacity, rather than at 75% of 1/3 bar. This does not affect the validity of the study.

The test compound was incompletely characterized. The following physico-chemical properties of tetraconazole should have been reported: UV absorption, dissociation constant (pK_a), octanol-water partition coefficient (K_{ow}/log K_{ow}) and stability at room temperature. This does not affect the validity of the study.

COMPLIANCE: This study was conducted in compliance with Italian Principles of GLP (1992, p. 3). Signed and dated Data Confidentiality,

GLP and Quality Assurance statements were provided (pp. 2-3, 5, Appendix E, pp. 100-103).

A. MATERIALS:

1. Test Material: [Triazole-U-^{14}C]-labeled (±)-2-(2,4-dichlorophenyl)-3-(1H-1,2,4-triazol-1-yl)propyl 1,1,2,2-tetrafluoroethyl ether (tetraconazole; p. 10; Appendix A, pp. 72, 75; Reviewer's Comment No. 9.i).

Chemical Structure: See DER Attachment 2.

Description: Technical; viscous liquid (pp. 10, 11).

Purity: Radiochemical purity: ≥95.6% (p. 10; Appendix B, pp. 80-82; Reviewer's Comment No. 9.ii).
Lot No.: 144 (p. 10).
Analytical purity: Not reported.
Specific activity: 136.63 µCi/mg (303,313 dpm/µg, 5.06 MBq/mg).
Location of radiolabel: Uniformly in the triazole ring.

Storage conditions of test chemical: At -20°C prior to use (p. 11).

Table 1: Physico-chemical properties of tetraconazole.

Parameter	Values	Comments
Molecular weight:	372.16 g/mol	
Chemical formula:	$C_{13}H_{11}Cl_2F_4N_3O$	
Water solubility:	159 mg/L	At 23°C.
Vapor pressure/volatility:	1.32×10^{-4} Pa	At 20°C.
UV absorption:	Not reported.	
pK_a:	Not reported.	
K_{ow}/log K_{ow}:	Not reported.	
Stability of compound at room temperature:	Not reported.	

Data obtained from p. 11 of the study report.

2. Soil Characteristics:

Table 2: Description of soil collection and storage.

Description	Speyer 2.1	Speyer 2.2	Speyer 2.3
Geographic location:	All three soils were supplied by the Agricultural Research Institute, Speyer, Germany, reportedly taken from their respective natural locations which were not specified.		
Pesticide use history at the collection site:	Not reported.		
Collection procedures:	Not reported.		
Sampling depth:	0- to 20-cm depth.		
Storage conditions:	At 4°C.		
Storage length:	Not reported.		
Preparation:	2-mm sieved.		

Data obtained from p. 12 of the study report.

Table 3: Properties of the soils.

Property	Speyer 2.1	Speyer 2.2	Speyer 2.3
Soil texture[1]:	Slightly humus sand.	Very humus loamy sand.	Slightly humus sandy loam.
% sand (2000-63 µm):	88.4	81.2	60.9
% silt (63-2 µm):	9.8	3.4	29.6
% clay (<2 µm):	1.9	5.5	9.5
pH in 0.01M $CaCl_2$:	5.9	5.6	6.4
Organic carbon (%)[2]:	0.62	2.32	1.22
CEC (meq/100 g soil):	5	10.9	1.2
Maximum water capacity (g/100 g soil):	31	48	39
Bulk density, disturbed (g/cm^3):	Not reported.		
Soil Taxonomic classification:	Not reported.		
Soil Mapping Unit:	Not reported.		

[1]Reviewer's Comment No. 3.
[2]Reviewer's Comment No. 9.iii.
Data obtained from p. 12; Tables 1-3, pp. 26-28; Appendix C, p. 83 of the study report.

B. EXPERIMENTAL CONDITIONS:

1. Preliminary experiments: None.

2. Experimental conditions:

Table 4: Study design.

