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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

10/12/1999

MEMORANDUM

SUBJECT: Isoxaflutole: Review of Shrimp and Bobwhite Studies for Isoxaflutole Degradate, RPA 203328; DP Barcode D252059, D251292

FROM: Michael Davy, Agronomist
Environmental Risk Branch II
Environmental Fate and Effects Branch (7505C)
Michael Davy 10-9-99

THRU: Pat Jennings, Acting Chief
Environmental Risk Branch II
Environmental Fate and Effects Branch (7505C)
Betsy Gin 10-12-99

TO: Joanne Miller, PM-23
Registration Division (H7506)

The Environmental Risk Branch II has reviewed 2 studies submitted by Phone-Poulenc Ag Co., Research Triangle, NC. These studies were submitted under DP Barcode D252059 and D251292 for conditional registration of Isoxaflutole.

Review of Submitted Studies
The following is a brief summary of the submitted studies:

- **CITATION:** Authors: S.P. Gallagher, J. Grimes, J.B. Beavers, and T.Z. Kendall
  Title: RPA 203328: A Dietary LC_{50} Study with the Northern Bobwhite
  Study Completion Date: October 15, 1998
  Laboratory: Wildlife International Ltd., Easton, MD
  Laboratory Report ID: 171-137
  Sponsor: Rhone-Poulenc Ag Company, Research Triangle Park, NC
  MRID No.: 446935-01
  DP Barcode: D251292

This study is scientifically sound and fulfills the guideline requirements. Based on the mean

measured concentration, the LC_{50} was >5265 ppm ai, which classifies RPA 203328 as practically non-toxic to the bobwhite.

Results Synopsis

LC_{50}: >5265 ppm ai 95% C.I.: N/A
NOAEC: 5265 ppm ai Probit Slope: N/A

Classification of study: Core

- **CITATION:** Author: J.V. Sousa
Title: RPA 203328 - Acute Toxicity to Mysids (*Mysidopsis bahia*) Under Static Acute Conditions
Study Completion Date: December 10, 1998
Laboratory: Springborn Laboratories, Inc., Wareham, MA
Sponsor: Rhone-Poulenc Ag Company, Research Triangle Park, NC
Laboratory Report ID: 98-10-7528
MRID No.: 447188-01
DP Barcode: D252059

This study is scientifically sound and fulfills the guideline requirements. The 96-hour LC_{50} for mysids exposed to RPA 203328 was 145 ppm ai, which classifies this compound as practically non-toxic to *Mysidopsis bahia*. The NOAEC was 25 ppm ai.

Results Synopsis

LC_{50} (95% C.I.)= 148 (120-200) ppm ai
NOAEC = 25 ppm ai Probit Slope = 5.8

Classification of study: Core

If you have any questions, please do not hesitate to contact Mike Davy at 305-7081.

1-EEB-11E
2/12/99

MRID No. 446935-01

DATA EVALUATION RECORD
§ 71-2 - UPLAND GAME BIRD DIETARY LC_{50} TEST

1. **CHEMICAL:** Isoxaflutole — PC Code No.: 123000

2. **TEST MATERIAL:** RPA 203328 — Purity: 99%

3. **CITATION:**

Authors:	S.P. Gallagher, J. Grimes, J.B. Beavers, and T.Z. Kendall
Title:	RPA 203328: A Dietary LC_{50} Study with the Northern Bobwhite
Study Completion Date:	October 15, 1998
Laboratory:	Wildlife International Ltd., Easton, MD
Laboratory Report ID:	171-137
Sponsor:	Rhone-Poulenc Ag Company, Research Triangle Park, NC
MRID No.:	446935-01
DP Barcode:	D251292

4. **REVIEWED BY:** Mark A. Mossler, M.S., Toxicologist, Golder Associates Inc.

Signature: Karl Butler for MAM **Date:** 2/11/99

APPROVED BY: Pim Kosalwat, Ph.D., Senior Scientist, Golder Associates Inc.

Signature: P. Kosalwat **Date:** 2/11/99

5. **APPROVED BY:**

Signature: Michael Dary **Date:** 10-9-99

6. **STUDY PARAMETERS:**

Scientific Name of Test Organism: Colinus virginianus
Age of Test Organisms at Test Initiation: 10 days
Definitive Study Duration: 8 days

7. **CONCLUSIONS:** This study is scientifically sound and fulfills the guideline requirements. Based on the mean measured concentration, the LC_{50} was >5265 ppm ai, which classifies RPA 203328 as practically non-toxic to the bobwhite.

