EPA Reg # 86865-1

NEW ACTIVE INGREDIENT (a.i.) OR FIRST FOOD USE OF OLD a.i. REGISTRATION APPLICATION CHECKLIST

Name of active ingredient: _____

EPA File Symbol/Reg. No. of product reviewed: _____

Date: _____

Note: If a section is not applicable to the application you are reviewing, write N/A.

NEW ACTIVE INGREDIENT SCREEN (ADMINISTRATIVE)

Did the application pass front end and PR Notice 86-5 screens? **YES___NO___**
If yes, enter into OPPIN, and proceed to do the RAL (PM) screen
If no, transfer deficient data to Team Leader or write to the registrant regarding deficiencies.

NEW ACTIVE INGREDIENT SCREEN (RAL/SCIENCE)

1. **Is the Application Form dated, signed and complete including:** **YES __ NO __**
   a) package size and type? YES __ NO __
   b) CRP certification? YES __ NO __

2. **Has the biochemical classification committee made a decision on classification and/or data requirements?** **YES __ NO __**

3. **Is proposed use a food or feed use?** **YES___ NO __**
   If yes, is there a petition for residue tolerance or exemption? (refer to tolerance petition checklist)
   If no, contact the applicant and indicate that the application is incomplete without a petition.

4. **Have tolerance petition fees been duly paid?** **YES___ NO___**
   If yes, refer to the tolerance petition checklist
   If no, wait for the fees to be deposited before putting data into review.

5. **Are all data requirements, as listed in 40 CFR adequately addressed?** **YES___ NO___**
   If Yes, inform the registrant about the screen outcome, prepare a Notice of Receipt in the Federal Register for the section 3 product application(s), and proceed to send the data for review.
   If No, write to the registrant regarding deficiencies.

Note: ***Do not publish Notice of Receipt or Notice of Filing until after the package passes new***

chemical screen

DATA REVIEW

1. Data segregated according to discipline	**YES___ NO___**
2. Data package bean sheets created in OPPIN for each discipline	**YES___ NO___**
3. Adequate instructions written in bean sheet for science reviewer	**YES___ NO___**
4. Efficacy data needed for public health uses	**YES___ NO___**

RAL PRELIMINARY DECISION

3.	Look over science reviews	YES ___ NO ___
4.	Additional data needed; if so, request it in a letter	YES ___ NO ___
5.	Label review	
a)	Agree with current Label Review Manual	YES ___ NO ___
b)	Acute toxicology, product chemistry, and efficacy data examined for labeling	YES ___ NO ___
c)	Nominal concentration of a.i. listed in ingredients statement (chemist's responsibility)	YES ___ NO ___
d)	Storage and disposal instructions agree with container types listed on application form	YES ___ NO ___
e)	Directions for use agree with container sizes on application form	YES ___ NO ___
6.	Confidential Statement of Formula review.	
a)	Completely filled out including pH, flashpoint, flammability, etc., if applicable	YES ___ NO ___
b)	Totals are accurate (everything adds up to 100%)	YES ___ NO ___
c)	Certified limits agree with 40 CFR 158.175 or 5 batch analysis	YES ___ NO ___
d)	PC codes assigned on CSF for inerts and 40 CFR 180.1001c, d, or e codes noted for products that have food or feed uses	YES ___ NO ___
e)	No inerts on list 1 present	YES ___ NO ___

f) **CSF is signed (original) and dated** **YES __ NO __**

7. Prepare a Biopesticide Registration Action Document (BRAD)

a) Review public comments in response to tolerance petition, Notice of Filing FR Notice and Application Receipt FR Notice

b) Write Biopesticide Registration Action Document (BRAD) using the following format:

I. Executive Summary

A. IDENTITY
B. USE/USAGE
C. RISK ASSESSMENT
D. DATA GAPS / LABELING RESTRICTIONS

II. Chemical Overview

A. ACTIVE INGREDIENT OVERVIEW
B. USE PROFILE
C. ESTIMATED USAGE
D. DATA REQUIREMENTS
E. REGULATORY HISTORY
D. FOOD CLEARANCES/TOLERANCES

III. Science Assessment

A. PHYSICAL/CHEMICAL PROPERTIES ASSESSMENT
1. **Product Identity and Mode of Action**
2. **Food Clearances/Tolerances**
3. **Physical and Chemical Properties Assessment**

B. HUMAN HEALTH ASSESSMENT
1. **Toxicology Assessment**
   a. **Acute Toxicology**
   b. **Subchronic and Chronic Tests**
   c. **Effects on Immune and Endocrine Systems**
2. **Dose Response Assessment**
3. **Dietary Exposure and Risk Characterization**
4. **Occupational, Residential, School and Day care Exposure and Risk Characterization**
5. **Drinking Water Exposure and Risk Characterization**
6. **Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and Children**

7. **Aggregate Exposure from Multiple Routes Including Dermal, Oral, and Inhalation**

C. ENVIRONMENTAL ASSESSMENT

1. **Ecological Effects Hazard Assessment**
2. **Environmental Fate and Ground Water Data**
3. **Ecological Exposure and Risk Characterization**

D. EFFICACY DATA

IV. Risk Management Decision

A. DETERMINATION OF ELIGIBILITY FOR REGISTRATION

B. REGULATORY POSITION

1. **Conditional/Unconditional Registration**
2. **Tolerance Reassessment**
3. **CODEX Harmonization**
4. **Nonfood Registrations**
5. **Risk Mitigation**
6. **Endangered Species Statement**

C. LABELING RATIONALE

1. **Human Health Hazard**
   a. **Worker Protection Standard**
   b. **Non-Worker Protection Standard**
   c. **Precautionary Labeling**
   d. **Spray Drift Advisory**
2. **Environmental Hazards Labeling**
   a. **End-Use Product Environmental Hazards Labeling**
   b. **Manufacturing-Use Product Environmental Hazard Labeling**

D. LABELING

e) Public Interest Finding (if a Conditional registration)

VI. Actions Required by Registrants

..... end of BRAD outline .....

6. Prepare Plain English Fact Sheet (PEF) - Have the PEF Coordinator sign-off on the "final" PEF. (Alan Reynolds will sign-off if Barbara is not available.) Attach to PEF a Buck Slip with the sign-off. Send electronic version of PEF to PEF Coordinator. YES __ NO __

7. Prepare Final Rule for tolerance establishment (refer to tolerance petition checklist) YES __ NO __

8. Route both Biopesticide Registration Action Document (BRAD) and draft Final Rule for science Reviewers, OGC, YES __ NO __

concurrence (Note: OGC has two weeks to review)

9. Prepare Decision Memorandum from Division Director To Deputy Office Director for signature — YES __ NO __

10. Send the whole package containing: DECISION MEMORANDUM, concurrence sheet, draft label(s), PEF, and BRAD for Branch Chief & DD concurrence, and DOD's signature — YES __ NO __

11. DOD signs off on Biopesticide Registration Action Document and Final Rule; Final Rule published — YES __ NO __

12. Prepare Notice of Registration for DD's signature (This step can proceed before actual publication of final rule.) — YES __ NO __

13. 30 Day Comment Period: Have the risk assessments been placed on the web for public comment for 30 days

YES __ NO __

Post Registration Activities

1. Inform PEF Coordinator that Registration has been issued and provide any changes to PEF from management review. PEF Coordinator will forward revised PEF to WebMaster for posting on the Website and will post PEF in share directory. — YES __ NO __

2. Stamp labels when Reg Notice is signed (Note: Be sure not to obliterate any part of the label text with stamp; only use "white" space.) — YES __ NO __

3. Mail Reg Notice and stamped label to registrant. Also, send copies of reviews and BRAD (with notice about checking for CBI before posting of BRAD on BPPD's Webpage) to registrant — YES __ NO __

4. Prepare and submit a "Weekly Report" item. — YES __ NO __

5. Prepare FR Notice announcing registration of new a.i. registration. **(Send to the FR Staff an electronic file of Registration Approval Notice.)** — **YES __ NO __**

6. Once registrant has agreed, post BRAD to BPPD's User Share and send electronic version of cleared BRAD to BPPD WebMaster for posting on the BPPD Website. — YES __ NO __

7. Close all records in OPPIN — YES __ NO __

8. File administrative materials, reviews, BRAD, PEF, Notice of Registration, and label in jacket. Return jacket to file room with note for transfer to SIG for coding. YES __ NO __

9. Place two copies of label(s) in "New Label" box for filing in BPPD's label file. YES __ NO __

10. Place a copy of Notice of Registration in chron file box YES __ NO __

11. Provide BPPD Gatekeeper with electronic copies of reviews, BRAD, PEF, and Notice of Registration. Don't forget to segregate CBI. YES __ NO __

12. Type of Registration: Unconditional____ Conditional_____

13. Does this registration have terms/conditions (ex: storage stability data)? YES __ NO _
IF THE REGISTRATION HAS TERMS/CONDITIONS THIS INFORMATION MUST BE ENTERED INTO THE LOGBOOK For BPPD Registrations with Terms/Conditions FOR THE APPROPRIATE BRANCH.

14. If there are term/conditions to the registration notice has this information been placed in the LOGBOOK For BPPD Registrations with Terms/Conditions
YES __ NO _

THE PLAYERS

BPPD Gatekeeper = Diana Hudson

BPPD WebMaster = Jim Skaptason

FR Staff (contact) = E-mail via Lotus Notes to: OPPTS FRStaff@EPA
FR Templates: http://intranet.epa.gov/oppthome/intrafrs/opptempl.htm#biopesticides (Linda Hollis coordinates for BPPD)

PEF Coordinator = Barbara Mandula (backup is Alan Reynolds)

Format for New Active Ingredient Decision Package

Left Panel	Center Panel	Right Panel
Two original (printed on Letterhead) Decision Memos with plastic *Executive Correspondence* cover Yellow concurrence sheet showing on bottom	Two complete copies of the Biopesticide Registration Action Document (include OGC Concurrence)	Two copies of the Plain English Fact Sheet (attach a Buck Slip signed by Barbara Mandula or Alan Reynolds - to be removed by BC before package goes on to OD's office) Label(s) - MUP and/or EP as appropriate

Note: The extra copies of the Decision Memo, BRAD, and PEF are for the OD's office.

Of course, if the new a.i. involves a food use, a separate tolerance/exemption rule package should accompany this package.