Parameter		All three soils
Duration of the test:		100 days.
Soil condition (air dried/fresh):		Fresh, moist.
Soil (g/replicate):		50 g dry wt.
Nominal application rate:		1.26 mg a.i/kg; 1.42 kg a.i./ha.
Actual application rate:		1.30 mg a.i./kg; 1.47 kg a.i./ha.
Control conditions, if used:		No sterile controls were used.
No. of Replications:	Controls, if used:	No sterile controls were used.
	Treatments:	For each soil type, duplicate soil samples for each collection interval.
Test apparatus (Type/material/volume):		250-mL Erlenmeyer flasks.
Details of traps for CO_2 and organic volatiles, if any:		Volatiles traps were not used.
If no traps were used, is the system closed/open?		Each flask was sealed with an air-permeable stopper.
Identity and concentration of co-solvent:	Identity:	Acetonitrile.
	Final concentration:	*ca.* 0.7% [1 mL of acetonitrile:water (16.7:33.3, v:v) test solution in 50 g soil].
Test material application:	Volume of test solution used/treatment:	1 mL of 64.833 µg/mL test solution.
	Application method:	Applied dropwise to soil surface.
	Is the co-solvent evaporated?	Not reported.
Any indication of the test material adsorbing to the walls of the test apparatus?		Not reported.
Biomass (mg microbial C/100 g, CFU or other) of control soil:		Initial: / Final:
		No sterile controls were used.
Biomass (mg microbial C/100 g, CFU or other) of treated soil:		Initial: / Final:
		Reviewer's Comment No. 4.
Experimental conditions:	Temperature (°C):	20 ± 2°C; method of temperature maintenance not described.
	Moisture content: Moisture maintenance method:	40% of field capacity. Determined by differential weight weekly and adjusted with distilled water as needed.

Parameter		All three soils
	Continuous darkness (Yes/No):	Yes.
Other details, if any:		None.

Data obtained from pp. 12, 14-15, 20; Appendix A, p. 77 of the study report.

3. Aerobic conditions: The flasks containing the treated soil were reportedly sealed with air-permeable stoppers (p. 15). No determinations were made, such as redox potentials, to verify that aerobic conditions were maintained.

4. Supplementary experiments: None.

5. Sampling:

Table 5: Sampling details.

Criteria		All three soils
Sampling intervals:		0, 7, 15, 30, 50, 70 and 100 days.
Sampling method:	Controls:	No sterile controls were used.
	Treated:	Duplicate flasks were collected at each interval.
Method of collection of CO_2 and volatile organic compounds:		Volatiles were not trapped.
Sampling intervals/times for: Sterility check, if sterile controls are used: Moisture content: Redox potential/other:		 Sterile controls were not used. Weekly. Not reported.
Sample storage before analysis:		Not reported.
Other observations, if any:		None.

Data obtained from p. 15 of the study report.

C. ANALYTICAL METHODS:

Extraction/clean up/concentration methods: Soil samples were sequentially extracted with acetone, methanol:water (1:1, v:v) and finally methanol:0.1N HCl (1:1, v:v); extraction solvent volumes were 200 mL per extraction (p. 16; Figure 1, p. 40). Each extraction was done using a horizontal shaker for 60 minutes, then soil and extract were separated by centrifugation (13,000 x g, 20 minutes) and duplicate aliquots (1 mL x 2) were analyzed for total radioactivity by LSC (pp. 12, 16). Aliquots (20 mL) of each extract were combined, then concentrated to 2-4 mL using rotary evaporation under vacuum (pressure not specified). Aliquots of the concentrated extract were analyzed by LSC (10 µL x 2, p. 16), TLC (10-20 µL, p. 18) and HPLC (10 µL, p. 19).

Nonextractable residue determination: Extracted soil was air-dried, then aliquots (1-4 g x 4) were analyzed for total radioactivity by LSC following combustion (p. 16).

Volatile residue determination: Volatiles were not collected.

Total ^{14}C measurement: Total ^{14}C residues were determined by summing the concentrations of residues measured in the soil extracts and extracted soil (p. 20).

Derivatization method, if used: A derivatization method was not employed.

Identification and quantification of parent compound: Soil extracts (10-20 µL) were analyzed using one-dimensional TLC on silica gel plates (Merck Kieselgel 60, F254, 0.25 mm) developed with ethyl acetate (solvent system 1, p. 18). Following development, areas of radioactivity were detected and quantified using a RITA 3200 TLC-Radioscanner at 1,450 V for 30 minutes. [^{14}C]Tetraconazole was identified by comparison to [^{14}C]tetraconazole reference standard (Figures 5-25, pp. 44-64).

