2.22.96

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Data review for RPA 201772 - Isoxaflutole (D219143, Chemical #123000, Case 286745)

FROM: Renée Costello, Biologist, ERCB, EFED (7507C) Renee Costello 2/22/96

THRU: Elizabeth M.K. Leovey, Chief, ERCB, EFED (7507C)

TO: Joanne Miller, PM 23, RD (7505C)

The Environmental Risk Characterization Branch (ERCB) has completed the review of the data submitted in support of registration of Isoxaflutole, chemical number 123000. The following is a brief summary of the data reviewed:

Citation: RPA 201772 Technical - Acute Toxicity to the freshwater diatom, *Navicula pelliculosa*, **EPA MRID #435732-44**, DP Barcode: D219143

Conclusions: This study is scientifically sound and fulfills the guideline requirement for an acute toxicity test with a freshwater diatom. Based on mean measured concentrations, the 120 hour EC_{50} of RPA 201772 is 0.38 mg ai/L and the NOEC is 0.0031 mg ai/L.

Citation: Laboratory testing for toxicity (acute contact and oral LD_{50}) of RPA 201772 to honeybees (*Apis mellifera L.*), **EPA MRID # 435732-48**, DP Barcode: D219143

Conclusions: This study is scientifically sound and fulfills the guideline requirement for an acute contact/acute oral study with the honeybee. The acute contact **LD50** > 100 ug/bee and the acute oral **LD50** > 168.7 ug/bee. Technical isoxaflutole is considered practically nontoxic to honeybees.

If there are any questions regarding this data review contact Renée Costello at 305-5294.

Peer reviewers:

Mike Davy, Agronomist

F. Nicholas Mastrota, Wildlife Biologist F. Nicholas Mastrota 2/22/96

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DATA EVALUATION RECORD
DIATOM EC_{50} TEST
GUIDELINE 122-2 OR 123-2 (TIER II)

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

2. **TEST MATERIAL:** Isoxaflutole technical Purity: 96.8%

3. **CITATION**

Authors: James R. Hoberg
Title: RPA 201772 Technical - Acute Toxicity to the freshwater diatom, *Navicula pelliculosa*
Study Completion Date: March 22, 1994
Laboratory: Springborn
Sponsor: Rhone-Poulenc
Laboratory Report ID: 94-4-5243
DP Barcode: D219143
MRID No.: 435732-44

4. **REVIEWED BY:** Renée Costello, Biologist, ERCB, EFED

Signature: Renée Costello **Date:** 2/20/96

5. **REVIEWED BY:** Mike Davy, Agronomist, ERCB, EFED

Signature: Michael P. Davy **Date:** 2-26-96

6. **STUDY PARAMETERS**

Definitive Test Duration: 120 hours
Type of Concentrations: Nominal and initial measured

7. **CONCLUSIONS:**

Results Synopsis

EC_{50}: 0.38 mg ai/L 95% C.I.: 0.26 - 0.49 mg ai/L
NOEC: 0.0031 mg ai/L

8. **ADEQUACY OF THE STUDY**

A. Classification: Core

B. Rationale: N/A

C. Repairability: N/A

9. **GUIDELINE DEVIATIONS:** 1. Dose range progression was 30% in order to achieve an EC_{50} and an NOEC.

This deviation did not effect the results of the study.

10. **SUBMISSION PURPOSE:** Product registration.

11. **MATERIALS AND METHODS**

A. Test Organisms

Guideline Criteria	Reported Information
Species *Skeletonema costatum* *Anabaena flos-aquae* *Selenastrum capricornutum* *Navicula pelliculosa*	*Navicula pelliculosa*
Initial Number of Cells 3,000 - 10,000 cells/mL	10,000 cells/mL
Nutrients Standard formula, e.g. 20XAAP	Standard AAP medium

B. Test System

Guideline Criteria	Reported Information
Solvent	Acetone
Temperature Skeletonema: 20°C Others: 24-25°C	24 - 25°C
Light Intensity Anabaena: 2.0 KLux (±15%) Others: 4.0-5.0 KLux (±15%)	3200 - 4800 Lux
Photoperiod Skeletonema: 14 h light, 10 h dark or 16 h light, 8 h dark Others: Continuous	Continuous
pH Skeletonema: approx. 8.0 Others: approx. 7.5	7.2 - 8.5

C. Test Design

Guideline Criteria	Reported Information
Dose range 2X or 3X progression	30% in order to achieve an NOEC and EC_{50}
Doses at least 5	0.0024, 0.0081, 0.027, 0.090, 0.30, and 1.0 mg ai/L

Guideline Criteria	Reported Information
Controls negative and/or solvent	solvent and negative
Replicates per dose 3 or more	3
Duration of test 120 hours	120 hours
Daily observations were made?	Yes every 24 hours
Method of Observations	Cellular counts
Maximum Labeled Rate	0.18 lb ai/acre