Label Review

File Symbol: _____ **Date:** ____/_____/_____ **Reviewer:**_____

[Site/Use]	[Res /Ag /Both] [Food /Non-Food /Both]				
[Tox Categories:]	[AcOral: /AcDerm: /AcInhl: /EyeIrr: /SkinIrr: DermSens:]				
Label Requirement	**Acceptable**	**Not Acceptable**	**N/A**	**Comments Recommendations**	**LRM3**
Restricted Use Pesticide	----------	----------	-----		**Ch 6**
Product Name					Pg 12-3
Compny Name and Info					Pg 15-1
Identification Numbers					**Ch 14**
Net Contents					**Ch 17**
Ingredients Statement					**Ch 5**
Label Claims					Pgs 4-5, 5-7 11-10 & **Ch 12**
Alternate Formula					5-12

Precautionary Statements					
Label Requirement	**Acceptable**	**Not Acceptable**	**N/A**	**Comments Recommendations**	**LRM3**
KOROC					3-1 & 9 7-3 & 4
Signal Word					**Ch 3 Ch 7** **Ch 10**
General Heading >PRECAUTIONARY STATEMENTS=					Ch 7
First Aid (PRN 20001-1)					**Ch 3 & 7**

Hazards to Humans and Domestic Animals					**Ch 3**, 7-3
PPE (WPS) Engineering Controls					Ch 7, Pg 7-12 Pgs 10-4, 15
User Safety Requirements					Ch 10
User Safety Recommendations					Ch 10
Environmental Hazards					Ch 8
Physical and Chemical Hazards					Pg 3-4 **Ch 9**

Directions for USE (FIFRA Text, WPS plus Storage and Disposal					
Label Requirement	Acceptable	Not Acceptable	N/A	Comments Recommendations	LRM3
Header >Directions for Use=					10-16
Violation of Federal Law text					10-26, 11-7
WPS Text (PPE)					Ch 10, 7-t 7-11
Non-WPS Text					7-12, Ch 10
Pesticide Storage and Disposal					11-16, Ch 13
Container Disposal & Batch Code					PRN 2007-4

Directions for Use (General Instructions and Information)					
Label Requirement	Acceptable	Not Acceptable	N/A	Comments Recommendations	LRM3
General Instructions and Sub-Header					
Chemigation / Prohibition					PRN
REI					Pg 10-20

Label Requirement	Acceptable	Not Acceptable	N/A	Comments Recommendations	LRM3
General Info. (non-site specific info. on uses, pests, mixing, and loading, tank mixing, etc.)					
General Precautions and Restrictions					
Directions for Use					
Directions for Application					
Warranty Information					
Consistency with label instructions					12-6
Not false or misleading					

"The warranty section contains an overly broad statement concerning limitations of liability. As such, this statement may be misleading and may constitute misbranding under the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA). It is suggested that the existing statement be preceded by the phrase, Ato the extent allowable by state law@, or otherwise qualified to make it clear that this warranty is not intended to be a statement of law which implies that the buyer has no legal rights to recover damages from the manufacturer if he/she suffered a loss or injury from the product and concludes that it would be futile to pursue what might in reality be a valid claim."

U.S. Environmental Protection Agency

Office of Pesticide Programs Information Network

ERROR REPORTING
- Report Data Errors

DETAILS
- Summary
- Registrations
- Sites / Pests
- Sites / Pests Unique
- Unique Approved Sites
- DCIs / REDs
- Tolerance Petitions
- Tolerances
- Data Requirements
- Data Requirements by Company
- Studies
- Attributes
- Synonyms
- Final Label Review

Back to Query

SUMMARY REPORTS
- Ingredients

OPTIONS
- Help
- Logout

Results

2 Items Found

PC Code
1) 000207
2) 800207

Summary Information For *Ingredient 000207 / 110-27-0 / Isopropyl myristate*

PC Code:	000207
CAS #:	110-27-0
Name:	Isopropyl myristate
Classification:	ESTER
Reregistration Case:	
Pesticide Category:	
Pesticide Type:	Antimicrobial
Active Ingredient?:	Y
Inert?:	N
First Registered Date:	31-Oct-1986
Current Status:	
Last Product Cancelled:	8082-2, 31-Dec-1987 7745-3, 31-Dec-1987

Risk Managers

Risk Manager	Team	Phone Number
Hutton, Phillip	RM 91	(703) 308-8260
Reilly, Sheryl	RM 91	(703) 308-8269
Torla, Robert	RM 91	(703) 308-8098
Hollis, Linda	RM 91	(703) 308-8733
Skaptason, James	RM 91	(703) 605-0584
Total Rows: 5		

Comments

Comment

Synonym Information For Ingredient
000207 / 110-27-0 / Isopropyl myristate

Name	Type
Isopropyl myristate	Other Common
Revenge, component of (with 000208 and 000209)	Trade
Tetradecanoic acid, 1-methylethyl ester	Other Systematic
Total Rows: 3	

ISB'S Front-end PRIA Completeness Screen

Draft 3; 10/25/07

EPA Receipt Date: DEC - 3 2009		EPA Reg. Number: 86865-R		
	Check List Item	Yes	No	N/A
1	Has the **PRIA Fee been Paid**; is a copy of the check or Pay.gov receipt included in the Submission Package? (FW)	X		
2	Is an **Application Form** (EPA Form 8570-1) Included in the Submission Package, is it completely filled out and signed including package type?	X		
3	Is a **Confidential Statement of Formula** (EPA Form 8570-29) Included in the Submission Package, is it completely filled out and signed (boxes 1-21)?	X		
4	Is a **Formulator's Exemption Statement** (EPA Form 8570-27) Included in the Submission Package?		X	
5	Is a **Certification with Respect to Citation of Data** (EPA Form 8570-34) Included in the Submission Package?		X	
6	Is a **Data Matrix** (EPA Form 8570-35) Included in the Submission Package?	X		
7	Is a **Label** Included in the Submission Package?	X		
8	Are **Data** Included in the Submission Package?	X		
9	**Is the Submission an Amendment?**		X	

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division
(7511P)
1200 Pennsylvania Avenue NW
Washington, DC 20460

EPA Reg. Number:	Date of Issuance:
86865-1	AUG 25 2011
Term of Issuance:	UNCONDITIONAL
Name of Pesticide Product:	Resultix™

NOTICE OF PESTICIDE:

__XX___ Registration ____ Re-registration
(under FIFRA, as amended)

Name and Address of Registrant (include ZIP Code):

Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Biopesticides and Pollution Prevention Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is unconditionally registered in accordance with FIFRA Sec. 3(c) provided you:

1. Submit and/or cite all data required for registration/ reregistration of your product under FIFRA section 3(c)(5) and section 4 when the Agency requires all registrants of similar products to submit such data.

2. Make the following label change before you release the product for shipment: Revise the EPA Registration Number to read, **"EPA Reg. No. 86865-1".**

3. Submit three (3) copies of the revised final printed labeling before you release the product for shipment.

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA Section 6(e). Your release for shipment of the product constitutes acceptance of these conditions. A stamped copy of the label is enclosed for your records.

Signature of Approving Official:

Keith A. Matthews, Director
Biopesticides and Pollution Prevention Division

Date: 25 August 2011

CONCURRENCES

SYMBOL ▶		7511P	7511P					
SURNAME ▶		Gaze	Hess					
DATE ▶		8/17/11	8/25/11					

EPA Form 8570-6

*U.S. Government Printing Office 2005

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

MEMORANDUM

SUBJECT: Consideration of a Section 3(c) (5) Unconditional Registration of a new active ingredient isopropyl myristate (PC Code 000207), EPA Identifying Symbol 86865-1.

----------**DECISION MEMORANDUM**----------

FROM: Keith A. Matthews, Director
Biopesticides and Pollution Prevention Division

TO: Steven Bradbury, Ph.D., Director
Office of Pesticide Programs

I. ISSUE

Should the Agency, under Section 3(c)(5) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), grant unconditional registrations for the new active ingredient isopropyl myristate (PC Code 000207), which is proposed for indoor use as a pediculocide on cats and dogs.

II. APPLICATION INFORMATION

On December 3, 2009, EPA received an application filed by Piedmont Animal Health, (204 Muirs Chapel Road, Suite 200, Greensboro, NC 27410) to register an end-use product (EP) containing the new active ingredient isopropyl myristate to kill ticks on cats and dogs. RESULTIX™, the EP, contains 50.0 % isopropyl myristate as an active ingredient. A notice of receipt of this application, allowing for a 30-day comment period, was published in the Federal Register on March 10, 2010 (75FR11175). No comments were received following this publication.

III. BACKGROUND AND CONCLUSIONS

The Biopesticides and Pollution Prevention Division (BPPD) reviewed the submitted data and information regarding the proposed use of isopropyl myristate. Evaluations of the data and conclusions are summarized and discussed in the attached Biopesticide Registration Action Document (BRAD).

The registration application was reviewed pursuant to the requirements of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Based on that review, BPPD determined that isopropyl myristate has a non-toxic mode of action and is generally effective at very low application rates. BPPD further determined that no unreasonable adverse effects to humans or the environment will result from the use of isopropyl myristate if used in accordance with label directions.

RCURRENCES								
	7511P							
	Greene							
	August 24, 2011							

Form 1320-1A(1/90)

OFFICIAL FILE COPY

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

IV. OFFICE DIRECTOR CONCURRENCE

Based on the discussion above, and the data and information presented in the attached BRAD, the Biopesticides and Pollution Prevention Division recommends unconditional registration of isopropyl myristate as an indoor insecticide to kill ticks on cats and dogs.

Concurrence: _____

Non-Concurrence: _____

Date: 8/25/11

CONCURRENCES								
➤	7511P							
➤	Greene							
➤	August 24, 2011							

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

AUG 25 2011

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

SUBJECT: Consideration of a Section 3(c) (5) Unconditional Registration of a new active ingredient isopropyl myristate (PC Code 000207), EPA Identifying Symbol 86865-1.

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FROM: Keith A. Matthews, Director
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The registration application was reviewed pursuant to the requirements of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Based on that review, BPPD determined that isopropyl myristate has a non-toxic mode of action and is generally effective at very low application rates. BPPD further determined that no unreasonable adverse effects to humans or the environment will result from the use of isopropyl myristate if used in accordance with label directions.

IV. OFFICE DIRECTOR CONCURRENCE

Based on the discussion above, and the data and information presented in the attached BRAD, the Biopesticides and Pollution Prevention Division recommends unconditional registration of isopropyl myristate as an indoor insecticide to kill ticks on cats and dogs.

Concurrence: Steve Bradbury

Non-Concurrence: _____

Date: 8/25/11

FRONT PANEL

RESULTIX™

Kills Ticks on Dogs and Cats

ACTIVE INGREDIENT	
Isopropyl Myristate	50.0%
OTHER INGREDIENT	50.0%
TOTAL	100.0%

KEEP OUT OF REACH OF CHILDREN

CAUTION

See Side/Back Panel for First Aid

STOP - READ LABEL BEFORE USE

EPA Reg. No. 86865-R

EPA Est. No. 71979-SC-001

Manufactured for
Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410
1-336-544-0320 x 207

NET CONTENTS
20 mL (0.65 oz.)