Results Synopsis:

LC_{50}: >5265 ppm ai — 95% C.I.: N/A
NOEC: 5265 ppm ai — Probit Slope: N/A

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LC_{50}: >5265 ppm ai
NOEC: 5265 ppm ai

95% C.I.: N/A
Probit Slope: N/A

8. **ADEQUACY OF THE STUDY:**

A. Classification: Core

B. Rationale: N/A

C. Repairability: N/A

9. **GUIDELINE DEVIATIONS:** No deviations were noted.

10. **SUBMISSION PURPOSE:**

11. **MATERIALS AND METHODS:**

A. Test Organisms

Guideline Criteria	Reported Information
Species: An upland game bird species, preferable the bobwhite (*Colinus virginianus*).	*Colinus virginianus*
Age at beginning of test: 10-14 days old	10 days old
Supplier	In-house production flock
Chicks appeared healthy and did not have excessive mortality before the test?	Birds appeared in good health at the initiation of testing
Acclimation period: As long as possible.	10 days

B. Test System

Guideline Criteria	Reported Information
Pen size: about 35 x 100 x 24 cm	72 x 90 x 23 cm

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Guideline Criteria	Reported Information
Brooder temperature: about 35°C (95°F)	38 ±1°C
Room temperature: 22-27°C (71-81°F)	27.6 ±1.1°C
Relative humidity: 30-80%	63 ±12%
Adequate ventilation?	Not reported
Photoperiod Minimum of 14 h of light.	16 hours of light per day
Diet: A commercial game bird feed.	In-house game bird diet

C. **Test Design**

Guideline Criteria	Reported Information
Range finding test?	Treatment concentrations based on known toxicity
Definitive Test **Nominal concentrations:** Four minimum, 5 or 6 strongly recommended, in a geometric scale, unless LC_{50} >5000 ppm.	562, 1000, 1780, 3160, and 5620 ppm active ingredient (ai)
Controls: Control group tested with diet containing the maximum amount of vehicle used in treated diets?	3 control groups offered diet containing 2% corn oil
Number of birds per group: 10 (strongly recommended)	10 birds per group
Vehicle: Distilled water, corn oil, propylene glycol, 1% carboxy-methylcellulose, gum arabic.	Material suspended in acetone and corn oil - acetone evaporated while blending
Vehicle amount (% of diet by weight): Not more than 2%	2% corn oil

Guideline Criteria	Reported Information
Test durations: 5 days with treated feed and at least 3 days observation with "clean" feed.	Five day exposure period followed by three day observation period
No mortality during last 72 hr of observations?	No mortality in any group during the test

12. REPORTED RESULTS:

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes
Body weights measured at beginning and end of study?	Individual body weights measured on day 0 (initiation), day 5, and day 8 (termination)
Estimated consumption per pen reported for pretreatment, treatment, and observation periods?	Average feed consumption determined for days 0-5 and 6-8
Control Mortality: Not more than 10%	No control mortality
Percent Recovery of Chemical Percent of nominal, Procedural recovery, Limit of quantitation (LOQ)	84-101%, Procedural recovery of 98%, LOQ = 100 ppm ai
Raw data included?	Yes
Signs of toxicity (if any) were described?	Yes

Analytical Results

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Concentration (ppm ai)	Measured concentrations (ppm ai)	
Nominal	Hour of Study	
	0	120
Control	<LOQ	<LOQ
562	545	470
1000	993	908
1780	1790	1510
3160	3110	2790
5620	5500	5030

Mortality

Conc. (ppm ai)	No. of Birds	Cumulative Number of Dead							
Nominal		Day of Study							
		1	2	3	4	5	6	7	8
Control	30	0	0	0	0	0	0	0	0
562	10	0	0	0	0	0	0	0	0
1000	10	0	0	0	0	0	0	0	0
1780	10	0	0	0	0	0	0	0	0
3160	10	0	0	0	0	0	0	0	0
5620	10	0	0	0	0	0	0	0	0

Other Significant Results: No mortalities or treatment-related signs of toxicity were observed in the control or treatment groups. There did not appear to be effects on body weight or feed consumption when control and treatment values were compared.

Statistical Results

Statistical Method: visual interpretation (based on nominal concentration)

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LC_{50}: >5620 ppm ai 95% C.I.: N/A
NOEC: 5620 ppm ai Probit Slope: N/A

13. **VERIFICATION OF STATISTICAL RESULTS:**

Statistical Method: visual interpretation (based on mean measured concentration)

LC_{50}: >5265 ppm ai 95% C.I.: N/A
NOEC: 5265 ppm ai Probit Slope: N/A

14. **REVIEWER'S COMMENTS:** This study is scientifically sound and fulfills the guideline requirements for an acute dietary toxicity test using the bobwhite. An LC_{50} value of >5265 ppm ai classifies the test material as practically non-toxic to the northern bobwhite. The NOEC was determined to be 5265 ppm ai. The study is classified as **Core**.