Additionally, 0- and 100-day extracts were analyzed by reverse-phase HPLC under the following conditions: Supelcosil LC-18 column (4.6 x 250 mm, 5 µm), isocratic mobile phase of acetonitrile:water (80:20, v:v), injection volume 10 µL, flow rate 1 mL/minute, Ramona 5 radioactivity detector (p. 19; Figures 26-27, pp. 65-66). [^{14}C]Tetraconazole was identified by comparison to [^{14}C]tetraconazole reference standard (Figures 26-27, pp. 65-66).

Identification and quantification of transformation products: No transformation products of [triazole-U-^{14}C]tetraconazole were detected.

Detection limits (LOD, LOQ) for the parent compound and transformation products: The limit of detection (LOD) for LSC analyses were determined as 0.057% of the applied for soil extracts and 0.06% for nonextractable [^{14}C]residues (p. 18).

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS: It was reported that aerobicity, moisture, temperature and other environmental conditions were maintained throughout the study (pp. 7, 22); however, no supporting records were provided.

B. MATERIAL BALANCE: Overall recovery of radiolabeled material in all three soils averaged 98.44 ± 1.02% (range 96.46-100.41%, n = 42) of the applied, with no significant declines in material balances for any sample set (Attachment 1). For each soil type, recoveries averaged (n = 14) 98.92 ± 1.10% (range 96.46-100.41%) of the applied in the Speyer 2.1 sand, 98.33 ± 0.87% (range 97.09-100.03%) in the Speyer 2.2 loamy sand, and 98.05 ± 0.85% (range 96.78-99.36%) in the Speyer 2.3 sandy loam (Tables 4-6, pp. 29-31; Attachment 1; Reviewer's Comment No. 2).

Table 6: Biotransformation of [triazole-U-^{14}C]tetraconazole, expressed as percentage of applied radioactivity (mean ± s.d.[1], n = 2), in German Speyer 2.1 sand soil under aerobic conditions.

Compound	Sampling times (days)						
	0	7	15	30	50	70	100
Tetraconazole	96.11 ± 0.50	95.20 ± 0.50	96.82 ± 1.00	93.22 ± 0.30	97.01 ± 0.17	88.45 ± 0.11	89.77 ± 3.06
[^{14}C]Polar compounds	1.65 ± 0.07	1.28 ± 0.14	1.53 ± 0.21	1.03 ± 0.62	1.66 ± 0.10	1.38 ± 0.28	1.50 ± 0.13
Total extractable residues	97.75 ± 0.43	96.48 ± 0.35	98.35 ± 0.79	94.25 ± 0.32	98.66 ± 0.07	89.83 ± 0.16	91.26 ± 3.19
CO_2	–[2]	--	--	--	--	--	--
Total volatile organics	--	--	--	--	--	--	--
Nonextractable residues	0.26 ± 0.00	2.42 ± 0.20	1.36 ± 0.35	5.12 ± 0.14	1.63 ± 0.18	8.17 ± 0.34	6.92 ± 1.47
Total % recovery	98.01 ± 0.42	98.90 ± 0.16	99.71 ± 0.44	99.37 ± 0.46	100.29 ± 0.12	98.00 ± 0.17	98.18 ± 1.72

[1]Means as reported by study authors, but standard deviations re-calculated by primary reviewer (Reviewer's Comment No. 2).
[2]Volatiles were not trapped.
Data obtained from Table 4, p. 29; Table 10, p. 35 of the study report.

Table 7: Biotransformation of [triazole-U-^{14}C]tetraconazole, expressed as percentage of applied radioactivity (mean ± s.d.[1], n = 2), in German Speyer 2.2 loamy sand soil under aerobic conditions.

Compound	Sampling times (days)						
	0	7	15	30	50	70	100
Tetraconazole	96.60 ± 0.79	95.57 ± 0.09	97.18 ± 0.10	95.36 ± 0.60	96.64 ± 0.25	93.73 ± 0.21	92.47 ± 0.74
[^{14}C]Polar compounds	0.53 ± 0.52	1.52 ± 0.32	0.34 ± 0.01	0.78 ± 0.44	1.38 ± 0.08	1.33 ± 0.05	1.18 ± 0.16
Total extractable residues	97.13 ± 0.28	97.09 ± 0.41	97.52 ± 0.10	96.14 ± 0.16	98.02 ± 0.17	95.06 ± 0.16	93.65 ± 0.58
CO_2	–[2]	--	--	--	--	--	--
Total volatile organics	--	--	--	--	--	--	--
Nonextractable residues	0.52 ± 0.08	2.47 ± 0.06	1.25 ± 0.27	1.11 ± 0.01	0.83 ± 0.08	2.37 ± 0.03	5.12 ± 0.21
Total % recovery	97.65 ± 0.36	99.56 ± 0.47	98.77 ± 0.37	97.25 ± 0.16	98.85 ± 0.09	97.43 ± 0.13	98.77 ± 0.38

