

(3-9-2006)

DATA EVALUATION RECORD

STUDY 6

PC No. 600074 Triazole
PC No. 128997 (degradate of Tebuconazole) §162-1
CAS No. 107534-96-3
DP Barcode D271910
FORMULATION-00-ACTIVE INGREDIENT

STUDY ID 45284027

Keller, A. 1984. Degradation of 1,2,4-triazole (CGA 71 019) in aerobic soil. Performing Laboratory ID 21/84. Bayer Report Number 110088. Unpublished study performed by Ciba-Geigy Limited, Basle, Switzerland; and submitted by Bayer Corporation, Kansas City, MO.

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CONCLUSIONS



Metabolism - Aerobic Soil

1. This study is scientifically valid and provides upgradable supplemental information on the aerobic soil metabolism of 1,2,3-triazole.

2. [3,5-¹⁴C]1,2,4-Triazole, at 1 ppm, degraded with a reviewer-calculated first order kinetics half-life ($t_{1/2}$) of 22 weeks (155 days; $r^2 = 0.96$) in silty loam soil that was moistened to 75% of the field capacity and incubated in the dark at 25°C for up to 168 days.
3. This study has a few deviations from the objectives of Subdivision N Guidelines requirements for aerobic soil metabolism for the following reasons:
 - A. confirmation analysis were not conducted to verify TLC results;
 - B. it is not sure whether the test soils were sieved;
 - C. dark control was not utilized;
 - D. only foreign soil was used; and
 - E. the soil was not classified according to the USDA Soil Classification System.

As the registrant submits the information concerning soil sieving, soil classification, and extraction efficiency data (percent spike recovery) the study may be upgraded to acceptable.

4. EFED notes that although this aerobic soil metabolism study does not fulfill Subdivision N Guidelines alone, there is sufficient information available from the other aerobic soil metabolism studies submitted by the registrant that support the results of this study. The registrant conducted four other aerobic soil metabolism studies with variety of experimental settings/conditions. All studies indicate that microbial degradation of 1,2,4-triazole appears to be rather slow process at higher application rates and faster at lower application rates. The half-lives ranged from 22 days to 375 days (Table 1). The aerobic soil metabolism degradation products were hydroxytriazole (3-hydroxy-1,2,4-triazole), triazolyl alanine (1,2,4-triazole-1-alanine), and triazolyl acetic acid (max. 18%; MRID 45297203 (Experiment II)), CO₂, and bound residues.

Table 1. Summary information of 1,2,4-Triazole aerobic soil metabolism study

Treatment Level	Soil type	Half-life ($T_{1/2}$) in days	Reference
ca. 0.06 ppm	German sandy loam	26.5	MRID 45284032
	German loamy sand	46.7	
	German silt loam	22.2	
50 ppm	Soil 2.2	343	MRID 45297203
	Soil 2.3	375	
1 ppm	Silty loam soil	155	MRID 45284027

Furthermore, it appears that 1,2,4-triazole residue may accumulate in crops after triazole application on the cropped soil. Total residues in the wheat plants were the maximum of 61.1-61.3% by 60-90 days after soil treatment with triazole (Experiment III, MRID 45297203). 1,2,4-Triazole was almost completely metabolized in 14 days via a bacteria culture, *Nocardia coralline* (MRID 45297203), and triazoly alanine was the principal metabolite isolated from the cultures.

ABSTRACT

[3,5-¹⁴C]1,2,4-Triazole, at 1 ppm, degraded with a reviewer-calculated first order kinetics half-life ($t_{1/2}$) of 22 weeks (155 days; $r^2 = 0.96$) in silty loam soil that was moistened to 75% of the field capacity and incubated in the dark at 25°C for up to 168 days. Based on TLC analysis, triazole was 78.7% of the applied at time 0, 65.2% (including 4.6% of bound residues) at 28 days, 52.5% (including 9.3% of bound residues) at 56 days, and 36.3% (including 6.7% of bound residues) at 168 days posttreatment. Unidentified degradates were a maximum of 8.9% of the applied at time 0. ¹⁴CO₂ totaled 1.9% of the applied at 168 days and organic [¹⁴C]volatiles were a maximum of 2.6% of the applied at 56 days posttreatment. Unextracted [¹⁴C]residues comprised 62.4% of the applied at 168 days posttreatment. Following further soil extraction with methanol/NaOH 0.1 N (4:1), an additional 10.6-17.1% of the applied radioactivity was extracted; 4.6-9.3% was identified as triazole and 1.5-5.8% were two unidentified degradates (unknown X and Z). Material balances ranged from 93.4 to 102.9% of the applied during the study.

MATERIALS AND METHODS

Samples of silty loam (16.5% sand, 75.1% silt, 8.4% clay, 1.3% organic carbon, pH 7.6, CEC 12.5 mmol/z/100 g; p. 5) soil from Les Barges, Switzerland, were weighed (200 g dry weight) into 1-L glass bottles equipped with inlet valves. The soil samples were thoroughly mixed, moistened to 75% of the field capacity, and treated with [3,5-¹⁴C]1,2,4-triazole (CGA 71 019; purity >97%, specific activity 65.4 μCi/mg, p. 4), dissolved in water, at a nominal rate of 1 ppm (p. 6). The treated samples were attached to a volatile trapping system and incubated in darkness at 25°C for up to 168 days posttreatment. Humidified, ambient air was drawn (60 mL/min) through the glass bottles, then sequentially through one bottle of ethylene glycol, one bottle containing 0.1 N sulfuric acid and two bottles containing 2 N NaOH (p. 5, Figure 1, p. 15). Soil moisture content was maintained by periodically weighing the soil samples and adding distilled water as needed (p. 6). Duplicate tubes of soil were removed for analysis at 0, 28, 56, 84, and 168 days posttreatment. The trapping solutions were collected and analyzed for total radioactivity every 2 weeks.

