# UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
## WASHINGTON, D.C. 20460

OFFICE OF PREVENTION,
PESTICIDES AND TOXIC
SUBSTANCES

PC Code: 123000
DP Barcode: D242856

**MEMORANDUM:**  Review of Environmental Fate Studies Submitted in Response to Section 3 Review of Isoxaflutole.

**TO:**  Joanne Miller, PM 23
Herbicide and Fungicide Branch
Registration Division (7505C)

**FROM:**  James Breithaupt
Agronomist, Environmental Risk Branch II
Environmental Fate and Ground Water Branch (7507C)    *James Breithaupt 2/5/98*

**PEER REVIEW:**  William Effland, Ph.D.
Soil Scientist, Environmental Risk Branch II
Environmental Fate and Ground Water Branch (7507C)    *William R. Effland*

**THRU :**  Elizabeth Leovey, Ph.D., Branch Chief    *Betsy Guin for 2/5/98*
Environmental Risk Branch II
Environmental Fate and Effects Division (7507C)

## General Conclusions

EFED has reviewed the aerobic aquatic metabolism (MRID 44291502, GLN 162-4) and leaching-adsorption-desorption (MRID 44291503, GLN 163-1) studies submitted in response to the Section 3. EFED has also reviewed the rainfall and pan evaporation upgrading information (MRID 44291504, GLN 164-1) for the terrestrial field dissipation studies as requested in the Section 3. The 163-1 and 164-1 data requirements are now satisfied for isoxaflutole and all metabolites. However, the aerobic aquatic metabolism study only satisfies the 162-4 data requirement for parent isoxaflutole and the metabolite RPA 202248. It does not provide adequate information on the degradation of the metabolite RPA 203328 under aerobic aquatic conditions. RPA 203328 appears to be the terminal metabolite in the environment, based on the laboratory studies submitted to date, and did not degrade significantly. Another 162-4 study will be required using dosing with the RPA 203328 metabolite. The DER's for the 162-4 and 163-1 studies and the information on rainfall and pan evaporation are attached to this memorandum. The pan evaporation and rainfall information are also attached.

In the terrestrial field dissipation studies, with the exception of the Washington site, all the studies for isoxaflutole and its metabolites had more total rainfall applied than total calculated Potential Evapotranspiration. This is known as a positive water balance, and indicates that leaching conditions existed in these field studies. For Nebraska, North Carolina, and California, EFED determined the Potential Evapotranspiration by multiplying the actual pan evaporation by 0.75 (Reference: Hydrology and the Management of Watersheds, Brooks et al., 1991). For Washington, the registrant had already calculated the Potential Evapotranspiration by the Penman Method, although they did not provide detailed information on how the values were calculated.

1

In general, the detections of the isoxaflutole metabolites RPA 202248 and RPA 203328 below the root zone (0-6 inches) were associated with the amount of rainfall and the treated soils. The soils ranged from loamy sand to silt loam in texture, and did not appear to have any impermeable layers that would restrict downward mobility. RPA 202248 was detected to 12 inches of depth, and RPA 203328 was detected to 30 inches of depth in the studies.

## Study-by Study Summary

Nebraska--There was very little relationship between dissipation and rainfall. RPA 203328 reached 6-12 inches of depth in Hasting silt loam soil (2.6-2.9 % OM) at 62 and 125 days (1 of 4 samples) with rainfall of 7.55-14.1 inches. The concentrations were <10 ppb

Washington,--There was some mobility between 59-122 days, and this mobility appeared to be associated with increased rainfall in this interval. Residues of RPA 203328 reached 6-12 inches of depth (<10-22 ppb) and <10 ppb at 12-18 inches of depth in Timmerman sandy loam soil (0.5-1.2 % OM) with 7.98-18.42 inches of rainfall.

North Carolina--The majority of RPA 203328 residues dissipated in the 0-6 inch soil depth between 13 and 30 days. RPA 203328 reached 6-12 inches of depth in Norfolk loamy sand soil (0.6-0.7 % OM) at 30, 64, and 126 days, with levels of 15, <10, <10 ppb, respectively. Rainfall between 30 and 126 days ranged from 4.38-17.47 inches.

California--RPA 202248 was observed at 12-18 inches of depth in Sorrento loam soil (0.8-1.0 % OM) as early as 6 days after treatment (0.94 inches of rainfall). This could have been sample contamination, since rainfall of <1 inch is not likely to cause detections to this depth. There were detections of RPA 203328 to 18-30 inches of depth by 239-496 days (32-62 inches of rainfall) at <10 ppb.