[1]Means as reported by study authors, but standard deviations re-calculated by primary reviewer (Reviewer's Comment No. 2).
[2]Volatiles were not trapped.
Data obtained from Table 5, p. 30; Table 11, p. 36 of the study report.

Table 8: Biotransformation of [triazole-U-^{14}C]tetraconazole, expressed as percentage of applied radioactivity (mean ± s.d.[1], n = 2), in German Speyer 2.3 sandy loam soil under aerobic conditions.

Compound	Sampling times (days)						
	0	7	15	30	50	70	100
Tetraconazole	95.56 ± 0.45	93.48 ± 0.20	95.85 ± 0.35	93.46 ± 0.24	93.32 ± 0.45	88.83 ± 0.24	92.19 ± 0.24
[^{14}C]Polar compounds	1.32 ± 0.03	1.28 ± 0.04	1.07 ± 0.38	1.52 ± 0.01	1.46 ± 0.05	1.30 ± 0.07	1.56 ± 0.01
Total extractable residues	96.88 ± 0.48	94.76 ± 0.24	96.92 ± 0.02	94.98 ± 0.25	94.78 ± 0.50	90.13 ± 0.31	93.75 ± 0.25
CO_2	–[2]	--	--	--	--	--	--
Total volatile organics	--	--	--	--	--	--	--
Nonextractable residues	0.61 ± 0.03	4.01 ± 0.07	1.89 ± 0.05	2.21 ± 0.11	2.43 ± 0.06	8.06 ± 0.87	4.95 ± 0.41
Total % recovery	97.49 ± 0.46	98.77 ± 0.17	98.81 ± 0.02	97.19 ± 0.15	97.21 ± 0.15	98.19 ± 1.17	98.70 ± 0.17

[1]Means as reported by study authors, but standard deviations re-calculated by primary reviewer (Reviewer's Comment No. 2).
[2]Volatiles were not trapped.
Data obtained from Table 6, p. 31; Table 12, p. 37 of the study report.

C. TRANSFORMATION OF PARENT COMPOUND: For all three soils, levels of [triazole-U-^{14}C]tetraconazole had only slightly decreased by the final (70- and 100-day) sampling intervals. In the German Speyer sand (2.1), loamy sand (2.2) and sandy loam (2.3) soils, [triazole-U-^{14}C]tetraconazole was detected at 95.61-96.61%, 95.81-97.40% and 95.11-96.01% of the applied, respectively, at day 0 posttreatment decreasing to 88.34-88.57%, 93.52-93.94% and 88.60-89.07%, respectively, at 70 days and was 86.71-92.82%, 91.73-93.21% and 91.96-92.43%, respectively at 100 days (Tables 10-12, pp. 35-37).

HALF-LIFE/DT50: Observed half-lives of [triazole-U-^{14}C]tetraconazole were >100 days in the German sand (2.1), loamy sand (2.2) and sandy loam (2.3) soils.

Table 9: Half-life ($t_{1/2}$) values of [triazole-U-^{14}C]tetraconazole in aerobic soil.

Soil type	First-order Linear		
	Half-life (days)	Regression equation	r^2
German 2.1 sand	>100 days		
German 2.2 loamy sand	>100 days		
German 2.3 sandy loam	>100 days		

TRANSFORMATION PRODUCTS: No major nonvolatile transformation products of [triazole-U-^{14}C]tetraconazole were detected. Minor unidentified [^{14}C]polar products were

detected in all three soil types at <2% of the applied at any sampling interval (Tables 10-12, pp. 35-37).

NONEXTRACTABLE AND EXTRACTABLE RESIDUES: In German sand (2.1) soil, extractable [^{14}C]residues were 97.33-98.18% of the applied at day 0, 93.93-98.73% at 7-50 days and 88.07-94.45% at 70-100 days, while nonextractable residues increased from 0.26% at day 0 to 7.83-8.50% at 70 days and were 5.44-8.39% at 100 days (Table 4, p. 29).