The soil samples were extracted five times with methanol:water (8:2, v:v) by strong agitation at room temperature (p. 7). The resulting sediment was Soxhlet-extracted with methanol for 6 hours. The methanol:water extracts were combined, concentrated, and partitioned with dichloromethane. The aqueous, organic, and methanol-Soxhlet soil extracts were analyzed by normal-phase one-dimensional TLC on silica gel plates developed in

chloroform:methanol:ammonia (50:50:5, v:v:v) or chloroform:methanol:formic acid:water (80:15:4:2, v:v:v:v), and by reverse-phase one-dimensional TLC on RP-18F plates developed in acetonitrile:water (1:1, v:v; p. 9). The samples were cochromatographed with an unlabeled reference standard of triazole that was visualized under UV light. Radioactive areas on the plates were located using a linear analyzer.

Unextracted [¹⁴C]residues were analyzed for total radioactivity by LSC following combustion (p. 8). A portion of the unextracted [¹⁴C]residues was extracted with methanol:0.1 N NaOH (4:1, v:v) in an ultrasonic bath at room temperature (pp. 7, 11). The resulting soil extracts were analyzed by normal- and reverse-phase TLC as described previously (pp. 8-9).

Aliquots of the ethylene glycol, sulfuric acid and NaOH trapping solutions were analyzed for total radioactivity using LSC (p. 9).

RESULTS/DISCUSSION

[3,5-¹⁴C]1,2,4-Triazole (purity >97%), at 1 ppm, degraded with a reviewer-calculated half-life of 22 weeks (the study author-calculated half-life of 14 weeks) in silty loam soil that was moistened to 75% of the field capacity and incubated in the dark at 25°C for up to 168 days. Based on TLC analysis, triazole was 78.7% of the applied at time 0, 65.2% at 28 days, 52.5% at 56 days, and 36.3% at 168 days posttreatment (summed data; Tables 1 and 2, pp. 13-14). Unidentified degradates ("Unknown metabolites") were a maximum of 8.9% of the applied at time 0. ¹⁴CO₂ totaled 1.9% of the applied at 168 days and organic [¹⁴C]volatiles were a maximum of 2.6% of the applied at 56 days posttreatment. Unextracted [¹⁴C]residues comprised 62.4% of the applied at 168 days posttreatment. Following Soxhlet and methanolic NaOH extractions of the unextracted soil, an additional 10.6-17.1% of the applied radioactivity was extracted; 4.6-9.3% was identified as triazole and 1.5-5.8% was two unidentified degradates (unknown metabolites X and Z; p. 11, Table 2, p.14). Material balances ranged from 93.4 to 102.9% of the applied during the study.

DEFICIENCIES/DEVIATIONS

1. No evidence was provided to demonstrate that the one-dimensional TLC system used in this study could adequately separate triazole and its degradates. No potential degradates were identified. Triazole was the only reference standard used on the plates.
2. Unextracted [¹⁴C]residues were extremely high following the methanol:water extraction, comprising 62.4% of the applied radioactivity at 168 days posttreatment. However, attempts were made to further extract the unextracted [¹⁴C]residues using Soxhlet and methanolic NaOH extractions. Following these extractions, an additional 10.6-17.1% of the applied radioactivity was extracted (p. 11).
3. It was not stated whether the entire volatile trapping solutions or aliquots of these trapping solutions were collected at each 2-week sampling interval.

4. The study author concluded that the unidentified degradates designated as “Unknown metabolites” following the methanol:water extraction were at least 3 polar metabolites (p. 10).
5. The registrant calculated a half-life of 14 weeks for [3,5-¹⁴C]1,2,4-triazole, apparently based on the data generated from the methanol:water extraction only (Table 1, p. 13). The reviewer-calculated half-life of 22 weeks was based on the combined results of the methanol:water and methanol:NaOH extractions, which most closely approximate the observed data (Tables 1 and 2, pp. 13-14).
6. The foreign test soil, designated as a “silty loam” soil, was not classified according to the USDA Soil Classification System, and was not compared to soils in the United States.
7. It was not stated whether the soil samples were sieved. Subdivision N Guidelines state that test soil should be sieved prior to use, and that the screen size should be ≤ 2 mm.
8. It was not stated whether control samples were used in the study.
9. The solubility of triazole in water was reported to be >2000 ppm (MRID 45284023, p. 6).
10. Good Laboratory Practice and Quality Assurance Statements were not included with the study.

ATTACHMENT 1
Data Critical to the Study Interpretation

THE FOLLOWING ATTACHMENT IS NOT AVAILABLE ELECTRONICALLY
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Page _____ is not included in this copy.

Pages 7 through 13 are not included in this copy.

The material not included contains the following type of information:

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ATTACHMENT 2
Excel Workbook

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Chemical Name Triazole degradate
 PC Code 600074
 MRID 45284027
 Guideline No. 162-1

Half-life (weeks) = 22

Days Posttreatment	[¹⁴ C]1,2,4-triazole (Percent of Applied)	Ln ([¹⁴ C]1,2,4-triazole)
0	78.7	4.365643155
28	65.2	4.177459469
56	52.5	3.96081317
84	48.7	3.88567903
168	36.3	3.591817741

Aerobic soil metabolism of [¹⁴C]1,2,4-triazole