Reference:

Brooks, K.N., P.F. Ffolliott, H.M. Gregersen, and J.L. Thames. 1991. Hydrology and the Management of Watersheds. Iowa State University Press, Ames, Iowa.

2

CHEM 123000            Isoxaflutole            §162-4
CAS No. 141112-29-0
FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 44291502

Ayliffe, J. M. and S. E. Newby. 1995. RPA 201772: Degradation and retention in two water/sediment systems. Laboratory Project ID P94/095. Unpublished study performed by Rhône-Poulenc Agriculture Limited, Essex, ENGLAND; and submitted by Rhône-Poulenc Ag. Co., Essex, ENGLAND.

DIRECT REVIEW TIME = 41    hours

| | | |
|---|---|---|
| REVIEWED BY: | D. E. Toland, M.S. | Signature: |
| TITLE: | Scientist | Date: |
| ORG: | Syracuse Research Corp. | |
| TEL: | 703/413-9369 | |

| | | |
|---|---|---|
| APPROVED BY: | James Breithaupt | Signature: |
| TITLE: | Agronomist | Date: |
| ORG: | ERB II/EFED/OPP | |
| TEL: | 703/305-5925 | |

*James Breithaupt*
*1/23/98*

SIGNATURE:

CONCLUSIONS

Metabolism - Aerobic Aquatic

1.     This is an acceptable study that satisfies the 162-4 data requirement for parent isoxaflutole and the metabolite RPA 202248, but does not satisfy the 162-4 data requirement for the metabolite RPA 203328. RPA 203328 did not form in significant ($\geq 10$ % of applied) quantities in this study, but was observed to reach significant levels in the aerobic soil metabolism study and would be predicted to reach water resources. The registrant has not shown that RPA 203328 actually degrades in aquatic systems. Therefore, EFED requires aerobic aquatic metabolism data derived from dosing with RPA 203328 using U.S. sediment and water, instead of the European sediments and waters used in this study. EFED does not normally accept studies conducted using European soils and sediments, but in this case the results are consistent with U.S. soils for both parent isoxaflutole and its metabolites. Parent isoxaflutole was not persistent, and the metabolite RPA 202248 was found to be persistent.

3

2. Uniformly-phenyl ring-labeled [$^{14}$C]isoxaflutole (RPA 201772), at a nominal concentration of 200 g ai/ha, degraded in Manningtree and River Roding aerobic sediment:water systems with registrant-calculated half-lives of 0.53 days ($r^2 = 0.98$) and 0.6 days ($r^2 = 0.85$). These systems were incubated in darkness at $20 \pm 2$ °C for up to 100 days. Parent compound was not detected in the sediment extracts, and was not detected past 7 days in the water. In the study, the major metabolites were RPA 202248 and RPA 205834 (cyano-reduced RPA 202248). The metabolite RPA 202248 was essentially stable in the aquatic systems, with calculated half-lives of 702 and 250 days for Manningtree and River Roding systems, respectively. RPA 202248 was present in the water phase at a maximum of 52-64 % of the applied by 1-2 days posttreatment, and decreased to 18-27 % by 100 days posttreatment. In the sediment extracts, RPA 202248 increased to a maximum of 22-39 % of applied by 62-100 days. The half-lives for the other major metabolite, RPA 205834, were 97 days for the Manningtree system and 52 days for the River Roding system. RPA 205834 was present in the water phase at a maximum of 15-20 % by 2-7 days, and decreased to 2-3 % of applied by 100 days posttreatment. In the sediment extracts, RPA 205834 reached maximums of 8-13.6 % of applied by 14-30 days posttreatment and declined to 4.3-9.6 % of applied by 100 days posttreatment. RPA 203328, the terminal metabolite in the aerobic soil metabolism study, and RPA 207048 did not exceed 4.7 % of applied in water or on sediment, and were not considered to be significant metabolites in this study. Nonextractable [$^{14}$C]residues were a maximum of 26.84% of the applied radioactivity at 30 days posttreatment and were 22.84% of the applied at 100 days posttreatment. Total [$^{14}$C]radioactivity in the water phase decreased throughout the incubation from a maximum of 96-97 % of the applied at 0 hours posttreatment to 49-52 % of the applied at 100 days posttreatment. Total [$^{14}$C]radioactivity in the sediment increased throughout the incubation and was 53-73 % of the applied by 100 days posttreatment. Radiolabeled volatiles were a maximum of 0.07-0.28 % of the applied at 100 days posttreatment.