In German loamy sand (2.2) soil, extractable [^{14}C]residues were 96.85-97.41% of the applied at day 0, 95.98-98.19% at 7-50 days and 93.07-94.24% at 100 days, while nonextractable residues increased from 0.44-0.60% at day 0 to 4.91-5.32% at 100 days (Table 5, p. 30).

In German sandy loam (2.3) soil, extractable [^{14}C]residues were 96.40-97.36% of the applied at day 0, 94.28-96.95% at 7-50 days and 89.83-94.00% at 70-100 days, while nonextractable residues increased from 0.59-0.64% at day 0 to 7.19-8.92% at 70 days and were 4.53-5.36% at 100 days (Table 6, p. 31).

VOLATILIZATION: Formation of volatilized ^{14}C]residues was not monitored.

TRANSFORMATION PATHWAY: Due to the lack of significant degradation, a transformation pathway was not proposed.

Table 10: Chemical names for identified transformation products of [triazole-^{14}C]-labeled tetraconazole in aerobic soil.

Applicant's code	CAS Number	Chemical Name(s)	Chemical formula	Molecular weight	SMILES string

D. SUPPLEMENTARY EXPERIMENT-RESULTS: None.

III. STUDY DEFICIENCIES: This study, conducted with [triazole-U-^{14}C]tetraconazole, provides supplemental information, but cannot be used towards fulfillment of the aerobic soil metabolism guideline, Subdivision N Guideline §162-1, data requirements for tetraconazole for the following reason:

1. The study was terminated after 100 days of incubation prior to establishment of the pattern of degradation of parent tetraconazole. Subdivision N guidelines requires that aerobic soil metabolism studies be conducted until either the pattern of degradation of the parent test compound and the patterns of formation and decline of all degradates are established, or for 1 year, whichever occurs first.

Additional deficiencies include the following:

2. The three foreign test soils were not characterized according to the USDA textural classification system and, therefore, not determined to be comparable to possible target soils found in the U.S.A.

3. Soil moisture was maintained at 40% of field capacity, rather than at 75% of 1/3 bar as required by Subdivision N guidelines.

4. The test compound was incompletely characterized. The following physico-chemical properties of tetraconazole should also be reported: UV absorption, dissociation constant (pK_a), octanol-water partition coefficient (K_{ow}/log K_{ow}) and stability at room temperature.

IV. REVIEWER'S COMMENTS:

1. This study was conducted using [triazole-U-^{14}C]-labeled tetraconazole. In the event that nonvolatile transformation products are formed during a longer incubation period (>100 days), a study investigating the aerobic soil metabolism of [phenyl-U-^{14}C]-labeled tetraconazole may be required.

2. The study authors calculated standard deviations using the "sample" standard deviation function equivalent to the "n-1 weighted" standard deviation which should only be used when data are taken from a sample of a population. The primary reviewer re-determined the standard deviations using the "population" standard deviation function which is used when data are taken from the entire population (Attachment 1).

3. Three foreign soils, German Speyer 2.1, 2.2 and 2.3, were used in this study and classified according to BBA soil classification guidelines. The test soils could not be classified according to USDA textural classifications because the particle size scale ranges differ from those used by the USDA soil classification system. According to BBA soil classification guidelines, particles in the range of 2.0-0.063 mm are categorized as sand, 0.063-0.002 mm as silt and <0.002 mm as clay.

   In addition, the textural analysis summation of the Speyer 2.2 soil was only 90.1% (2000-63 µm = 81.2%, 63-2 µm = 3.4% and <2 µm = 5.5%; Table 2, p. 27).

4. The study authors reported that the microbial biomass of the three test soils were determined prior to use and at study termination, but it was not specified whether the microbial biomass determinations were conducted using untreated or treated soils (p. 12; Appendix A, p. 75). The microbial biomass for the Speyer 2.1, 2.2 and 2.3 soils were reported as 7.44, 39.90 and 10.14 mg C/100 g soil, respectively, at study initiation and 41.58, 34.66 and 17.19 mg C/100 g soil, respectively, at study termination (Tables 1-3, pp. 26-28).

5. Storage conditions and intervals of the soil samples prior to extraction and of extracts prior to TLC and HPLC analyses were not specified.