ACCEPTED

AUG 24 2011
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 86865-1

SIDE PANEL

FIRST AID

If on skin:	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor immediately for treatment advice.
If in eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. • Call a poison control center or doctor immediately for treatment advice.
If inhaled:	• Move person to fresh air. • If person is not breathing, call 911 or an ambulance; then give artificial respiration, preferably mouth-to-mouth if possible. • Call a poison control center or doctor immediately for treatment advice.
If swallowed:	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by a poison control center or doctor. • Do not give anything by mouth to an unconscious person.

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-222-1222 (American Association of Poison Control Centers) any time day or night for emergency medical treatment information.

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION. May cause dermal and eye irritation. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet.

ENVIRONMENTAL HAZARDS

This pesticide is toxic to invertebrates and fish. Do not discharge this product into lakes, streams, ponds, estuaries, oceans, or other waters where aquatic invertebrates or fish may be found.

BACK PANEL

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

RESULTIX™, when used as instructed below, will dissolve the outer wax layer coving the hard shell (cuticle) of the tick resulting in uncontrollable water loss and death of the tick.

For the removal and killing of attached and crawling ticks on dogs and cats

APPLICATION AND USE INSTRUCTIONS

For external use only.

Do not use near dog's or cat's eyes.

Do not use on irritated skin.

Stop treatment with this product and consult a veterinarian if skin irritation or skin infection develops during use of product.

- Use when you see a tick or ticks on your dog or cat.
- Remove cap and hold bottle upright. Direct nozzle at tick and spray until tick is covered with solution (2 sprays).
- The tick will be dead within 3 hours; it will fall off of the dog or cat or will be immobile when removed.
- If tick falls off indoors within 3 hours of application, carefully pick up and dispose of tick using gloves or tweezers.
- After 3 hours, if the tick has not fallen off, remove carefully with gloves or tweezers and dispose of tick.
- Dispose of ticks by placing in sealable plastic bag, sealing the bag, and placing it in an outdoor garbage can.
- Wash hands after accidental exposure to any ticks.

STORAGE AND DISPOSAL

Do not contaminate water, food, or feed by storage and disposal.

Pesticide Storage:

Store in a dry place away from extreme heat and cold (tightly closed between 59° F – 86° F (15° C – 30° C). Keep container closed when not in use. Always store pesticide in the original container. Store away from food and pet food. Keep away from open flames.

In case of fire or other emergency, report at once by toll-free telephone to CHEMTREC (800-424-9300).

Pesticide Disposal and Container Handling:

Nonrefillable container. Do not reuse or refill this container.
When empty: place in trash or offer for recycling if available.
Never place unused product down any indoor or outdoor drain.

NOTICE: Seller warrants that the product conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use. To the extent permitted by applicable law, this warranty or any other warranty of merchantability or fitness for a particular purpose, express or implied, does not extend to the use of this product contrary to label instructions, or under abnormal conditions, or under conditions not reasonably foreseeable to Seller. To the extent permitted by applicable law, buyer assumes the risk of any such use.

ANY PANEL (Do not substitute these for required statements)

Label Claims (one or more in various combinations, located in various places throughout the box and bottle/insert labels)

Breakthrough in tick killing for attached and crawling ticks

Convenient and easy to apply

For the Killing of Ticks on Dogs and Cats

Free of conventional pesticides

Patented spray formula softens the waterproof outer waxy layer of the tick's body, resulting in dehydration

Direct spray formula is safe to use on pets

Can be used as often as needed

Can be part of your tick prevention regimen

Tick Killing Solution™

NEW ACTIVE INGREDIENT (a.i.) OR FIRST FOOD USE OF OLD a.i. REGISTRATION APPLICATION CHECKLIST

Name of active ingredient: Isopropyl Myristate

EPA File Symbol/Reg. No. of product reviewed: 86865-1

Date: 8/22/11

Note: If a section is not applicable to the application you are reviewing, write N/A.

NEW ACTIVE INGREDIENT SCREEN (ADMINISTRATIVE)

Did the application pass front end and PR Notice 86-5 screens? YES ✓ NO ___
If yes, enter into OPPIN, and proceed to do the RAL (PM) screen
If no, transfer deficient data to Team Leader or write to the registrant regarding deficiencies.

NEW ACTIVE INGREDIENT SCREEN (RAL/SCIENCE)

1. **Is the Application Form dated, signed and complete including:** YES ✓ NO ___
   a) package size and type? YES ✓ NO ___
   b) CRP certification? YES ✓ NO ___

2. **Has the biochemical classification committee made a decision on classification and/or data requirements?** YES ✓ NO ___

3. **Is proposed use a food or feed use?** YES ___ NO ✓
   If yes, is there a petition for residue tolerance or exemption? (refer to tolerance petition checklist)
   If no, contact the applicant and indicate that the application is incomplete without a petition.

4. **Have tolerance petition fees been duly paid?** N/A YES ___ NO ✓
   If yes, refer to the tolerance petition checklist
   If no, wait for the fees to be deposited before putting data into review.

5. **Are all data requirements, as listed in 40 CFR adequately addressed?** YES ✓ NO ___
   If Yes, inform the registrant about the screen outcome, prepare a Notice of Receipt in the Federal Register for the section 3 product application(s), and proceed to send the data for review.
   If No, write to the registrant regarding deficiencies.

Note: ***Do not publish Notice of Receipt or Notice of Filing until after the package passes new***

chemical screen

DATA REVIEW

1. Data segregated according to discipline	**YES** ✓ **NO** ___
2. Data package bean sheets created in OPPIN for each discipline	**YES** ✓ **NO** ___
3. Adequate instructions written in bean sheet for science reviewer	**YES** ✓ **NO** ___
4. Efficacy data needed for public health uses	**YES** ✓ **NO** ___

RAL PRELIMINARY DECISION

3.	Look over science reviews	YES ✓ NO ___
4.	Additional data needed; if so, request it in a letter Done	YES ✓ NO ___
5.	Label review	
a)	Agree with current Label Review Manual	YES ✓ NO ___
b)	Acute toxicology, product chemistry, and efficacy data examined for labeling	YES ✓ NO ___
c)	Nominal concentration of a.i. listed in ingredients statement (chemist's responsibility)	YES ✓ NO ___
d)	Storage and disposal instructions agree with container types listed on application form	YES ✓ NO ___
e)	Directions for use agree with container sizes on application form	YES ✓ NO ___
6.	Confidential Statement of Formula review.	
a)	Completely filled out including pH, flashpoint, flammability, etc., if applicable	YES ✓ NO ___
b)	Totals are accurate (everything adds up to 100%)	YES ✓ NO ___
c)	Certified limits agree with 40 CFR 158.175 or 5 batch analysis	YES ✓ NO ___
d)	PC codes assigned on CSF for inerts and 40 CFR 180.1001c, d, or e codes noted for products that have food or feed uses	YES ✓ NO ___
e)	No inerts on list 1 present	YES ✓ NO ___

f) **CSF is signed (original) and dated** **YES ✓ NO __**

7. Prepare a Biopesticide Registration Action Document (BRAD)

a) Review public comments in response to tolerance petition, Notice of Filing FR Notice and Application Receipt FR Notice

b) Write Biopesticide Registration Action Document (BRAD) using the following format:

I. Executive Summary

A. IDENTITY
B. USE/USAGE
C. RISK ASSESSMENT
D. DATA GAPS / LABELING RESTRICTIONS

II. Chemical Overview

A. ACTIVE INGREDIENT OVERVIEW
B. USE PROFILE
C. ESTIMATED USAGE
D. DATA REQUIREMENTS
E. REGULATORY HISTORY
D. FOOD CLEARANCES/TOLERANCES

III. Science Assessment

A. PHYSICAL/CHEMICAL PROPERTIES ASSESSMENT
1. **Product Identity and Mode of Action**
2. **Food Clearances/Tolerances**
3. **Physical and Chemical Properties Assessment**

B. HUMAN HEALTH ASSESSMENT
1. **Toxicology Assessment**
   a. **Acute Toxicology**
   b. **Subchronic and Chronic Tests**
   c. **Effects on Immune and Endocrine Systems**
2. **Dose Response Assessment**
3. **Dietary Exposure and Risk Characterization**
4. **Occupational, Residential, School and Day care Exposure and Risk Characterization**
5. **Drinking Water Exposure and Risk Characterization**
6. **Acute and Chronic Dietary Risks for Sensitive Subpopulations Particularly Infants and Children**

7. **Aggregate Exposure from Multiple Routes Including Dermal, Oral, and Inhalation**

C. ENVIRONMENTAL ASSESSMENT

1. **Ecological Effects Hazard Assessment**
2. **Environmental Fate and Ground Water Data**
3. **Ecological Exposure and Risk Characterization**

D. EFFICACY DATA

IV. Risk Management Decision

A. DETERMINATION OF ELIGIBILITY FOR REGISTRATION

B. REGULATORY POSITION

1. **Conditional/Unconditional Registration**
2. **Tolerance Reassessment**
3. **CODEX Harmonization**
4. **Nonfood Registrations**
5. **Risk Mitigation**
6. **Endangered Species Statement**

C. LABELING RATIONALE

1. **Human Health Hazard**
   a. **Worker Protection Standard**
   b. **Non-Worker Protection Standard**
   c. **Precautionary Labeling**
   d. **Spray Drift Advisory**
2. **Environmental Hazards Labeling**
   a. **End-Use Product Environmental Hazards Labeling**
   b. **Manufacturing-Use Product Environmental Hazard Labeling**

D. LABELING

e) Public Interest Finding (if a Conditional registration)

VI. Actions Required by Registrants

..... end of BRAD outline .....