## METHODOLOGY

Water and sediment samples were obtained from two streams (Manningtree: 6.2% organic carbon, pH 6.6, CEC 12.6 meq/100 g; and Roding: 3.6% organic carbon, pH 7.9, CEC 50.7 meq/100 g) located in Essex, England. Characteristics of the sediment samples are reported in Table 7.2 (p. 27) based on the BBA system (see Comment #3). Sieved (2 mm) sediment samples (EFED calculated 24 g soil using a bulk density of 1.3 g/cm$^3$), were placed in glass containers to a depth of 2.5 cm, and flooded with an EFED-estimated amount of 45 ml of filtered (0.2 mm) river water (Manningtree: pH 6.5, hardness 319.8 mg/L as CaCO$_3$, TOC 22.66 mg/L, redox potential 520 mV; and Roding: pH 7.35, hardness 370.1 mg/L as CaCO$_3$, TOC 67.88 mg/L, redox potential 439 mV; conductivity and total dissolved solids not reported; Tables 7.1 and 9.4; pp. 27, 75) from the corresponding sample collection site (pp. 13, 14). The sediment/water systems were pre-incubated in darkness at $20 \pm 2$ °C for approximately 7 weeks; CO$_2$-free air was passed through the water during the pre-incubation period. Following the pre-incubation period,

2

*y*

the sediment/water samples were treated with uniformly-phenyl ring-labeled [$^{14}$C]isoxaflutole (RPA 201772; 5-cyclopropyl-4-(2-methanesulphonyl-4-trifluoromethylbenzoyl) isoxazole; radiochemical purity 98.7%, specific activity 909.1 MBq/mmol), dissolved in acetone, at a nominal rate of 200 g ai/ha. The sediment/water ratio was not reported. Sediment/water systems were incubated in darkness at $20 \pm 2\,°C$ for up to 100 days. Humid $CO_2$-free air was passed through the water and then through ethylene glycol and two KOH volatile traps. Duplicate samples were removed for analysis at 0, 6, 24, and 48 hours; and at 7, 14, 30, 62, and 100 days posttreatment (p. 14). Prior to sampling at each interval, the sediment and water redox potentials and the pH and dissolved oxygen content of the water were measured. Microbial biomass was measured at the beginning and end of the incubation.

The water phase was decanted from the sediment and analyzed for total radioactivity by LSC (p. 15). The water was concentrated by freeze drying and reconstituted in acetonitrile:water (1:1, v:v). Sample aliquots were analyzed by HPLC (Ultrabase C8 column) using a mobile phase of acetonitrile:water plus 0.5% trifluoroacetic acid (45:55, v:v) with radioactiveflow and UV (275 nm) detection (p. 17); the limit of detection was 0.01% of the applied radioactivity (Table 7.6, p. 30). Samples were co-chromatographed with nonradiolabeled reference standards. Sample aliquots were also analyzed by TLC using silica gel plates developed with chloroform:methanol:trifluoroacetic acid (90:5:5, v:v:v). Aliquots were co-chromatographed with nonradiolabeled reference standards which were located with UV light (254 nm); radiolabeled residues were located and quantified using a radioanalytic imaging system (p. 17).

Sediment samples were extracted by shaking with acetonitrile:water (1:1, v:v) for 20 minutes, centrifuged and decanted (p. 15). The extraction was repeated twice and the combined extracts were measured for total radioactivity by LSC and filtered as required. The extract was concentrated by rotary evaporation or rotary evaporation followed by freeze drying and reconstituted in acetonitrile:water (1:1, v:v) prior to HPLC and TLC analysis as described above. One 100-days posttreatment sediment sample from each sediment/water system was further extracted by shaking with acidified acetonitrile:water (1:1, v:v; pH 3.0); extracts were concentrated and analyzed by HPLC and TLC as described above. The samples undergoing further extraction were also used to determine radioactivity associated with the humic acid, fulvic acid and humin fractions. Subsamples of air-dried sediment were shaken for 24 hours with 0.5 M NaOH, centrifuged and decanted, and the sediment was washed twice with NaOH and three times with water (p. 16). The combined extracts were analyzed for total radioactivity by LSC. The solution was acidified with 6 M HCl and centrifuged. The supernatant was analyzed directly by LSC, and the precipitate was dissolved in 0.1 M NaOH and analyzed by LSC for total radioactivity. Post-extracted sediment samples were air-dried and analyzed for total radioactivity by LSC following combustion (p. 16).