6. Detection limits (LOD, LOQ) for the TLC and HPLC analyses were not specified.

7. The study authors reported that the treatment rate for this study was based on the recommended maximum field application rate for tetraconazole of 125 g a.i./ha (p. 15).

8. (RS)-2-(2,4-Dichlorophenyl)-3-(1H-1,2,4-triazol-1-yl)propyl 1,1,2,2-tetrafluoroethyl ether and 1-[2-(2,4-dichlorophenyl)-3-(1,1,2,2-tetrafluoroethoxy)propyl]-1H-1,2,4-triazole were identified as the IUPAC anc CAS names, respectively, of tetraconazole by the Compendium of Pesticide Common Names (http://www.hclrss.demon.co.uk/tetraconazole.html). CAS Reg. No. 112281-77-3 for tetraconazole was obtained from the USEPA/OPP Chemical Database (http://www.cdpr.ca.gov/cgi-bin/epa/chemidetriris.pl?pccode=120603).

9. The following typographical errors/discrepancies were noted in this study:

   i. In section 12. MATERIALS, 12.1 TEST SUBSTANCES (p. 11), the chemical name for tetraconazole was incorrectly reported as -2-(2,4-dichlorophenyl)-3-(1H-1,2,4-triazol-1-yl)-1-propyl 1,1,2,2-tetrafluoroethyl ether, with the correct chemical name, (±)-2-(2,4-dichlorophenyl)-3-(1H-1,2,4-triazol-1-yl)propyl 1,1,2,2-tetrafluoroethyl ether provided in Appendix A (p. 72).

   ii. In section 12. MATERIALS, 12.1 TEST SUBSTANCES (p. 10) and 14. RESULTS AND DISCUSSION, 14.1 CONCENTRATION AND RADIOCHEMICAL PURITY OF ^{14}C-TETRACONAZOLE IN TEST SOLUTION (p. 20), the study authors reported the radiochemical purity of the test substance as determined by TLC as 99.50%; however, the TLC chromatograms provided indicate determined radiochemical purities of 95.65-96.38% (%Total column; Appendix B, pp. 80-81).

   iii. In Tables 1-3 (pp. 26-28), the reported percent organic matter content of each soil is actually the percent organic carbon (Appendix C, p. 83).

V. REFERENCES:

1. U.S. Environmental Protection Agency. 1982. Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate, Section 162-1, Aerobic Soil Metabolism Studies. Office of Pesticide and Toxic Substances, Washington, DC. EPA 540/9-82-021.

2. U.S. Environmental Protection Agency. 1989. FIFRA Accelerated Reregistration, Phase 3 Technical Guidance. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 540/09-90-078.

3. U.S. Environmental Protection Agency. 1993. Pesticide Registration Rejection Rate Analysis - Environmental Fate. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 738-R-93-010.

Attachment 1

Quattro Pro Graphs and Spreadsheets

Aerobic Metabolism of [Triazole-U-^{14}C]Tetraconazole in Three German Soils.
MRID 45851801

Speyer 2.1 Sand Soil.

Determination of [^{14}C]residues means/standard deviations[1].

Day	Extracts			Nonextractable			Total		
	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.
0	97.33			0.26			97.59		
0	98.18	97.76	0.43	0.26	0.26	0.00	98.44	98.02	0.42
7	96.83			2.23			99.06		
7	96.13	96.48	0.35	2.62	2.43	0.20	98.75	98.91	0.16
15	99.14			1.01			100.15		
15	97.56	98.35	0.79	1.72	1.37	0.35	99.28	99.72	0.44
30	94.57			5.26			99.83		
30	93.93	94.25	0.32	4.98	5.12	0.14	98.91	99.37	0.46
50	98.60			1.81			100.41		
50	98.73	98.67	0.07	1.44	1.63	0.18	100.17	100.29	0.12
70	89.67			8.50			98.17		
70	90.00	89.84	0.16	7.83	8.17	0.34	97.83	98.00	0.17
100	88.07			8.39			96.46		
100	94.45	91.26	3.19	5.44	6.92	1.47	99.89	98.18	1.72

Determination of [^{14}C]Tetraconazole means/standard deviations[1].