6. Prepare Plain English Fact Sheet (PEF) - Have the PEF Coordinator sign-off on the "final" PEF. (Alan Reynolds will sign-off if Barbara is not available.) Attach to PEF a Buck Slip with the sign-off. Send electronic version of PEF to PEF Coordinator. YES ✓ NO __

7. Prepare Final Rule for tolerance establishment N/A (refer to tolerance petition checklist) YES __ NO __

8. Route both Biopesticide Registration Action Document (BRAD) and draft Final Rule for science Reviewers, OGC, YES ✓ NO __

concurrence (Note: OGC has two weeks to review)

9. Prepare Decision Memorandum from Division Director To Deputy Office Director for signature — YES ✓ NO __

10. Send the whole package containing: DECISION MEMORANDUM, concurrence sheet, draft label(s), PEF, and BRAD for Branch Chief & DD concurrence, and DOD's signature — YES __ NO __

11. DOD signs off on Biopesticide Registration Action Document and Final Rule; Final Rule published — YES __ NO __

12. Prepare Notice of Registration for DD's signature (This step can proceed before actual publication of final rule.) — YES __ NO __

13. 30 Day Comment Period: Have the risk assessments been placed on the web for public comment for 30 days

YES __ NO __

Post Registration Activities

1. Inform PEF Coordinator that Registration has been issued and provide any changes to PEF from management review. PEF Coordinator will forward revised PEF to WebMaster for posting on the Website and will post PEF in share directory. — YES __ NO __

2. Stamp labels when Reg Notice is signed (Note: Be sure not to obliterate any part of the label text with stamp; only use "white" space.) — YES __ NO __

3. Mail Reg Notice and stamped label to registrant. Also, send copies of reviews and BRAD (with notice about checking for CBI before posting of BRAD on BPPD's Webpage) to registrant — YES __ NO __

4. Prepare and submit a "Weekly Report" item. — YES __ NO __

5. Prepare FR Notice announcing registration of new a.i. registration. **(Send to the FR Staff an electronic file of Registration Approval Notice.)** — **YES __ NO __**

6. Once registrant has agreed, post BRAD to BPPD's User Share and send electronic version of cleared BRAD to BPPD WebMaster for posting on the BPPD Website. — YES __ NO __

7. Close all records in OPPIN — YES __ NO __

8. File administrative materials, reviews, BRAD, PEF, Notice of Registration, and label in jacket. Return jacket to file room with note for transfer to SIG for coding. YES __ NO __

9. Place two copies of label(s) in "New Label" box for filing in BPPD's label file. YES __ NO __

10. Place a copy of Notice of Registration in chron file box YES __ NO __

11. Provide BPPD Gatekeeper with electronic copies of reviews, BRAD, PEF, and Notice of Registration. Don't forget to segregate CBI. YES __ NO __

12. Type of Registration: Unconditional____ Conditional_____

13. Does this registration have terms/conditions (ex: storage stability data)? YES __ NO __
IF THE REGISTRATION HAS TERMS/CONDITIONS THIS INFORMATION MUST BE ENTERED INTO THE LOGBOOK For BPPD Registrations with Terms/Conditions FOR THE APPROPRIATE BRANCH.

14. If there are term/conditions to the registration notice has this information been placed in the LOGBOOK For BPPD Registrations with Terms/Conditions
YES __ NO __

THE PLAYERS

BPPD Gatekeeper = Diana Hudson

BPPD WebMaster = Jim Skaptason

FR Staff (contact) = E-mail via Lotus Notes to: OPPTS FRStaff@EPA
FR Templates: http://intranet.epa.gov/oppthome/intrafrs/opptempl.htm#biopesticides (Linda Hollis coordinates for BPPD)

PEF Coordinator = Barbara Mandula (backup is Alan Reynolds)

Format for New Active Ingredient Decision Package

Left Panel	Center Panel	Right Panel
Two original (printed on Letterhead) Decision Memos with plastic *Executive Correspondence* cover Yellow concurrence sheet showing on bottom	Two complete copies of the Biopesticide Registration Action Document (include OGC Concurrence)	Two copies of the Plain English Fact Sheet (attach a Buck Slip signed by Barbara Mandula or Alan Reynolds - to be removed by BC before package goes on to OD's office) Label(s) - MUP and/or EP as appropriate

Note: The extra copies of the Decision Memo, BRAD, and PEF are for the OD's office.

Of course, if the new a.i. involves a food use, a separate tolerance/exemption rule package should accompany this package.

RE: TGAI CSF FOR ISOPROPYL MYRISTATE - RESULTIX -- EPA Reg. No. 86865-R

Cheryl Greene to Jacob Moore 05/12/2011 05:04 PM

Hi Jacob,

I'm dropping in your chair the CSF for the above referenced action. Before you review it please take a look at the email message below from the registrant's consultant. she has made changes to the certified limits since your original review of the CSF. If this is not acceptable, please let me know and I will ask her to resend the CSF without the certified limit changes. let me know if you have questions or need more information.

Personal privacy information

From: Susan Phillips:

I am sorry about the delay. The CSF I have attached contains all the revisions you requested in the deficiency letter; however, it also includes lower certified limits for the impurities, down to 0%. This is proposed because as the TGAI purity approaches 100.0%, the percent impurities will logically go down, and based on the manufacturing process, one or both of these impurities may not be found based on the analytical limits of quantification or detection.

If this reasonable approach does not meet with your approval I can immediately send you a CSF containing all requested changes but no changes to the lower certified limits for the impurities.

Regards,
Susan
[redacted]

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, May 12, 2011 1:27 PM
To: Susan Phillips; Susan Phillips; Matt Schneider
Subject: Fw: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Hi Susan:

This is a follow-up to our May 4, 2011 phone conversation and my May 5 follow-up email (see below) in which I explained that EPA needs a copy of the TGAI CSF for RESULTIX (Reg. # 86865-R). We cannot complete our review of your recently submitted data for this action until we receive the CSF for the TGAI. Please send it to me as soon as possible by email or fax using the contact information below. If you have questions or need additional information, let me know.

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov
----- Forwarded by Cheryl Greene/DC/USEPA/US on 05/12/2011 02:19 PM -----

From: Cheryl Greene/DC/USEPA/US
To: "Susan Phillips" <SPhillips@gsblaw.com>
Date: 05/05/2011 02:19 PM
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Hi Susan:

This is a follow-up to the email I sent earlier today and the voice message I left for you a short while ago. I have discussed your question with our managing science reviewer and essentially the answer to your question is YES, you must submit a CSF for the TGAI even if you are not getting the TGAI registered. The reason a CSF is required in part is so that the Agency can confirm that the CSF corresponds with the all data/information submitted in support of the product.
As such, please send me a copy of the CSF for the TGAI in your product as soon as possible. You may send the CSF by email or by fax. My fax information is listed below.

I apologize if you were inadvertently given incorrect information during our conference calls or meetings. Let me now if you have questions or need additional information.

Regards.
Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Hi Susan:

Sorry for the delay in getting back to you on this. I don't have an answer to your question yet but I wanted to ask if you could send me another copy of the meeting minutes you submitted that documented what we said. I can't recall if you sent the minutes or if Matt did. (I don't have the answer to your question in my notes and I'm hoping that something in your meeting minutes will jar my memory.) Also, would you include your telephone number/contact information at the end of your emails. When folks include their contact information in the emails it saves so much time when we need to contact them quickly.

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

Date: June 1, 2011

OFFICE OF CHEMICAL SAFETY AND POLUTION PREVENTION

JUN 0 1 2011

MEMORANDUM

SUBJECT: Science Review in Support of the Registration of Resultix, containing 50 % Isopropyl Myristate as Active Ingredient.

Decision Number: 424225
DP Number: 383262
EPA File Symbol Number: 86865-R
Chemical Class: Biochemical
PC Code: 000207
CAS Number: 110-27-0
Active Ingredient Tolerance Exemptions: N/A non-food
MRID Numbers: 483482-04 and 483482-03

FROM: Clara Fuentes, Entomologist
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

TO: Cheryl Greene, Regulatory Action Leader
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

ACTION REQUESTED

Piedmont Animal Health LLC (Piedmont) is submitting data in MRIDS 483482-04 and 483482-03 to determine safety of the product Resultix on companion animals, dogs and cats, in response to study deficiencies identified in previously submitted studies MRID 47925317 and 47925318.

RECOMMENDATIONS AND CONCLUSIONS

A. MRIDs 483482-03 and 483482-04 are acceptable pending resolution of the following deficiencies, and revision of proposed label claims:

1a. Clinical pathology and hematology values parameters were not addressed completely in the dog and cat studies; blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count are not reported.

2a. Dogs' efficacy data shows that mortality rates of control ticks, *R. Sanguineus* and *D. variabilis,* are 11.1% and 14.4%, respectively. In IPM treated dogs, the reported percentage mortality rates for each tick species were 95.6% and 106.1%, respectively. These percentages result from dividing total dead ticks, *R. sanguneous* = 153 by total number of ticks treated =160, and total dead ticks, *D. variabilis*=157 divided by total number of ticks treated = 148. Calculation of efficacy does not take into account percent mortality in control group, which need to be factored in and subtracted from the percentages of efficacy being reported. In control group, 11.1% and 14.4% *R. sanguineus* and *D. variabilis,* respectively, were counted dead by causes unrelated to treatment. Furthermore, Table 4a on page 24 in MRID 5483482-03 shows that more ticks were dead than were treated. That natural mortality factor cannot be excluded from the calculation of efficacy. The efficacy of the product on dogs is up to 85% for both tick species. In addition, Table 4a does not specify whether these counts correspond to 3, 6 or 24 hours. The registrant should specify how long it takes for the product to reach its maximum efficacy, which is approximately 85% for both tick species on dogs.

3a. On cats, the product is 96% effective on *D. variabilis* ticks, and approximately 90% on *R. sanguine* ticks at 24 hours. It is inconsistent that mortality due to treatment diminishes from 92.4% to 90.9 % from 3 to 24 hours.

B. The following label claims (***in bold letters***) are not supported by data:

1b. ***Clinically proven*** is unsupported since data on companion animal safety deviates from OPPTS 870.7200 guideline's recommendations as follows: a) observations and measurements of possible treatment related effects on dogs and cats for 14 days post-treatment were not reported; b) individual body weights of dogs and cats were not measured consistently with guidelines recommendations, which are once during acclimation period, once immediately prior to test initiation, and next, on days 7 and 14 post-treatment; c) individual food consumption was not measured on a daily basis, and d) blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), and reticulocyte count are not reported.

2b. ***Even kills "super ticks", the ones that have built up resistance to traditional pesticide treatments.*** This claim has not been tested and demonstrated to be true.

c. The word "adult" should be added to this label statement, ***For the treatment of Ticks on "***adult***" Dogs and Cats,*** because only adults dogs age from 39 to 41 months old, and cats, from 11 to 140 months old, were tested for safety of the product

3b. ***...softens the waterproof outer waxy layer of the tick's body, resulting in rapid dehydration.*** How rapid? The registrant needs to specify how long it takes to kill the ticks on dogs. Neither the report text nor Table 4a on page 24 of MRID 483482-03 (form which efficacy is calculated) specify whether the tabulated dead tick counts correspond to 3, 6 or 24 hours.

4b. ***Safe for you and your family.*** Safety of this product has not been evaluated on people.

5b. ***Works to reduce human exposure to tick borne diseases*** This statement needs to be supported with efficacy data on most predominant tick vectors of human pathogens such as species of both genera, *Ixodes* and *Amblioma* species, which have not been tested.

C. <u>The previously identified study deficiencies have been addressed as indicated below</u>:

1c. The amount of product applied to each dog and cat is reported in terms of exposure to Isopropyl Myristate (IPM). For dogs, the exposure dose ranged from 149 to 278 and 134 to 263 mg/kg bw/day on treatment days 0 (when *Rhipicephalus sanguineus* ticks were treated) and 7 (when *Dermacentor variabilis* ticks were treated), respectively. For cats, the exposure dose ranged from 97 to 510 and 30 to 974 mg /kg bw/day on treatment days 0 and 7, respectively.