Radioactivity in the volatile trapping solutions was determined by LSC at each sampling interval (p. 16).

## DATA SUMMARY

### Manningtree Sediment/Water System

Uniformly-phenyl ring-labeled [$^{14}$C]isoxaflutole (RPA 201772; radiochemical purity 98.7%), at a nominal concentration of 200 g ai/ha, degraded with a registrant-calculated half-life (incorrectly described in the study as a DT$_{50}$) of 0.53 days ($r^2 = 0.98$) in aerobic flooded sediment that was incubated in darkness at $20 \pm 2\,°C$ for up to 100 days (Table 7.16, p. 41). All reported data were determined using HPLC analysis. The parent compound was present in the water phase at 84.44% of the applied radioactivity at 0 hours posttreatment, decreased to 31.88% of the applied by 1 day posttreatment and was not detected by 7 days posttreatment (Table 7.16, p. 41). Parent compound was not detected in the sediment extracts. The major metabolite

    2-cyano-3-cyclopropyl-4-(2-methylsulfonyl-4-trifluoromethylphenyl)propan-1,3-dione (RPA 202248)

was present in the water phase at 11.83% of the applied radioactivity at 0 hours posttreatment, increased to a maximum of 52.07% of the applied by 2 days posttreatment, then decreased to 36.14% by 14 days posttreatment and was 18.09% at 100 days posttreatment. The calculated, extrapolated half-lives in the study were 702 and 254 days in the whole aquatic systems. In the sediment extracts, RPA 202248 was initially present at 8.18% of the applied radioactivity at 6 hours posttreatment, increased to 20.49% of the applied by 14 days posttreatment, was a maximum of 38.88% at 62 days posttreatment and was 37.97% at 100 days posttreatment. The major metabolite

    2-aminomethylene-1-cyclopropyl-3-(2-methylsulphonyl-4-trifluoromethyl-phenyl)propan-1,3-dione (RPA 205834)

was initially detected in the water phase at 0.87% of the applied radioactivity at 6 hours posttreatment, increased to a maximum of 15.17% of the applied by 2 days posttreatment and was 1.99% at 100 days posttreatment. In the sediment extracts, RPA 205834 was initially present at 6.28% of the applied radioactivity at 6 hours posttreatment, increased to a maximum of 13.59% of the applied by 14 days posttreatment and was 9.55% at 100 days posttreatment. The minor metabolite 2-methanesulphonyl-4-trifluoromethyl benzoic acid (RPA 203328) was a maximum of 1.92% of the applied radioactivity in the water phase and 1.56% of the applied in the sediment extracts, both at 100 days posttreatment (Tables 7.6, 7.7; pp. 30, 31). The minor metabolite RPA 207048 was a maximum of 3.68% of the applied radioactivity at 7 days posttreatment in the water phase, and was a maximum in the sediment extracts of 1.87% of the applied at 62 days posttreatment. One

4

unidentified minor metabolite was present at a maximum of 0.44% of the applied radioactivity in the water phase.

Nonextractable [$^{14}$C]residues were a maximum of 26.84% of the applied radioactivity at 30 days posttreatment and were 22.84% of the applied at 100 days posttreatment (Table 7.4, p. 28). At 100 days posttreatment, 10.84%, 5.25%, and 2.50% of the applied were associated with the fulvic acid, humic acid, and humin fractions, respectively (Table 9.6, p. 79). Total [$^{14}$C]radioactivity in the water phase decreased throughout the incubation from a maximum of 96.27% of the applied at 0 hours posttreatment to 49.10% of the applied at 14 days posttreatment and 22.43% at 100 days posttreatment. Total [$^{14}$C]radioactivity in the sediment increased throughout the incubation and was 33.45% of the applied at 7 days posttreatment and 73.43% at 100 days posttreatment.

Radiolabeled volatiles were a maximum of 0.07% of the applied at 100 days posttreatment (Table 7.4, p. 28). Material balances ranged from 95.93% to 98.99% of the applied radioactivity throughout the incubation.