Day	Tetraconazole			[^{14}C]Polars		
	% AR	Mean	s.d.	% AR	Mean	s.d.
0	95.61			1.72		
0	96.61	96.11	0.50	1.57	1.65	0.07
7	95.70			1.13		
7	94.71	95.21	0.50	1.42	1.28	0.14
15	97.82			1.32		
15	95.83	96.83	1.00	1.73	1.53	0.21
30	92.92			1.65		
30	93.52	93.22	0.30	0.41	1.03	0.62
50	96.84			1.76		
50	97.18	97.01	0.17	1.55	1.66	0.10
70	88.57			1.10		
70	88.34	88.46	0.11	1.66	1.38	0.28
100	86.71			1.36		
100	92.82	89.77	3.06	1.63	1.50	0.13

[1]Reviewer's Comment No. 2.
Results (% of applied radioactivity) from Table 4, p. 29; Table 10, p. 35 of the study report.
Means and standard deviations calculated using Corel Quattro Pro 8 program functions @avg(A1..A2) and @std (A1..A2).

Aerobic Metabolism of [Triazole-U-^{14}C]Tetraconazole in Three German Soils.
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Speyer 2.2 Loamy Sand Soil.

Determination of [^{14}C]residues means/standard deviations[1].

Day	Extracts			Nonextractable			Total		
	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.
0	97.41			0.60			98.01		
0	96.85	97.13	0.28	0.44	0.52	0.08	97.29	97.65	0.36
7	97.50			2.53			100.03		
7	96.69	97.10	0.41	2.41	2.47	0.06	99.10	99.57	0.47
15	97.63			1.52			99.15		
15	97.42	97.53	0.10	0.98	1.25	0.27	98.40	98.78	0.37
30	96.31			1.10			97.41		
30	95.98	96.15	0.16	1.11	1.11	0.01	97.09	97.25	0.16
50	97.85			0.91			98.76		
50	98.19	98.02	0.17	0.75	0.83	0.08	98.94	98.85	0.09
70	94.90			2.40			97.30		
70	95.22	95.06	0.16	2.35	2.38	0.03	97.57	97.44	0.13
100	93.07			5.32			98.39		
100	94.24	93.66	0.58	4.91	5.12	0.21	99.15	98.77	0.38

Determination of [^{14}C]Tetraconazole means/standard deviations[1].

Day	Tetraconazole			[^{14}C]Polars		
	% AR	Mean	s.d.	% AR	Mean	s.d.
0	97.40			0.01		
0	95.81	96.61	0.79	1.04	0.53	0.52
7	95.66			1.84		
7	95.49	95.58	0.09	1.20	1.52	0.32
15	97.28			0.35		
15	97.08	97.18	0.10	0.34	0.35	0.01
30	95.97			0.34		
30	94.76	95.37	0.60	1.22	0.78	0.44
50	96.39			1.46		
50	96.90	96.65	0.25	1.29	1.38	0.08
70	93.52			1.38		
70	93.94	93.73	0.21	1.28	1.33	0.05
100	91.73			1.34		
100	93.21	92.47	0.74	1.03	1.19	0.16

[1]Reviewer's Comment No. 2.
Results (% of applied radioactivity) from Table 5, p. 30; Table 11, p. 36 of the study report.
Means and standard deviations calculated using Corel Quattro Pro 8 program functions @avg(A1..A2) and @std (A1..A2).

Aerobic Metabolism of [Triazole-U-^{14}C]Tetraconazole in Three German Soils.
MRID 45851801

Speyer 2.3 Sandy Loam Soil.

Determination of [^{14}C]residues means/standard deviations[1].

Day	Extracts			Nonextractable			Total		
	% AR	Mean	s.d.	% AR	Mean	s.d.	% AR	Mean	s.d.
0	96.40			0.64			97.04		
0	97.36	96.88	0.48	0.59	0.62	0.03	97.95	97.50	0.46
7	94.52			4.08			98.60		
7	95.00	94.76	0.24	3.94	4.01	0.07	98.94	98.77	0.17
15	96.90			1.93			98.83		
15	96.95	96.93	0.02	1.84	1.89	0.05	98.79	98.81	0.02
30	95.24			2.10			97.34		
30	94.73	94.99	0.25	2.32	2.21	0.11	97.05	97.20	0.15
50	95.28			2.37			97.65		
50	94.28	94.78	0.50	2.50	2.44	0.06	96.78	97.22	0.43
70	89.83			7.19			97.02		
70	90.44	90.14	0.31	8.92	8.06	0.87	99.36	98.19	1.17
100	93.50			5.36			98.86		
100	94.00	93.75	0.25	4.53	4.95	0.41	98.53	98.70	0.17

Determination of [^{14}C]Tetraconazole means/standard deviations[1].