2c. Food consumption is addressed and reported as not measured in terms of daily quantities of food eaten. Animals were observed daily for adverse effects including inappetance and aneroxia, which were not observed. Body weights were taken prior to treatment on Day 7 (August 26, 2009), and again after completion of the study (January 07, 2011) more than a year later as stated on page 14 of MRID 483482-03. However, table 3 on page 22 of the same study report, shows that body weight was not significantly different between these dates. In fact, the study was not completed on January 2011; this is the date for the final report amendment date. The actual study ended on November 2009.

3c. Food consumption was not measured on cats; however, cats were observed daily and no eating disorders such as inappetance or anorexia were observed during the study. Cats were weighed at the beginning of the study in August, 2009. All treated cats and 2 controls were weighed again in January, 2011.

4c. Some individual data parameters for hematology and clinical chemistry analysis were addressed in response to deficiencies. The following previously requested, hematological parameters were reported: platelet count, mean corpuscular HGB, MCH and concentration (MCHC). Explanation is provided on page 15 of MRID 483482-03 for some of the clinical pathology values (CK (U/L; GGT (U/L); Choesterol (mg/dL); Total CO2 (MeQ/l); Chloride (mEq/L), and Potassium (mEq/L)), and hematological values (monocytes, monocites percentage and absolute counts, WBC and HGB counts, neutrophils, lymphocytes, MCHC, eosinophil percentage, and auto platelet counts) that are marginally outside reference ranges for dogs.

5c. Explanation for clinical pathology values (Alk Phos, creatine, calcium, sodium, ALT, BUN, phosphorus, CK, GGT, albumin, cholesterol, glucose, potassium, B/C and A/G ratios), and hematological values (Lymphocytes, monocytes, WBC, MCV, neutrophils, Abs eosinophils, RCB, HGB, HCT, and auto platelet counts) that are marginally outside reference ranges for cats is provided ON PAGE 115 IN mrid 483482-04. However, the following hematological arameters were not addressed for neither dogs nor cats: blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), and reticulocyte count.

cc: *Clara Fuentes*, Cheryl Greene, BPPD Chron File, IHAD/ARS
, FT, PY-S: June 1, 2011.

Material Sent for Data Extraction

Reg. # 66865-1

Description: New Registration

☐ Material(s) Sent to Data Extraction Contractors:

- ☑ New Stamped Label Dated Aug 24, 2011
- ☐ Notification Dated _____
- ☑ New CSF(s) Dated Jan 9, 2011
- ☐ Other: _____

☐ Decision #: _____

☐ Other Action/Comments: Please Extract label and Registration Notice and Scan to PPIS and Return Jacket to me. Thanks

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: Cheryl Greene

Phone: 703 308-0352 Division: BPPD

Date: August 1, 2012

Greene.Cheryl@EPA.gov

Material Sent for Data Extraction

Reg. # 86865-R

Description: _____

☐ Material(s) Sent to Data Extraction Contractors:

- ☑ New Stamped Label Dated _____
- ☐ Notification Dated _____
- ☑ New CSF(s) Dated Jan 9, 2011
- ☐ Other: _____

☐ Decision #: _____

☐ Other Action/Comments: There is one or more labels that need to be added to PPLS

File this coversheet and attached materials in the jacket. It must be well organized and clipped together, NOT STAPLED. Then give the jacket with the coversheet and materials to staff in the Information Services Center (ISC) (Room S-4900). If a jacket is full or only available as an image, please file materials in a new jacket and bring it down to the (ISC). For further information please call 703-605-0716.

Reviewer: Cheryl Greene

Phone: _____ Division: _____

Senedu Date: _____

Please request transfer back to Cheryl Greene when finished with this jacket.

RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Cheryl Greene to: Susan Phillips 05/05/2011 02:19 PM

Bcc: Angela Gonzales, Clara Fuentes, Jacob Moore, Russell Jones

---

Hi Susan:

This is a follow-up to the email I sent earlier today and the voice message I left for you a short while ago. I have discussed your question with our managing science reviewer and essentially the answer to your question is YES, you must submit a CSF for the TGAI even if you are not getting the TGAI registered. The reason a CSF is required in part is so that the Agency can confirm that the CSF corresponds with the all data/information submitted in support of the product. As such, please send me a copy of the CSF for the TGAI in your product as soon as possible. You may send the CSF by email or by fax. My fax information is listed below.

I apologize if you were inadvertently given incorrect information during our conference calls or meetings. Let me now if you have questions or need additional information.

Regards.
Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Hi Susan:

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Thanks.

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

"Susan Phillips" Thanks -----Original Message----- 04/27/2011 10:50:09 AM

From: "Susan Phillips" <SPhillips@gsblaw.com>
To: Cheryl Greene/DC/USEPA/US@EPA
Date: 04/27/2011 10:50 AM
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Tuesday, April 26, 2011 4:54 PM
To: Susan Phillips
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Hi Susan:

Let me verify this with my scientist and get back to you. I should have an answer by cob tomorrow.

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

From: "Susan Phillips" <SPhillips@gsblaw.com>
To: Cheryl Greene/DC/USEPA/US@EPA
Cc: "Matt Schneider" <MSchneider@gsblaw.com>
Date: 04/26/2011 02:48 PM
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

I thought in the teleconference your reviewers decided that the CSF was not needed because we are not getting the TGAI registered. If this is incorrect I will send you the CSF as soon as possible.

Thanks,
Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [
mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Monday, April 25, 2011 6:02 PM
To: Susan Phillips
Subject: RE: Request for meeting with BPPD to discuss deficiency letter

for RESULTIX -- EPA Reg. No. 86865-R

Hi Susan:

We are steadily working through our review of your January 2011 submitted information. Portions of the review are complete but not everything is done. At this point I am aiming to respond on the status of the newly submitted information by the end of May. In the meantime, I don't appear to have a copy of your revised CSF for the TGAI being used in your proposed product. (I probably passed it on to one of my reviewers but they work at alternate worksites) Can you forward me a copy of the referenced CSF by fax (see below for number) or by email. Let me know if you have questions or need more information.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

From: "Susan Phillips" <SPhillips@gsblaw.com>
To: Cheryl Greene/DC/USEPA/US@EPA
Cc: "Matt Schneider" <MSchneider@gsblaw.com>, "Kathy Palma" <kpalma@piedmontpharma.com>
Date: 04/25/2011 10:25 AM
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Good morning,
We haven't heard anything from you concerning the submission of additional information in support of the registration of RESULTIX that was done in January. We would appreciate an update on the status of this submission.

Thank you for your time on this project.

Regards,
Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov)
Sent: Friday, December 10, 2010 12:06 PM
To: Susan Phillips
Cc: Hollis.Linda@epamail.epa.gov; Gonzales.Angela@epamail.epa.gov; Fuentes.Clara@epamail.epa.gov; Moore.Jacob@epamail.epa.gov

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

Thanks for your response. A meeting time of 11:00 am to 12:00 noon on Tuesday, December 14, 2010 works for us. If the three of you will be calling in from the same number the call-in number is 703 305-0123 repeat 703 305-0123. If you will be calling from separate numbers, please let me know as soon as you can so that I can get a multiple-line call in number for the meeting. Also, thanks for the agenda information. I will get it out to the folks here ASAP.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA

Cc: "Matt Schneider" <MSchneider@gsblaw.com>, Linda Hollis/DC/USEPA/US@EPA

Date: 12/10/2010 07:02 AM

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks for your prompt reply. A teleconference on Tuesday from 11-12 is the best for us. I will be at GSB on Tuesday for this telcon and therefore Matt's number can be used for this purpose (202 298 1787). We can add Dr. Palma to the call from our end. If you need to contact me before Tuesday, my home number is [redacted].

As for the agenda on Tuesday, the major issues are toxicology and the two safety and efficacy studies in cats and dogs (MRID 479253-17 and -18). Product chemistry and the draft label deficiencies are easily corrected and we see no reason to discuss these during the teleconference.

Personal privacy information

The safety and efficacy studies were submitted to fulfill both product performance and companion animal toxicity requirements. Based on the EPA deficiency letter, these two studies may not fulfill the companion animal toxicity requirements; however, product performance issues only concern label statement claims, which are easily correctible by revising the product label.

As for the toxicology deficiencies, the requested citation concerning dermal irritation will be submitted to the EPA in its entirety (approximately 84 pages) with an introduction indicating where the specific information is located in this review article. In addition, we are prepared to discuss additional rationales for requesting data waivers for the developmental toxicity and the in vitro mammalian cell assay data requirements.

Consequently, the agenda for the teleconference only concern toxicity data requirements for dogs, cats and humans. Please feel free to contact me or Matt if you have further questions in advance of our call and we would appreciate confirmation once the conference call time is firmed up.

Thanks very much for fitting this in during a very busy time of the year.

Regards,
Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov (
mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 5:10 PM
To: Susan Phillips
Cc: Matt Schneider; Hollis.Linda@epamail.epa.gov
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

Please see Linda Hollis's email below. Since Linda is not available next weed for a face-to face meeting, our next best option is a conference call. I'm working on pulling that together now. Please verify with your people that a conference call is acceptable. Also, please send me -- as soon as you possibly can -- a list containing the specific deficiencies/information Piedmont wishes to discuss or have clarified during the conference call. I need this list as soon as possible to ensure that I include the appropriate science folks on the call. At this point, I have identified two possible times for the call they are Monday, December 13, from 11:30 am to 12:30 PM or Tuesday December 14, 11:00 am to 12"00 noon. Please let me know which of these times best suite your people.

Also , the attachment below contains a pdf copy of the signed deficiency letter for RESULTIX. As I explained in my email earlier this month, this signed letter does not deviate in any significant way from the draft copy I forwarded to you on December 3, 2010.

The original deficiency letter went out to you in the mail today.

Please let me know if you have questions or need more information.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Susan: I just left a very detailed message with Matt. I would like your telephone number. At any rate, we can not accommodate a face to face meeting at anytime next week due to juggling schedules and previous commitments. However, my voice message to Matt was that we could entertain a conf call with all key players. I would like to do this preferably on Monday. I am available most of the morning and most of Tuesday. Wed - Friday are not options for me. I asked Matt that you forward a detailed list of topics for discussion. I am assuming that you really want to discuss product performance. Please let me know, we would be happy to provide further guidance as to how to move forward. Also, we recognize that the PRIA2 due date falls on a holiday (the 24th). This essentially means that we will need to wrap this up with regard to a renegotiation days prior to that. Please work with Cheryl Greene and forward your telephone number.