12. REPORTED RESULTS

Guideline Criteria	Reported Information
Initial and 120 h cell densities were measured?	Yes
Control cell count at 120 hr ≥2X initial count?	> 2x from 24 hours
Initial chemical concentrations measured?	Yes
Raw data included?	Yes

Dose Response

Initial measured concentration (mg ai/L)	Mean Cell Density (x 10^4 cells/mL)	% Inhibition	120-Hour pH
Control	93	N/A	8.5
Solvent Control	96	N/A	8.5
0.0031	96	-1.5	8.3
0.0093	89	6.3	8.0
0.030	83	13	7.5
0.096	81	15	7.5
0.29	66	30	7.2

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0.64	12	87	7.2

Statistical Results

Statistical Method: William's test and linear regression

EC_{50}: 0.38 mg ai/L 95% C.I.: 0.26 - 0.49 mg ai/L
EC_{25}: 0.18 mg ai/L 95% C.I.: 0.066 - 0.29 mg ai/L
NOEC: 0.0031 mg ai/L

13. Verification of Statistical Results

Statistical Method: Nuthatch

EC_{50}: 0.36 mg ai/L 95% C.I.: 0.36 - 0.42 mg ai/L
EC_{25}: 0.28 mg ai/L 95% C.I.: 0.25 - 0.32 mg ai/L
NOEC: 0.0031 mg ai/L

NAV.DAT : 120 hour cell densities for navicula pelliculosa

Williams Test

[One-Sided Test for Decrease, alpha = 0.050000]

Dose	Isotone Means	T-bar	P-value	Significance
0	95.6	.		
0.0031	95.6	-0.2272	N.S.	
0.0093	89.3	2.317	0.018	*
0.03	82.7	5.043	<0.005	*
0.096	81.3	5.589	<0.005	*
0.29	66.3	11.72	<0.005	*
0.64	12	33.94	<0.005	*

"*"=Significant; "N.S."=Not Significant.

Estimates of EC%

Parameter	Estimate	95% Bounds Lower	95% Bounds Upper	Std.Err.	Lower Bound /Estimate
EC5	0.18	0.15	0.22	0.037	0.84
EC10	0.22	0.18	0.25	0.032	0.86
EC25	0.28	0.25	0.32	0.024	0.89
EC50	0.39	0.36	0.42	0.016	0.93