Microbial biomass was 199 μg C/g soil and 276 μg C/g soil at the beginning and end of the incubation, respectively (Table 7.3, p. 27). The redox potential during the incubation ranged from 64 to 255 mV (moderately reducing to moderately oxidizing) in the water and from -307 to -98 mV (reducing to strongly reducing) in the sediment (Table 7.14, p. 38). The dissolved oxygen content ranged from 39% to 53% of saturation except for 77% of saturation at 6 hours posttreatment. The pH ranged from 6.57 to 8.69.

River Roding Sediment/Water System

Uniformly-phenyl ring-labeled [$^{14}$C]isoxaflutole (RPA 201772; radiochemical purity 98.7%), at a nominal concentration of 200 g ai/ha, degraded with a registrant-calculated half-life (incorrectly described in the study as a $DT_{50}$) of 0.60 ($r^2$ = 0.85) days in aerobic flooded sediment that was incubated in darkness at 20 ± 2 °C for up to 100 days (Table 7.17, p. 44). All reported data were determined using HPLC analysis. The parent compound was present in the water phase at 82.59% of the applied radioactivity at 0 hours posttreatment, decreased to 44.25% of the applied by 6 hours posttreatment and was not detected by 7 days posttreatment (Table 7.17, p. 44). The parent compound was not detected in the sediment extracts. The major metabolite

2-cyano-3-cyclopropyl-4-(2-methylsulfonyl-4-trifluoromethylphenyl)propan-1,3-dione (RPA 202248)

was present in the water phase at 14.48% of the applied radioactivity at 0 hours posttreatment, increased to a maximum of 63.87% of the applied by 1 day posttreatment, then decreased to 47.19% by 7 days posttreatment and was 27.63% at 100 days posttreatment. In the sediment extracts, RPA 202248 was initially present at 2.88% of the

5

7

applied radioactivity at 6 hours posttreatment, increased to 11.75% of the applied by 7 days posttreatment and was a maximum of 22.87% at 100 days posttreatment. The major metabolite

2-aminomethylene-1-cyclopropyl-3-(2-methylsulphonyl-4-trifluoromethyl-phenyl)propan-1,3-dione (RPA 205834)

was initially detected in the water phase at 0.74% of the applied radioactivity at 6 hours posttreatment, increased to a maximum of 20.44% of the applied by 7 days posttreatment and was 3.10% at 100 days posttreatment (Table 7.17, p. 45). In the sediment extracts, RPA 205834 was initially present at 2.72% of the applied radioactivity at 6 hours posttreatment, increased to a maximum of 7.95% of the applied by 30 days posttreatment and was 4.33% at 100 days posttreatment. The minor metabolite 2-methanesulphonyl-4-trifluoromethyl benzoic acid (RPA 203328) was a maximum of 7.10% of the applied radioactivity in the water phase and 3.71% of the applied in the sediment extracts, both at 100 days posttreatment (Tables 7.8, 7.9; pp. 32, 33). The minor metabolite RPA 207048 was a maximum of 4.73% of the applied radioactivity at 14 days posttreatment in the water phase, and was a maximum of 2.48% of the applied at 100 days posttreatment in the sediment extracts. Two unidentified minor metabolites were present at a maximum of ≤0.57% of the applied radioactivity in the water and sediment phases.

Nonextractable [$^{14}$C]residues were a maximum of 20.12% of the applied radioactivity at 62 days posttreatment and were 18.89% of the applied at 100 days posttreatment (Table 7.5, p. 29). At 100 days posttreatment, 13.71%, 2.64%, and 0.11% of the applied were associated with the fulvic acid, humic acid, and humin fractions, respectively (Table 9.6, p. 79). Total [$^{14}$C]radioactivity in the water phase decreased throughout the incubation from a maximum of 97.44% of the applied at 0 hours posttreatment to 51.75 % of the applied at 30 days posttreatment and 41.17% at 100 days posttreatment. Total [$^{14}$C]radioactivity in the sediment increased throughout the incubation and was 25.84% of the applied at 7 days posttreatment and 52.66% at 100 days posttreatment.

Radiolabeled volatiles were a maximum of 0.28% of the applied at 100 days posttreatment (Table 7.5, p. 29). Material balances ranged from 94.11% to 99.21% of the applied radioactivity throughout the incubation.

Microbial biomass was 50 µg C/g soil and 103 µg C/g soil at the beginning and end of the incubation, respectively (Table 7.3, p. 27). The redox potential during the incubation ranged from 40 to 187 mV (reducing to moderately reducing) in the water and from -168 to -25 mV (reducing) in the sediment (Table 7.15, p. 40). The dissolved oxygen content ranged from 43% to 65% of saturation and the pH ranged from 7.67 to 8.44 (Table 7.15, pp. 39, 40).