Linda A. Hollis, MS
Chief, Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division Office of Pesticide Programs (7511P) U.S. Environmental Protection Agency One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202
hollis.linda@epa.gov
(703) 308-8733 (phone)
(703) 308-7026 (fax)
Visit http://www.epa.gov/pesticides

"The journey of 1000 miles begins with one step.....Take the step"

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA, "Matt Schneider" <MSchneider@gsblaw.com>

Cc: Linda Hollis/DC/USEPA/US@EPA

Date: 12/09/2010 03:55 PM

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks very much for your prompt response.

Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 3:19 PM
To: Susan Phillips; Matt Schneider
Cc: Hollis.Linda@epamail.epa.gov
Subject: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

This email is to acknowledge receipt of Matt's email requesting for a meeting with BPPD to discuss the deficiency letter for RESULTIX. I hope to discuss this with my Branch Chief either later today or early tomorrow. As soon as I know her availability and the availability of the associated science folks, I will get back to you to let you know if Wednesday the 15th is possible and if so the time. In the meantime, let me know if you have questions or need more information.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352

Fax 703 308-7026
Email: greene.cheryl@epa.gov

Re: Product: RESULTIX

EPA Registration # 86865-R

Your December 3, 2009 application for Section 3 Registration

PRIAII Code B600 EPA Decision # 424225

Good Morning Cheryl,

I am writing to you in response to your December 3 email to my colleague Susan Phillips containing a draft of a the deficiency letter pertaining to the above captioned matter. As you know, the draft letter states that if the PRIA 2 deadline is not renegotiated by December 17, 2010, EPA will issue a can not grant letter. While we have not yet received a final deficiency letter, we see that the timeframe available to take action before December 17 is very short and so we very much appreciate your forwarding the draft. On the assumption that the final deficiency letter will be similar or identical to the draft, we need to move quickly. Accordingly, on behalf of our client, Piedmont Animal Health, we urgently and respectfully request a meeting to discuss the issues raised in the letter to clarify certain matters and hopefully reach agreement on a new PRIA 2 deadline in advance of December 17. In order for our client, Dr. Kathleen G. Palma, Vice President of Research and Development, Piedmont Animal Health, to be in attendance we were hoping that you would be able to schedule a meeting for Wednesday, December 15. I recognize this is short notice however, we only received the draft notice 14 days in advance of the deadline. We will make ourselves available any time on December 15 at your convenience. We very much appreciate whatever you can do to arrange the meeting at which Dr. Palma, Susan Phillips and I will be in attendance on behalf of Piedmont Animal Health.

Best regards,

Matt

MATTHEW R. SCHNEIDER

Owner and Managing Director D.C. and NY Offices | 202.965.7880 x 1787 Tel | 202.965.1729 Fax | mschneider@gsblaw.com

GARVEY SCHUBERT BARER | 5th Floor | 1000 Potomac Street NW | Washington, DC 20007 | ► GSBLaw.com

Unless expressly stated otherwise, any federal tax advice contained in this communication (including attachments) is not intended to be used, and cannot be used, for the purpose of avoiding federal tax penalties.

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RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Cheryl Greene to: Susan Phillips 05/05/2011 01:28 PM

Hi Susan:

Sorry for the delay in getting back to you on this. I don't have an answer to your question yet but I wanted to ask if you could send me another copy of the meeting minutes you submitted that documented what we said. I can't recall if you sent the minutes or if Matt did. (I don't have the answer to your question in my notes and I'm hoping that something in your meeting minutes will jar my memory.) Also, would you include your telephone number/contact information at the end of your emails. When folks include their contact information in the emails it saves so much time when we need to contact them quickly.

Thanks.

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

"Susan Phillips" Thanks -----Original Message----- 04/27/2011 10:50:09 AM

From: "Susan Phillips" <SPhillips@gsblaw.com>
To: Cheryl Greene/DC/USEPA/US@EPA
Date: 04/27/2011 10:50 AM
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Tuesday, April 26, 2011 4:54 PM
To: Susan Phillips
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Hi Susan:

Let me verify this with my scientist and get back to you. I should have an answer by cob tomorrow.

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency

1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

From: "Susan Phillips" <SPhillips@gsblaw.com>
To: Cheryl Greene/DC/USEPA/US@EPA
Cc: "Matt Schneider" <MSchneider@gsblaw.com>
Date: 04/26/2011 02:48 PM
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

I thought in the teleconference your reviewers decided that the CSF was not needed because we are not getting the TGAI registered. If this is incorrect I will send you the CSF as soon as possible.

Thanks,
Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Monday, April 25, 2011 6:02 PM
To: Susan Phillips
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Hi Susan:

We are steadily working through our review of your January 2011 submitted information. Portions of the review are complete but not everything is done. At this point I am aiming to respond on the status of the newly submitted information by the end of May. In the meantime, I don't appear to have a copy of your revised CSF for the TGAI being used in your proposed product. (I probably passed it on to one of my reviewers but they work at alternate worksites) Can you forward me a copy of the referenced CSF by fax (see below for number) or by email. Let me know if you have questions or need more information.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

From: "Susan Phillips" <SPhillips@gsblaw.com>
To: Cheryl Greene/DC/USEPA/US@EPA
Cc: "Matt Schneider" <MSchneider@gsblaw.com>, "Kathy Palma"
<kpalma@piedmontpharma.com>
Date: 04/25/2011 10:25 AM
Subject: RE: Request for meeting with BPPD to discuss deficiency
letter for RESULTIX -- EPA Reg. No. 86865-R

Good morning,
We haven't heard anything from you concerning the submission of additional information in support of the registration of RESULTIX that was done in January. We would appreciate an update on the status of this submission.

Thank you for your time on this project.

Regards,
Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Friday, December 10, 2010 12:06 PM
To: Susan Phillips
Cc: Hollis.Linda@epamail.epa.gov; Gonzales.Angela@epamail.epa.gov; Fuentes.Clara@epamail.epa.gov; Moore.Jacob@epamail.epa.gov
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

Thanks for your response. A meeting time of 11:00 am to 12:00 noon on Tuesday, December 14, 2010 works for us. If the three of you will be calling in from the same number the call-in number is 703 305-0123 repeat 703 305-0123. If you will be calling from separate numbers, please let me know as soon as you can so that I can get a multiple-line call in number for the meeting. Also, thanks for the agenda information. I will get it out to the folks here ASAP.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA

Cc: "Matt Schneider" <MSchneider@gsblaw.com>, Linda Hollis/DC/USEPA/US@EPA

Date: 12/10/2010 07:02 AM

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks for your prompt reply. A teleconference on Tuesday from 11-12 is the best for us. I will be at GSB on Tuesday for this telcon and therefore Matt's number can be used for this purpose (202 298 1787). We can add Dr. Palma to the call from our end. If you need to contact me before Tuesday, my home number is [redacted].

As for the agenda on Tuesday, the major issues are toxicology and the two safety and efficacy studies in cats and dogs (MRID 479253-17 and -18). Product chemistry and the draft label deficiencies are easily corrected and we see no reason to discuss these during the teleconference.

The safety and efficacy studies were submitted to fulfill both product performance and companion animal toxicity requirements. Based on the EPA deficiency letter, these two studies may not fulfill the companion animal toxicity requirements; however, product performance issues only concern label statement claims, which are easily correctible by revising the product label.

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Consequently, the agenda for the teleconference only concern toxicity data requirements for dogs, cats and humans. Please feel free to contact me or Matt if you have further questions in advance of our call and we would appreciate confirmation once the conference call time is firmed up.

Thanks very much for fitting this in during a very busy time of the year.

Regards,
Susan

-----Original Message-----

Personal privacy information

From: Greene.Cheryl@epamail.epa.gov [
mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 5:10 PM
To: Susan Phillips
Cc: Matt Schneider; Hollis.Linda@epamail.epa.gov
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

Please see Linda Hollis's email below. Since Linda is not available next weed for a face-to face meeting, our next best option is a conference call. I'm working on pulling that together now. Please verify with your people that a conference call is acceptable. Also, please send me -- as soon as you possibly can -- a list containing the specific deficiencies/information Piedmont wishes to discuss or have clarified during the conference call. I need this list as soon as possible to ensure that I include the appropriate science folks on the call. At this point, I have identified two possible times for the call they are Monday, December 13, from 11:30 am to 12:30 PM or Tuesday December 14, 11:00 am to 12"00 noon. Please let me know which of these times best suite your people.

Also , the attachment below contains a pdf copy of the signed deficiency letter for RESULTIX. As I explained in my email earlier this month, this signed letter does not deviate in any significant way from the draft copy I forwarded to you on December 3, 2010. The original deficiency letter went out to you in the mail today.

Please let me know if you have questions or need more information.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Susan: I just left a very detailed message with Matt. I would like your telephone number. At any rate, we can not accommodate a face to face meeting at anytime next week due to juggling schedules and previous committments. However, my voice message to Matt was that we could entertain a conf call with all key players. I would like to do this preferably on Monday. I am available most of the morning and most of Tuesday. Wed - Friday are not options for me. I asked Matt that you forward a detailed list of topics for discussion. I am assuming that you really want to discuss product performance. Please let me know, we would be happy to provide further guidance as to how to move forward. Also, we recognize that the pria due date falls on a holiday (the 24th). This essentially means that we will need to wrap this up with regard to a renegotiation days prior to that. Please work with Cheryl Greene and forward your telephone number.

Linda A. Hollis, MS
Chief, Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division Office of Pesticide Programs (7511P) U.S. Environmental Protection Agency One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202
hollis.linda@epa.gov
(703) 308-8733 (phone)
(703) 308-7026 (fax)
Visit http://www.epa.gov/pesticides

"The journey of 1000 miles begins with one step.....Take the step"

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA, "Matt Schneider" <MSchneider@gsblaw.com>

Cc: Linda Hollis/DC/USEPA/US@EPA

Date: 12/09/2010 03:55 PM

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks very much for your prompt response.

Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [
mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 3:19 PM
To: Susan Phillips; Matt Schneider
Cc: Hollis.Linda@epamail.epa.gov
Subject: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

This email is to acknowledge receipt of Matt's email requesting for a meeting with BPPD to discuss the deficiency letter for RESULTIX. I hope to discuss this with my Branch Chief either later today or early tomorrow. As soon as I know her availability and the availability of the associated science folks, I will get back to you to let you know if Wednesday the 15th is possible and if so the time. In the meantime, let me know if you have questions or need more information.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Re: Product: RESULTIX

EPA Registration # 86865-R

Your December 3, 2009 application for Section 3 Registration

PRIAII Code B600 EPA Decision # 424225

Good Morning Cheryl,

I am writing to you in response to your December 3 email to my colleague Susan Phillips containing a draft of a the deficiency letter pertaining to the above captioned matter. As you know, the draft letter states that if the PRIA 2 deadline is not renegotiated by December 17, 2010, EPA will issue a can not grant letter. While we have not yet received a final deficiency letter, we see that the timeframe available to take action before December 17 is very short and so we very much appreciate your forwarding the draft. On the assumption that the final deficiency letter will be similar or identical to the draft, we need to move

quickly. Accordingly, on behalf of our client, Piedmont Animal Health, we urgently and respectfully request a meeting to discuss the issues raised in the letter to clarify certain matters and hopefully reach agreement on a new PRIA 2 deadline in advance of December 17. In order for our client, Dr. Kathleen G. Palma, Vice President of Research and Development, Piedmont Animal Health, to be in attendance we were hoping that you would be able to schedule a meeting for Wednesday, December 15. I recognize this is short notice however, we only received the draft notice 14 days in advance of the deadline. We will make ourselves available any time on December 15 at your convenience. We very much appreciate whatever you can do to arrange the meeting at which Dr. Palma, Susan Phillips and I will be in attendance on behalf of Piedmont Animal Health.