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1-ECD-11E
2/12/99

MRID No. 447188-01

DATA EVALUATION RECORD
ACUTE LC_{50} TEST WITH AN ESTUARINE/MARINE SHRIMP
§ 72-3

1. **CHEMICAL:** Isoxaflutole — PC Code No.: 123000

2. **TEST MATERIAL:** RPA 203328 — Purity: 99%

3. **CITATION:**

Author:	J.V. Sousa
Title:	RPA 203328 - Acute Toxicity to Mysids (Mysidopsis bahia) Under Static Acute Conditions
Study Completion Date:	December 10, 1998
Laboratory:	Springborn Laboratories, Inc., Wareham, MA
Sponsor:	Rhone-Poulenc Ag Company, Research Triangle Park, NC
Laboratory Report ID:	98-10-7528
MRID No.:	447188-01
DP Barcode:	D252059

4. **REVIEWED BY:** Mark Mossler, M.S., Toxicologist, Golder Associates Inc.

Signature: for MAM **Date:** 2/12/99

APPROVED BY: Pim Kosalwat, Ph.D., Senior Scientist, Golder Associates Inc.

Signature: P. Kosalwat **Date:** 2/12/99

5. **APPROVED BY:**

Signature: Michael Dang **Date:** 2/12/99

6. **STUDY PARAMETERS:**

Age or Size of Test Organism:	≤24 hours old
Definitive Test Duration:	96 hours
Study Method:	Static
Type of Concentrations:	Mean measured

7. **CONCLUSIONS:** This study is scientifically sound and fulfills the guideline requirements. The 96-hour LC_{50} for mysids exposed to RPA 203328 was 145 ppm ai, which classifies this compound as practically non-toxic to Mysidopsis bahia. The NOEC was 25 ppm ai.

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8. **ADEQUACY OF THE STUDY:**

   A. Classification: Core.

   B. Rationale: N/A.

   C. Repairability: N/A.

9. **GUIDELINE DEVIATIONS:** The age of the test mysids was not reported. However, the test protocol attached to the report as Appendix I indicates that ≤24-hour-old mysids would be used.

10. **SUBMISSION PURPOSE:**

11. **MATERIALS AND METHODS:**

   A. Test Organisms

Guideline Criteria	Reported Information
Species Preferred species are *Mysidopsis bahia*, *Penaeus setiferus*, *P. duorarum*, *P. aztecus* and *Palaemonetes sp.*	*Mysidopsis bahia*
Age Juvenile, mysids should be ≤ 24 hours old	≤24 hours old
Supplier	In-house cultures
All shrimp are from same source?	Yes
All shrimp are from the same year class?	Yes

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B. Source/Acclimation

Guideline Criteria	Reported Information
Acclimation Period minimum 10 days	Adult mysids were cultured under the same temperature, salinity, and pH as that used during the study.
Wild caught organisms were quarantined for 7 days?	N/A
Were there signs of disease or injury?	No
If treated for disease, was there no sign of the disease remaining during the 48 hours prior to testing?	N/A
Feeding No feeding during the study and no feeding for 24 hours before the beginning of the test if organisms are over 0.5 g each.	Mysids were fed brine shrimp nauplii once daily during the study.
Pretest Mortality <3% mortality 48 hours prior to testing	Not reported

C. Test System

Guideline Criteria	Reported Information
Source of dilution water Soft reconstituted water or water from a natural source, **not** dechlorinated tap water	Filtered seawater
Does water support test animals without observable signs of stress?	Yes

Guideline Criteria	Reported Information
Salinity 30-34 ‰ for marine (stenohaline) shrimp and 10-17 ‰ for estuarine (euryhaline) shrimp, weekly range < 6 ‰	31-35‰
Water Temperature Approx. 22 ± 1 °C	24-25°C
pH 8.0-8.3 for marine (stenohaline) shrimp, 7.7-8.0 for estuarine (euryhaline) shrimp, monthly range < 0.8	7.0-8.0
Dissolved Oxygen Static: ≥ 60% during 1st 48 hrs and ≥ 40% during 2nd 48 hrs, Flow-through: ≥ 60%	≥61% of saturation
Total Organic Carbon	<2.0 mg/L
Test Aquaria 1. Material: Glass or stainless steel 2. Size: 19.6 L is acceptable for organisms ≥ 0.5 g (e.g. pink shrimp, white shrimp, and brown shrimp), 3.9 L is acceptable for smaller organisms (e.g. mysids and grass shrimp). 3. Fill volume: 15 L is acceptable for organisms ≥ 0.5 g, 2-3 L is acceptable for smaller organisms.	1. Glass 2. 1-L vessels 3. 0.9 L
Type of Dilution System Must provide reproducible supply of toxicant	N/A