6

## COMMENTS

1. The calculated half-lives for RPA 202248 were 702 and 254 days in the study for the whole systems. These half-lives are extrapolated beyond the 100 days of the study duration, and show that this metabolite is persistent.

2. The foreign sediment was not adequately compared to domestic (U.S.) sediments. The study authors reported that the sand-silt-clay distributions of the Manningtree and Roding sediments were 54-34-12 and 48-22-30, respectively (Table 7.2, p. 27). However, particle size fractions were reported in size fraction classes not used in the USDA system, and it could not be determined what the USDA texture classifications of the two sediments would be. The registrant should adequately compare European and U.S. sediments in the future.

3. The study authors stated that the $DT_{50}$ and $DT_{90}$ values were calculated using linear regression analysis (first order kinetics; p. 10). The reviewer notes, therefore, that the values reported by the study author as $DT_{50}$'s are actually half-life calculations ($t_{1/2}$) rather than true $DT_{50}$'s.

4. The study authors reported $DT_{50}$ and $DT_{90}$ values (see Comment #5) for the parent material and major metabolites. The $DT_{50}$ and $DT_{90}$ values for the metabolites are of questionable validity due to the likely formation and degradation of the metabolites at the same time, making degradation rates difficult to determine. The reviewer notes that the $r^2$ value associated with the registrant-calculated $DT_{50}$'s for RPA 202248 in the Manningtree flooded sediment system was very low, at 0.19 (pp. 41,42). In the Roding flooded sediment system, an $r^2$ value of 0.67 was calculated for the metabolite RPA 202248.

5. Data were reported for both HPLC and TLC analyses. The reviewer chose to report HPLC data because the study authors used the HPLC data to determine the half-lives ($DT_{50}$'s). The reviewer notes that the HPLC and TLC results were similar.

6. The water was not adequately characterized; the conductivity and total dissolved solids were not reported.

7. The study authors did not indicate if the samples were stored prior to analysis. Clarification by the registrant would be appropriate.

8. The study authors did not submit concentration data for the parent material and its metabolites in the water and sediment; data were reported only as percentages of the applied radioactivity. Future studies submitted by the registrant should included concentration data.

9. The redox potential during the incubation ranged from 40 to 187 mV (reducing to

7

moderately reducing) in the water and from -168 to -25 mV (reducing) in the sediment (Table 7.15, p. 40). The classification of the redox potentials was determined by the reviewer using Wolfe, N.L. et. al. 1990. *Pesticides in the Soil Environment*. Soil Science Society of America book series no. 2. pp. 103-168.

10

CHEM 123000            Isoxaflutole            §163-1

CAS No. 142994-06-7

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 44291503

Burr, C. M. 1996. [$^{14}$C]-RPA 203328: Adsorption/desorption to and from four soils and a sediment. Laboratory Project ID: 11487. Unpublished study performed by Rhône-Poulenc Agriculture Limited, Essex, ENGLAND; and submitted by Rhône-Poulenc Ag. Co., Essex, ENGLAND.

DIRECT REVIEW TIME = 34   hours

| REVIEWED BY: | D. A. Saccone, B.S. | Signature: |
| TITLE: | Scientist | Date: |
| ORG: | Syracuse Research Corp. | |
| TEL: | 703/413-9369 | |

| APPROVED BY: | James Breithaupt | Signature: | _James Breithaupt_ |
| TITLE: | Agronomist | Date: | _1/22/98_ |
| ORG: | ERB II/EFED/OPP | | |
| TEL: | (703)-305-5925 | | |

SIGNATURE:

## CONCLUSIONS

### Mobility - Leaching and Adsorption/Desorption

1.  This study is acceptable and satisfies the aged portion of the 163-1 data requirement for the isoxaflutole metabolite, RPA 203328 (2-methylsulphonyl-4-trifluoromethylbenzoic acid). The 163-1 data requirement is now satisfied with acceptable studies for parent isoxaflutole and the primary metabolites RPA 202248 and RPA 203328. It should be noted that none of the soils or the sediment used in the study came from the Midwestern U.S., where most U.S. corn is grown. Nevertheless, it is apparent that RPA 203328 is very mobile in the tested soils.