Best regards,

Matt

MATTHEW R. SCHNEIDER

Owner and Managing Director D.C. and NY Offices | 202.965.7880 x 1787 Tel | 202.965.1729 Fax | mschneider@gsblaw.com

GARVEY SCHUBERT BARER | 5th Floor | 1000 Potomac Street NW | Washington, DC 20007 | ► GSBLaw.com

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86865-R (isopropyl myristate - RESULTIX) Efficacy resubmitted data needs to be reviewed.

Cheryl Greene to: Clara Fuentes 04/25/20 t1 05:33 PM
Cc: Linda Hollis, Russell Jones, Cole.Leonard

Hi Clara:

See my email to Russ below.

I'm placing on your file room shelf the resubmitted efficacy data for the above referenced product. When the full resubmitted data package was beaned back in January, the efficacy part of the package did not get beaned to you. Can you review the resubmitted data and let me know if it is now acceptable for the registration of the product (?). If you recall, one of the big issues with the data is that the applicant did not adequately address companion animal safety. Along with the efficacy data package I have also included a copy of the deficiency letter that we sent out to the applicant back in December 2010 and a copy of the revised CSF for your reference. i will stop by tomorrow to discuss. Thanks

Best regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov
----- Forwarded by Cheryl Greene/DC/USEPA/US on 04/25/2011 05:23 PM -----

From:	Cheryl Greene/DC/USEPA/US
To:	Russell Jones/DC/USEPA/US@EPA
Cc:	Linda Hollis/DC/USEPA/US@EPA
Date:	04/25/2011 03:49 PM
Subject:	Fw: 86865-R Efficacy and Product chemistry resubmitted data needs to be reviewed .

Hi Russ:

I'm placing in your file room in box the resubmitted product chemistry and efficacy data for the above referenced action. Leonard beaned this package to you back in January on my behalf. However, I neglected to alert you that the package needed to be broken up with the tox, product chemistry and efficacy data sets getting reviewed separately. Consequently, the entire package got assigned to Angela who was only responsible for the tox section of the data package. Angela has completed her review back in March. I just started reading Angela's review and realized that the product chemistry and efficacy reviews have not been done. Hence, I am placing them on your shelf to be parsed out to Jacob and Clara respectively. Based on our the initial product chemistry and efficacy deficiencies , I don't expect that Jacob and Clara will have much trouble with the reviews or take too much time. Unfortunately, the PRIA 2 due date for this action is May 24, so, I do need to ask for a quick turn-a-round. Is this possible? Should we talk?

Cheryl F. Greene

Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov
----- Forwarded by Cheryl Greene/DC/USEPA/US on 04/25/2011 03:36 PM -----

From: Russell Jones/DC/USEPA/US
To: Angela Gonzales/DC/USEPA/US@EPA, Leonard Cole/DC/USEPA/US@EPA, Cheryl Greene/DC/USEPA/US@EPA
Date: 01/24/2011 03:05 PM
Subject: 86865-R transferred to Angela - Not sure who RAL is; Bean says Leonard, but I thought Cheryl had this one - Please clarify

Transferred to Angela 01/24/2011

Review Date

Priority	A. I. (Reg. No.)	RAL	Study Type	Status	Date Rec'd **Pria Date**
5	Ispropyl Myristate ()	L. Cole? C. Greene?	Response to Deficiencies	InQueue	(

REVIEW DUE DATE = 08/25/2011

86865-R (isopropyl myristate - RESULTIX) Efficacy resubmitted data needs to be reviewed.

Cheryl Greene to Jacob Moore 04/25/2011 05:51 PM

Cc: Linda Hollis, Russell Jones, Cole.Leonard

Hi Jacob:

See my email to Russ below.

I'm placing on your file room shelf the applicant's response to the product chemistry deficiencies noted in your December 2010 deficiency letter for the referenced product. When the full resubmitted data package was beaned back in January, the applicant's response to product chemistry deficiencies did not get beaned to you. Can you review the response (revised CSF) let me know if it is now acceptable for the registration of the product (?). If you recall, the deficiencies were pretty much minor (incorrect certified limit values, missing information on the source of the AI, etc.) Along with the product chemistry resubmission (CSF), I have also included a copy of the deficiency letter that we sent out to the applicant back in December 2010 for your reference. Is it possible to get your response to the new CSF by May 15, 11? I will stop by tomorrow to discuss. Thanks

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

----- Forwarded by Cheryl Greene/DC/USEPA/US on 04/25/2011 05:23 PM -----

From:	Cheryl Greene/DC/USEPA/US
To:	Russell Jones/DC/USEPA/US@EPA
Cc:	Linda Hollis/DC/USEPA/US@EPA
Date:	04/25/2011 03:49 PM
Subject:	Fw: 86865-R Efficacy and Product chemistry resubmitted data needs to be reviewed .

Hi Russ:

I'm placing in your file room in box the resubmitted product chemistry and efficacy data for the above referenced action. Leonard beaned this package to you back in January on my behalf. However, I neglected to alert you that the package needed to be broken up with the tox, product chemistry and efficacy data sets getting reviewed separately. Consequently, the entire package got assigned to Angela who was only responsible for the tox section of the data package. Angela has completed her review back in March. I just started reading Angela's review and realized that the product chemistry and efficacy reviews have not been done. Hence, I am placing them on your shelf to be parsed out to Jacob and Clara respectively. Based on our the initial product chemistry and efficacy deficiencies, I don't expect that Jacob and Clara will have much trouble with the reviews or take too much time. Unfortunately, the PRIA 2 due date for this action is May 24, so, I do need to ask for a quick turn-a-round. Is this possible? Should we talk?

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov
----- Forwarded by Cheryl Greene/DC/USEPA/US on 04/25/2011 03:36 PM -----

From:	Russell Jones/DC/USEPA/US
To:	Angela Gonzales/DC/USEPA/US@EPA, Leonard Cole/DC/USEPA/US@EPA, Cheryl Greene/DC/USEPA/US@EPA
Date:	01/24/2011 03:05 PM
Subject:	86865-R transferred to Angela - Not sure who RAL is; Bean says Leonard, but I thought Cheryl had this one - Please clarify

Transferred to Angela 01/24/2011

Review Date

Priority	A. I. (Reg. No.)	RAL	Study Type	Status	Date Rec'd **Pria Date**
5	Ispropyl Myristate ()	L. Cole? C. Greene?	Response to Deficiencies	InQueue	(

REVIEW DUE DATE = 08/25/2011

To BPPD

DATA PACKAGE BEAN SHEET

Date: 25-Apr-2011

Decision #: 424225
DP #: (386086)
PRIA
Parent DP #:
Submission #: 888652

* * * Registration Information * * *

Registration: 86865-R - RESULTIX TM

Company: 86865 - PIEDMONT ANIMAL HEALTH

Risk Manager: RM 91 - Andrew Bryceland - (703) 305-6928 Room# PY1 S-8911

Risk Manager Reviewer: Leonard Cole LCOLE02

Sent Date: 11-Jan-2011 Calculated Due Date: 25-Aug-2011 Edited Due Date: MAY 15

Type of Registration: Product Registration - Section 3

Action Desc: (B600) NEW AI;NON-FOOD USE;MICROBIAL/BIOCHEMICAL;

Ingredients: 000207, Isopropyl myristate[redacted]

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 21-Jan-2011 Due Back: MAY 15

DP Ingredient: 000207, Isopropyl myristate

DP Title:

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

	Assigned To	Date In	Date Out
Organization:	BPPD / BPB		
Team Name:	RM 91		
Reviewer Name:	Gonzales, Angela		
Contractor Name:			

Last Possible Science Due Date: ~~30-Aug-2010~~ MAY 15

Science Due Date:

Sub Data Package Due Date:

* * * Studies Sent for Review * * *

Printed on Page 2

* * * Additional Data Package for this Decision * * *

Can be printed on its own page

* * * Data Package Instructions * * *

Attention Russell Jones, Ph.O.: Russ, would you forward this data package to your reviewer for evaluation. This is information submitted in response to a deficiency letter sent to Piedmont Animal Health. The product is Resultix with the new active ingredient is Isopropyl myristate. The Phase IV due date is MAY 25, 2011.

Product ingredient source information may be entitled to confidential treatment

DP#: (386086) *** Studies Sent for Review *** Decision#: (424225)

MRID	MRID Status	Citation Reference	Guideline
48348202		Phillips, S.; Barer, G. (2011) Published Articles Concerning the Safety of Myristic Acid and its Derivatives, Including Isopropyl Myristate. Unpublished study prepared by Piedmont Animal Health. 123 p.	870.7200/Companion animal safety
48348204		Young, D. (2011) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray Against Rhipicephalus sanguineus and Dermacentor variabilis on Cats: Amended Final Report. Project Number: PAH/09/0065. Unpublished study prepared by Young Veterinary Research Services. 85 p.	870.7200/Companion animal safety
48348202		Phillips, S.; Barer, G. (2011) Published Articles Concerning the Safety of Myristic Acid and its Derivatives, Including Isopropyl Myristate. Unpublished study prepared by Piedmont Animal Health. 123 p.	870.5300/In vitro mammalian cell gene mutation test
48348201		Phillips, S.; Barer, G. (2011) Discussion of Submitted Information: (RESULTIX End-Use Product). Unpublished study prepared by Piedmont Animal Health. 67 p.	870.5375/In vitro mammalian chromosome aberration test
48348202		Phillips, S.; Barer, G. (2011) Published Articles Concerning the Safety of Myristic Acid and its Derivatives, Including Isopropyl Myristate. Unpublished study prepared by Piedmont Animal Health. 123 p.	870.5375/In vitro mammalian chromosome aberration test
48348201		Phillips, S.; Barer, G. (2011) Discussion of Submitted Information: (RESULTIX End-Use Product). Unpublished study prepared by Piedmont Animal Health. 67 p.	870.3700/Prenatal developmental toxicity study
48348204		Young, D. (2011) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray Against Rhipicephalus sanguineus and Dermacentor variabilis on Cats: Amended Final Report. Project Number: PAH/09/0065. Unpublished study prepared by Young Veterinary Research Services. 85 p.	810.3300/Treatments to control pests of humans and pets
48348201		Phillips, S.; Barer, G. (2011) Discussion of Submitted Information: (RESULTIX End-Use Product). Unpublished study prepared by Piedmont Animal Health. 67 p.	870.5300/In vitro mammalian cell gene mutation test
48348201		Phillips, S.; Barer, G. (2011) Discussion of Submitted Information: (RESULTIX End-Use Product). Unpublished study prepared by Piedmont Animal Health. 67 p.	870.7200/Companion animal safety
48348203		Young, D. (2011) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanguineus and Dermacentor variabilis on Dogs: Amended Final Report. Project Number: PAH/09/0036. Unpublished study prepared by Young Veterinary Research Services. 83 p.	810.3300/Treatments to control pests of humans and pets
48348202		Phillips, S.; Barer, G. (2011) Published Articles Concerning the Safety of Myristic Acid and its Derivatives, Including Isopropyl Myristate. Unpublished study prepared by Piedmont Animal Health. 123 p.	870.3700/Prenatal developmental toxicity study
48348203		Young, D. (2011) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanguineus and Dermacentor variabilis on Dogs: Amended Final Report. Project Number: PAH/09/0036. Unpublished study prepared by Young Veterinary Research Services. 83 p.	870.7200/Companion animal safety

BACK PANEL

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

For the treatment of ticks on dogs and cats.