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Guideline Criteria	Reported Information
Flow Rate Consistent flow rate of 5-10 vol/24 hours, meter systems calibrated before study and checked twice daily during test period	N/A
Biomass Loading Rate Static: ≤ 0.8 g/L at ≤ 17°C, ≤ 0.5 g/L at > 17°C; flow-through: ≤ 1 g/L/day	Not reported
Photoperiod 16 hours light, 8 hours dark	16 h light, 8 h dark
Solvents Not to exceed 0.5 mL/L for static tests or 0.1 mL/L for flow-through tests	Solvent: acetone Maximum conc.: 0.5 mL/L

D. **Test Design**

Guideline Criteria	Reported Information
Range Finding Test If LC_{50} >100 mg/L with 30 shrimp, then no definitive test is required.	Mysids exposed at 50, 150, and 200 ppm active ingredient (ai) - mortality of 0, 50, and 80%, respectively after 96 hours
Nominal Concentrations of Definitive Test Control & 5 treatment levels; a geometric series in which each concentration is at least 60% of the next higher one.	Control, solvent control, 9.3, 16, 26, 43, 72, 120, and 200 ppm ai
Number of Test Organisms Minimum 20/level, may be divided among containers	10 mysids per test vessel; 2 replicate test vessels per treatment and control
Test organisms randomly or impartially assigned to test vessels?	Yes

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Guideline Criteria	Reported Information
Biological observations made every 24 hours?	Observations were made daily
Water Parameter Measurements 1. Temperature Measured constantly or, if water baths are used, every 6 hrs, may not vary > 1°C 2. DO and pH Measured at beginning of test and ever 48 h in the high, medium, and low doses and in the control	1. Temperature was measured continuously throughout the test period in the water bath. Temperature was also measured daily in each test vessel. 2. DO and pH were measured daily in each control and treatment vessel.
Chemical Analysis needed if solutions were aerated, if chemical was volatile, insoluble, or known to absorb, if precipitate formed, if containers were not steel or glass, or if flow-through system was used	Test solutions were analyzed for the test material using HPLC. Samples were collected from each group at 0 and 96 hours after initiation.

12. **REPORTED RESULTS:**

A. General Results

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes
Recovery of Chemical: Percent of nominal, Procedural recovery, Limit of quantitation (LOQ)	88-105% of nominal, Procedural recovery of 98%, LOQ = 0.68 ppm ai
Control Mortality Not more than 10% of control organisms may die or show abnormal behavior.	0% mortality

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Guideline Criteria	Reported Information
Raw data included?	Yes
Signs of toxicity (if any) were described?	Yes

Analytical Results

Concentration (ppm ai)	Measured Concentrations (ppm ai)	
Nominal	Hour of Study	
	0	96
Control	<LOQ	<LOQ
Sol. Con.	<LOQ	<LOQ
9.3	9.0	9.4
16	14	16
26	23	26
43	39	45
72	67	72
120	110	120
200	180	210

Mortality

Concentration (ppm ai)		Number of Shrimp	Cumulative Number Dead			
Nominal	Mean Measured		Hour of Study			
			24	48	72	96
Control	<0.68	20	0	0	0	0
Sol. Con.	<0.68	20	0	0	0	0
9.3	9.2	20	0	0	0	0
16	15	20	0	0	0	0

Concentration (ppm ai)		Number of Shrimp	Cumulative Number Dead			
			Hour of Study			
Nominal	Mean Measured		24	48	72	96
26	25	20	0	0	0	0
43	42	20	0	0	0	1
72	70	20	0	0	0	0
120	120	20	0	1	1	3
200	200	20	3	17	19	19

Other Significant Results: Signs of test material toxicity including surfacing, lethargy, darkened pigmentation, partial/complete loss of equilibrium were noted at the four highest-concentration treatment levels.

B. Statistical Results

Methods: nonlinear interpolation and binomial probability

96-hr LC_{50}: 150 ppm ai
Probit Slope: N/A
95% C.I.: 120-200 ppm ai
NOEC: 25 ppm ai

13. **VERIFICATION OF STATISTICAL RESULTS:**

Parameter	Result
Binomial Test LC_{50} (95% C.I.)	148 (120-200) ppm ai
Moving Average Angle LC_{50} (95% C.I.)	145 (129-168) ppm ai
Probit LC_{50} (95% C.I.)	141 (0-∞) ppm ai
Probit Slope	5.8
NOEC	25 ppm ai

14. **REVIEWER'S COMMENTS:** This study is scientifically sound, fulfills the guideline requirements, and is classified as **Core**. The 96-hour LC_{50} for mysids exposed to RPA 203328 is 145 ppm ai, which classifies the test material as practically non-toxic to mysids. The NOEC was 25 ppm ai.

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