2.  Uniformly phenyl ring-labeled [$^{14}$C]RPA 203328 exhibited low adsorption to the tested clay, sand, loamy sand and silt loam soil:solution slurries (1:2.5, w:v) and a loam sediment:solution slurry that were equilibrated in darkness for 2 hours at 20 °C. Freundlich $K_{ads}$ values ranged from 0.31-1.15 ml/g for the soils and sediment that ranged from sand to clay textures and 0.34-4.98 OC%. These adsorption values as classified in the McCall classification system indicate that RPA 203328 is highly to very highly mobile in soil. The Koc values ranged from 23-100 mL/g ($r^2$=0.96). Respective 1/N values

/ /

associated with the adsorption phase were 0.98-1.00 for the soils and 0.76 for the sediment. Freundlich $K_{des}$ values ranged from 0.27-1.17, and corresponding $K_{oc}$ values were 23-137 ml/g. Respective 1/N values associated with the desorption phase of the study were 0.88-1.00 and 0.67 for the loam sediment. Freundlich $K_{des}$ values could not be calculated for the silt loam soil because all of the adsorbed radioactivity was desorbed following the first desorption cycle for one replicate.

## METHODOLOGY

Based on a preliminary study for the adsorption of uniformly phenyl ring-labeled [$^{14}$C]RPA 203328 (2-methylsulphonyl-4-trifluoromethylbenzoic acid; radiochemical purity 98%, specific activity 921.7 MBq/mmol) to Sharkey clay, Norfolk sand, Norfolk loamy sand, Dundee silt loam soils and loam sediment (Table 7.1, p. 26), an equilibration period of 2 hours was chosen for all four soils and the sediment; data were submitted in graphical form (Figure 7.1, p. 41). Based on a preliminary study for the desorption of the parent compound from the soils, an equilibration period of 1 hour was chosen for all four soils and the sediment (p. 18). A preliminary study to determine the adsorption of the parent compound to the borosilicate glass tubes was performed using radiolabeled [$^{14}$C]RPA 203328, at 1.0 mg/L, in 0.01 $\underline{M}$ CaCl$_2$ solution. Following 24 hours of agitation at 20 °C, [$^{14}$C]RPA 203328 was present in solution at 99.62% of the applied radioactivity (determined by LSC analysis), indicating that adsorption to the glass tubes did not occur (p. 27).

For the adsorption phase of the study, duplicate sieved (2 mm) oven-dried subsamples (20 g) of clay, sand, loamy sand, silt loam soils and loam sediment were placed into glass tubes and mixed with 50 mL of 0.01 $\underline{M}$ CaCl$_2$ solution treated with uniformly phenyl ring-labeled [$^{14}$C]RPA 203328 at nominal concentrations of 0.04, 0.2, 1.0, and 5.0 mg/L (pp. 16, 27). The soil:solution slurries (1:2.5, w:v) were mechanically shaken in darkness for 2 hours at 20 °C (p. 16). Following the equilibration period, samples were centrifuged and the supernatant was decanted. Triplicate aliquots of the supernatant from each sample were analyzed for total radioactivity by LSC; no detection limits were reported.

For the desorption phase of the study, 50 ml of pesticide-free 0.01 $\underline{M}$ CaCl$_2$ solution were added to the glass tubes containing soil from the adsorption phase of the study (p. 16). The samples were shaken for 1 hour and maintained as previously described. Following the equilibration period, samples were centrifuged and the supernatant was decanted. The desorption process was performed serially four more times. Triplicate aliquots of the supernatant from each sample were analyzed for total radioactivity by LSC. One replicate from each soil type and the sediment fortified at the highest application rate (5.0 mg/L) was extracted with acetonitrile:water (1:1, v:v) by shaking for 20 minutes followed by centrifuging. The supernatant was removed and triplicate aliquots were analyzed for total radioactivity by LSC. Following desorption, soil pellets were air dried, ground and analyzed for total radioactivity by LSC following combustion.

2

To determine compound stability during the adsorption and desorption phases of the study, duplicate adsorbates and desorbates from systems treated at 5.0 mg/L and 1.0 mg/L were analyzed using reverse-phase HPLC (KR100 5C8 column) with a mobile phase gradient of acetonitrile:water plus 0.5% trifluoroacetic acid (30:70, v:v); UV (275 nm) and $\beta$-ram radioactiveflow detection were utilized (p. 17). Method detection limits were not reported.