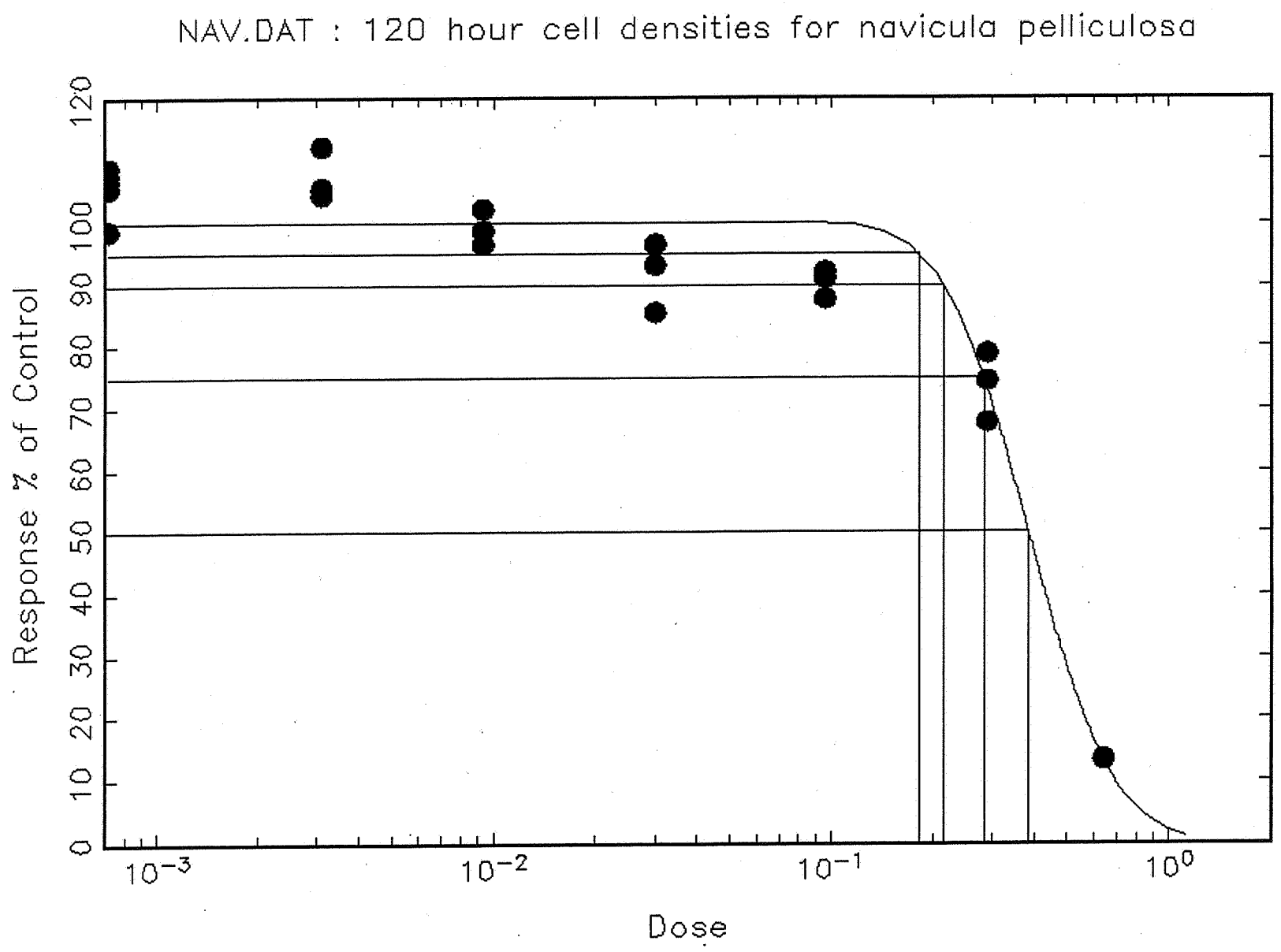
Slope = 5.05 Std.Err. = 0.387

!!!Poor fit: p < 0.001 based on DF= 4.00 17.0

NAV.DAT : 120 hour cell densities for navicula pelliculosa

Observed vs. Predicted Treatment Group Means

Dose	#Reps.	Obs. Mean	Pred. Mean	Obs. -Pred.	Pred. %Control	%Change
0.00	6.00	95.0	90.0	4.96	100.	0.00
0.00310	3.00	96.7	90.0	6.63	100.	1.58e-14
0.00930	3.00	89.3	90.0	-0.708	100.	1.58e-14
0.0300	3.00	82.7	90.0	-7.37	100.	1.04e-06
0.0960	3.00	81.3	89.9	-8.61	99.9	0.113
0.290	3.00	66.3	66.2	0.175	73.5	26.5
0.640	3.00	12.0	12.0	-0.0281	13.4	86.6


NAV.DAT : 120 hour cell densities for navicula pelliculosa
Response % of Control
0
10
20
30
40
50
60
70
80
90
100
120
10^{-3}
10^{-2}
10^{-1}
10^{0}
Dose

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DP Barcode: D219143 MRID No.: 435732-48

DATA EVALUATION RECORD
ACUTE CONTACT TOXICITY TEST WITH THE HONEY BEE
§ 141-1

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

2. **TEST MATERIAL:** RPA 201772 Purity: 96.8%

3. **CITATION**

Authors: Dr. Ralf Petto
Title: Laboratory testing for toxicity (acute contact and oral LD_{50}) of RPA 201772 to honeybees (*Apis mellifera L.*)
Study Completion Date: May 27, 1994
Laboratory: RCC Umweltchemie GmbH & Co KG, D-64380 RoBdorf
Sponsor: Rhone-Poulenc Agro
Laboratory Report ID: 463500
MRID No.: 435732-48
DP Barcode: D219143

4. **REVIEWED BY:** C. Renée Costello, Biologist, EFED

Signature: C. Renée Costello **Date:** 2/20/96

5. **REVIEWED BY:** F. Nicholas Mastrota, Wildlife Biologist, EFED

Signature: F. Nicholas Mastrota **Date:** 2/22/96

6. **STUDY PARAMETERS**

Test Species: *Apis mellifera L.*
Age of Test Organisms at Test Initiation: Similar age
Exposure Duration: 48 hours

7. **CONCLUSIONS:** Acute contact **LD50** >100 ug/bee
Acute oral **LD50** > 168.7 ug/bee
Toxicity category Practically nontoxic

8. **ADEQUACY OF THE STUDY**

A. **Classification:** Core

B. **Rationale:** N/A

C. **Repairability:** N/A

9. **GUIDELINE DEVIATIONS:** N/A

10. 10. **SUBMISSION PURPOSE:** Registration.