Day	Tetraconazole			[^{14}C]Polars		
	% AR	Mean	s.d.	% AR	Mean	s.d.
0	95.11			1.29		
0	96.01	95.56	0.45	1.35	1.32	0.03
7	93.28			1.24		
7	93.68	93.48	0.20	1.32	1.28	0.04
15	96.20			0.70		
15	95.50	95.85	0.35	1.45	1.08	0.38
30	93.71			1.53		
30	93.22	93.47	0.24	1.51	1.52	0.01
50	93.76			1.51		
50	92.87	93.32	0.45	1.41	1.46	0.05
70	88.60			1.23		
70	89.07	88.84	0.24	1.37	1.30	0.07
100	91.96			1.54		
100	92.43	92.20	0.24	1.57	1.56	0.01

[1]Reviewer's Comment No. 2.
Results (% of applied radioactivity) from Table 6, p. 31; Table 12, p. 37 of the study report.
Means and standard deviations calculated using Corel Quattro Pro 8 program functions @avg(A1..A2) and @std (A1..A2).

Aerobic Metabolism of [Triazole-U-^{14}C]Tetraconazole in Three German Soils.
MRID 45851801

Determination of overall [^{14}C]residues mean/standard deviation for all three soils.

	Total Recovery			
	Speyer 2.1	Speyer 2.2	Speyer 2.3	
Day	% AR	% AR	% AR	
0	97.59	98.01	97.04	
0	98.44	97.29	97.95	
7	99.06	100.03	98.60	
7	98.75	99.10	98.94	
15	100.15	99.15	98.83	
15	99.28	98.40	98.79	
30	99.83	97.41	97.34	
30	98.91	97.09	97.05	
50	100.41	98.76	97.65	
50	100.17	98.94	96.78	
70	98.17	97.30	97.02	
70	97.83	97.57	99.36	
100	96.46	98.39	98.86	
100	99.89	99.15	98.53	**All three soils:**
Mean	98.92	98.33	98.05	98.44
std. dev.	1.10	0.87	0.85	1.02
n =	14	14	14	42

Results (% of applied radioactivity) from Tables 4-6, pp. 29-31 of the study report.
Means and standard deviations calculated using Corel Quattro Pro 8 program functions @avg(A1..A2) and @std (A1..A2).

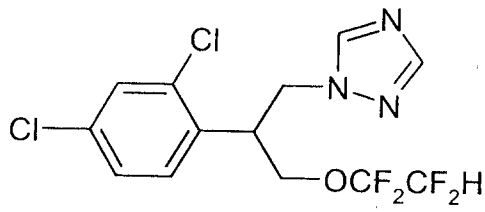
Attachment 2

Structures of Parent and Transformation Products

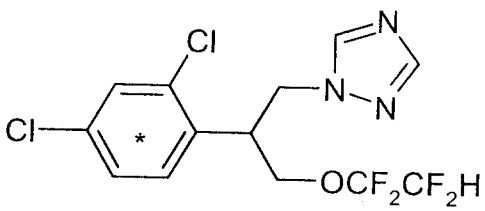
Tetraconazole

IUPAC name: (RS)-2-(2,4-Dichlorophenyl)-3-(1H-1,2,4-triazol-1-yl)propyl 1,1,2,2-tetrafluoroethyl ether
CAS name: 1-[2-(2,4-Dichlorophenyl)-3-(1,1,2,2-tetrafluoroethoxy)propyl]-1H-1,2,4-triazole.
CAS No: 112281-77-3

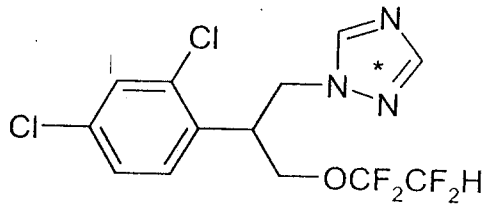
Unlabeled



[Phenyl-U-^{14}C] label



[Triazole-U-^{14}C]label



* Position of the radiolabel.