## DATA SUMMARY

Uniformly phenyl ring-labeled [$^{14}$C]RPA 203328 (radiochemical purity 98%), at nominal concentrations of 0.04, 0.2, 1.0, and 5.0 mg/L, exhibited low adsorption to the tested clay, sand, loamy sand and silt loam soil:solution slurries (1:2.5, w:v) and a loam sediment:solution slurry that were equilibrated in darkness for 2 hours at 20 °C. Freundlich $K_{ads}$ values ranged from 0.31-1.15 ml/g for the soils and sediment that ranged from sand to clay textures and 0.34-4.98 OC%. These adsorption values as classified in the McCall classification system indicate that RPA 203328 is highly to very highly mobile in soil. The Koc values ranged from 23-100 mL/g ($r^2$=0.96). Respective 1/N values associated with the adsorption phase were 0.98-1.00 for the soils and 0.76 for the sediment (Table 7.5 p. 28). Freundlich $K_{des}$ values ranged from 0.27-1.17, and corresponding $K_{oc}$ values were 23-137 ml/g. Respective 1/N values associated with the desorption phase of the study were 0.88-1.00 and 0.67 for the loam sediment (Table 7.6, p. 28). Freundlich $K_{des}$ values could not be calculated for the silt loam soil because all of the adsorbed radioactivity was desorbed following the first desorption cycle. Table 1 presents the adsorption and desorption information.

Data from the HPLC analysis indicated that uniformly phenyl ring-labeled [$^{14}$C]RPA 203328 was stable in soil:solution and sediment:solution slurries treated at the two highest application rates (5.0 and 1.0 mg/L) during the adsorption and desorption equilibration periods (Table 7.17, p. 37).

/3

Table 1. Adsorption and Desorption Constants for RPA 203328.

| Soil[1] (% OC, Location) | $K_f$ (adsorption) | $K_{oc}$ (adsorption) | 1/n (adsorption) | $K_f$ (desorption) | $K_{oc}$ (desorption) | 1/n (desorption) |
|---|---|---|---|---|---|---|
| Norfolk Sand, 0.38 % OC, NC | 0.31 | 82 | 0.996 | 0.27 | 72 | 0.88 |
| Norfolk Loamy Sand, 0.34 % OC, NC | 0.31 | 91 | 1.00 | 0.47 | 137 | 1.00 |
| Loam[2], 4.98, NC | 1.15 | 23 | 0.76 | 1.17 | 23 | 0.67 |
| Dundee Silt Loam, 0.47 % OC, MS | 0.47 | 100 | 0.99 | 3 | 3 | 3 |
| Sharkey Clay, 1.22 % OC, MS | 0.58 | 47 | 0.98 | 0.8 | 65 | 0.94 |

[1] The soils came from the Clayton Research Farm in North Carolina and the Delta Research Farm in Mississippi. It should be noted that the soils chosen were not the Midwest, where most corn is grown.

[2] This was a sediment, and the contributing soil series were not specified.

[3] Desorption coefficients could not be calculated, since $\geq$ 100 % of residues were desorbed in the first step.

Material balances across all application rates were 99.23-100.12% for the sand soil, 99.64-100.63% for the sand soil, 99.39-101.09% for the loamy sand soil, 99.70-103.80% for the silt loam soil, and 97.87-100.32% for the loam sediment (Tables 7.18-7.22, pp. 38-39).

## COMMENTS

1.     Method detection limits were not reported.

2.     The study authors used a Norfolk sandy loam in the aerobic soil metabolism study (MRID 43588006). The EFED reviewer compared the Norfolk soils between the studies and found that they were very similar, except that the Norfolk sandy loam soil in the aerobic soil metabolism study had a higher organic carbon content.

3.     The qualitative classifications of soil mobility reported in the data summary were determined by the reviewer using "Table III: The general relationship between the soil/solution partition coefficient K, $R_f$ and soil mobility" (*Federal Register*, Vol. 44, No. 53) and are based on the $K_{ads}$ values reported by the registrant. The qualitative

14

determinations reported by the registrant in the form of a McCall mobility class were based on the $K_{oc}$ values associated with the adsorption phase of the experiment; these class determinations were not reported by the reviewer.

4.  The study author stated that desorption coefficient values could not be calculated for the silt loam soil because all of the adsorbed radioactivity was desorbed following the first desorption cycle for one replicate (p. 20). Raw data for the desorption of the test compound from silt loam soil during the first desorption cycle are presented in Table 7.15 (p. 15).

5.  The aqueous solubility of RPA 203328 was reported as 8.5 g/L (p. 12).