11. MATERIALS AND METHODS

A. Test Organisms

Guideline Criteria	Reported Information
Species	Honey Bee (*Apis mellifera L.*)
Age at beginning of test Worker bees of uniform age.	Worker bees of similar age
Source	RCC
Were bees from disease-free colonies?	Not reported
Were bees kept in conditions conforming to proper cultural practices?	Yes

B. Test System

Guideline Criteria	Reported Information
Test Chambers	Stainless steel (10 x 8.5 x 5.5 cm). Front closed with removable glass sheets, bottom with perforated ventilation holes. Top had 2 openings for food, inner sides were covered with filter paper.
Temperature during exposure	26 to 28°C
Relative humidity during exposure	54 to 64%
Lighting	Darkness except for observation period.
Feeding	No food for 1-2 hours prior to testing; then *ad libitum*.

C. Test Design

Guideline Criteria	Reported Information
Nominal dosage levels tested	Contact test: 100, 50, 25, 12.5, and 6.25 ug/bee Oral test: 168.7. 68.4, 33.8, 19.4, and 11.2 ug/bee
Number of bees exposed per dosage level	30
Other experimental design information	10 bees/chamber; 3 reps
Bees randomly or impartially assigned to test groups	Not reported
Control	Solvent, untreated and positive control (dimethoate).
Solvent control	Acetone/ready to use syrup 20 µl per bee (this is in excess of the recommended amount of 5 ul per bee).
Total observation period and frequency of interim observations	48 hours total, continuous for 1st 30 minutes, then 45 and 60 minutes, 2 hours, and 4 hours 1st day, then 24 hours, 48 hours the 2nd day.

12. REPORTED RESULTS

Guideline Criteria	Reported Information
Quality assurance and GLP compliance statements were included in the report?	Yes
Observed adverse effects on bees at respective dosages	Contact test: the only mortalities occurred in the positive control (100% after 4 hours). No behavioral anomalies. Oral test: No mortalities with the exception of the positive control (100% after 2 hours). Increased cleaning behavior at all levels until the 4 hour check, then nothing abnormal.
Control and Solvent Control Mortality	0%
Were raw data included?	Yes

Mortality and Observations

No mortalities with the exception of the positive control (contact test 100% after 4 hours; oral test 100% after 2 hours).

Agency Statistical Analysis

Visual observation.

10.

RHÔNE-POULENC

RHÔNE-POULENC AG COMPANY

February 14, 1996

RENEE,
HOPE THIS
HELPS!
-DAN

Mr. Dan Kenny
U.S. Environmental Protection Agency
Office of Pesticide Programs
Registration Division
Crystal Mall Building 2, Room 266A
1921 Jefferson Davis Highway
Arlington, VA 22202

Dear Mr. Kenny:

Re: Technical Isoxaflutole, EPA File Symbol 264-LAA, PP# 6F4664
Honeybee Acute Toxicity Study

This letter is in response to the reviewer's question regarding the purity of the active ingredient used as test material in the isoxaflutole (RPA 201772) honeybee acute toxicity study (Study no. 463500, RCC), MRID no. 43573248. We have reviewed the study and found that there was a transcription error in reporting the purity of the test material. The purity should be reported as 968 g/kg instead of 968 kg/kg as stated in the final report. Enclosed is a copy of the certificate of analysis which corresponds to the batch of test product used in the study.

If you have any questions, please contact me at telephone number 919-549-2365.

Sincerely,

Karen S. Shearer

Karen S. Shearer
Registration Manager

kss/96/033

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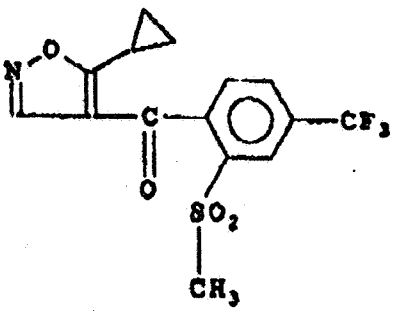
CERTIFICATE OF ANALYSIS

Active Ingredient

Name or Code : RPA201772

Alias :



Storage Log N° : DA874

Chemical Name (IUPAC) : 5-cyclopropyl-4-(2-methylsulfonyl-4-trifluoromethylbenzoyl) isoxazole

Molecular Weight : 359.53 N° Cas :

Location of Synthesis : DECINES

Synthesis Batch N° : 39 ADM 93

Purity : 968 g/Kg Appearance : yellow powder

Date of Analysis : 25/06/93 Reference of Analysis : AMA1966

Date of Retest : 25/06/95

- Storage Conditions -	- Toxicity Classification -
Store at about ambient	Xn R20/21/22
Date of Emission : Jun 25, 1993 Certificate N° : AGMA93621	I certify that this material was analyzed in a laboratory following Good Laboratory Practice Standards. The characterization data for this material are archived at RHONE-POULENC Secteur Agro-LYON-FRANCE. File Location : A489 Authorization : Name and Signature : J.COUSIN

END

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