- Use when you see a tick or ticks on your dog or cat.
- Remove cap and hold pump bottle upright, direct nozzle at tick and spray until tick is covered with solution (2 sprays).
- Dispose of dead ticks.

For external use only.

Wash hands after use.

Do not use near dog's or cat's eyes.

Stop and ask a vet if skin irritation or infection is present or develops during use of product.

Keep away from open flames

Store at 59° F – 86° F (15° C – 30° C)

STORAGE AND DISPOSAL

Do not contaminate water, food, or feed by storage and disposal.

Pesticide Storage:

Store in a dry place away from extreme heat and cold (tightly closed at or below +30°C). Keep container closed when not in use. Always store pesticide in the original container. Store away from food and pet food.

In case of fire or other emergency, report at once by toll-free telephone to CHEMTREC (800-424-9300).

Pesticide Disposal and Container Handling:

Nonrefillable container. Do not reuse or refill this container.

If empty: place in trash or offer for recycling if available.

If partly filled: call your local solid waste agency for disposal instructions.

Never place unused product down any indoor or outdoor drain.

NOTICE: Seller warrants that the product conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use. Neither this warranty nor any other warranty of merchantability or fitness for a particular purpose, express or implied, extends to the use of this product contrary to label instructions, or under abnormal conditions, or under conditions not reasonably foreseeable to Seller, and Buyer assumes the risk of any such use.

ANY PANEL (Do not substitute these for required statements)

Label Claims (one or more in various combinations, located in various places throughout the box and bottle/insert labels)

Breakthrough in tick treatments

Clinically proven

Convenient and easy to apply as soon as you see a tick on your pet

Even kills "super ticks", the ones that have built up resistance to traditional pesticide treatments

For the Treatment of Ticks on Dogs and Cats

Free of conventional pesticides

Guaranteed effective

Kills ticks on pets

No conventional pesticides

Patented spray formula softens the waterproof outer waxy layer of the tick's body, resulting in rapid dehydration

Recommended to use on its own or in conjunction with other flea and tick control medications

Safe for you and your family

Safe to use on pets

Simple way to kill more than 90% of ticks on your pet that's completely non-toxic to animals, odorless and pesticide-free

Tick Killing Solution™

Works to reduce human exposure to tick-borne diseases (when used in conjunction with safe tick removal practices)

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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: March 28, 2011

SUBJECT: Science Review in Support of Resultix™, Containing 50% Isopropyl Myristate As Its Active Ingredient.

Decision Number: 424225
DP Number: 383262 and 386086
EPA File Symbol Number: 86865-R
Chemical Class: Biochemical
PC Code: 000207
CAS Number: 110-27-0
Active Ingredient Tolerance Exemptions: Nonfood-use
MRID Numbers: 47925309- 47925316, 47925319, 48348201-48348202

FROM: Angela L. Gonzales, Biologist Angela L Gonzales 3/28/11
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

TO: Cheryl Greene, Regulatory Action Leader
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

ACTION REQUESTED

In response to the request for additional mammalian toxicology data and information discussed in a memorandum from A. L. Gonzales to C. Greene dated November 16, 2010 and relayed in a letter to the registrant dated December 9, 2010, the registrant has submitted a revised proposed label and additional information in MRIDs 48348201-48348202 and in a cover letter dated January 10, 2011. This memorandum is a review of the submitted information. Summaries of studies (MRIDs 47925309-47925316, 47925319) that accompanied the original submission are also provided.

RECOMMENDATIONS AND CONCLUSIONS

1. The toxicology submission is ACCEPTABLE.

MRID 47925309-SUPPLEMENTAL	MRID 47925310-ACCEPTABLE
MRID 47925311-ACCEPTABLE	MRID 47925312-ACCEPTABLE
MRID 47925313-ACCEPTABLE	MRID 47925314-ACCEPTABLE
MRID 47925315-UNACCEPTABLE	MRID 47925316-ACCEPTABLE
MRID 47925319-NOT REVIEWED	MRID 48348201-ACCEPTABLE
MRID 48348202-ACCEPTABLE	

Regarding Isopropyl Myristate:

a. All data requirements have been satisfied at this time.

Regarding Resultix™:

a. All data requirements have been satisfied at this time.

RISK ASSESSMENT AND STUDY SUMMARIES FOR ISOPROPYL MYRISTATE

I. Introduction

Isopropyl myristate is an ester that is synthesized from the reaction of myristic acid and isopropyl alcohol. The proposed end-use product (EP) is intended for use on cats and dogs to kill ticks. The mode of action of the active ingredient is desiccation; the chemical dissolves the cuticle on the surface of the insect.

The chemical is exempt from the requirement of a tolerance under 40 CFR 180.910 as an inert ingredient in pesticide formulations applied to growing crops or raw agricultural commodities after harvest. It is also approved for use in nonfood pesticide formulations as an inert ingredient. Isopropyl myristate is used in a variety of personal care products including antiperspirants, lotions, make-up, hand-sanitizers and anti-itch creams (Household Products Database, 2010) and in otic and topical pharmaceutical products (FDA Inactive Ingredients Database, 2011). The chemical is used in approximately 881 cosmetic products at concentrations ranging from 0.00008-78% (MRID 48348202).

II. Human Health Assessment

A. Toxicology (MRIDs 47925309, 47925316, 47925319, 48348201-48348202)

All toxicology data requirements have been satisfied per 40 CFR 158.2050. The data presented in Table 1 below are a summary of the toxicity data and selected endpoints for isopropyl myristate. Refer to the DERs for more information. DERs were not created for MRIDs 48348201-48348202; these MRIDs contain information and data to support data and information presented in MRID 47925309. Refer below for more detailed information regarding data submitted.

Table 1. Mammalian Toxicology Data and Selected Endpoints for *isopropyl myristate* (40 CFR § 158.2050)

Study/OCSPP Guideline No.	Results[1]	Toxicity Category/Description	MRID
Acute oral toxicity (rat) (870.1100)	LD_{50} > 13.6 g/kg	IV	47925309 48348202
Acute dermal toxicity (rabbit) (870.1200)	LD_{50} = 5000 mg/kg	III	47925309 48348202 HSDB, 2011
Acute inhalation toxicity (rat) (870.1300)	LC_{50} > 33-41 mg/L[2]	IV	47925309 48348202 HSDB, 2011
Primary eye irritation (rabbit) (870.2400)	Minimally irritating	III	47925309 48348202 HSDB, 2011
Primary dermal irritation (rabbit, guinea pig, rat) (870.2500)	Minimally - severely irritating[3]	II	47925309 48348202 HSDB, 2011
Dermal sensitization (guinea pig) (870.2600)	Not a sensitizer	N/A	47925309 48348202 HSDB, 2011
Hypersensitivity incidents (885.3400)	Must be reported	N/A	N/A
90-Day oral toxicity (870.3100)	Repeat human oral exposure is not expected based on the use pattern. A 28-day non-guideline oral toxicity study was submitted on the EP but is classified as unacceptable due to deficiencies in the study. A 28-day oral toxicity study conducted in rats at 0, 100, 500 or 1000 mg/kg bw-day resulted in a NOAEL of ≥ 1000 mg/kg bw. The LOAEL could not be determined (no adverse effects at the highest dose tested).[3]		47925315 HSDB, 2011
90-Day dermal toxicity (pig) (870.3250)	No purposeful application to the human skin based on use pattern. Prolonged dermal exposure is not expected. A 28-day non-guideline dermal toxicity study in pigs was submitted on the EP. The dermal LOAEL could not be determined (no adverse effects at the highest dose tested) and the NOAEL ≥ 196.3-321.3 mg/kg bw.[3]		48348201 47925316

Table 1. Mammalian Toxicology Data and Selected Endpoints for *isopropyl myristate* (40 CFR § 158.2050)

Study/OCSPP Guideline No.	Results[1]	Toxicity Category/Description	MRID
90-Day inhalation toxicity (870.3465)	No likelihood of significant repeat inhalation exposure based on use pattern and low volatility of the active ingredient. A 13-week inhalation study conducted in guinea pigs with an aerosol formulation containing 16-20% isopropyl myristate at 0, 63.3, or 224 mg/m^3 resulted in increased absolute and relative lung weights. No other treatment-related effects were observed.[3] A 13-week inhalation study conducted in cynomolgus monkeys with the same formulation at 0, 5.3, 8.4, 33.6, or 37.0 mg/m^1 resulted in accumulations of macrophages within the bronchiolar and alveolar walls that were dose-related in treated monkeys. No other treatment-related effects were noted.[3]		47925309 48348201 HSDB, 2011
Mutagenicity-bacterial reverse mutation test (Ames) (870.5100)	Negative at 4, 20, 100, 500, 2500 µg/plate with and without metabolic activation in *Salmonella typhimurium*.[3]		HSDB, 2011
Mutagenicity-*in vitro* mammalian cell assay (870.5300 and 870.5375)	No data were submitted. However, significant human exposure is unlikely; isopropyl myristate is not structurally related to a known mutagen and does not belong to a chemical class of compounds containing a known mutagen. A life-time dermal carcinogenicity study conducted in mice at 10%, 50% and 100% isopropyl myristate diluted in acetone resulted in no difference in skin tumor frequency when compared to controls.[3]		48348201 47925309 HSDB, 2011
Developmental toxicity (870.3700)	No data submitted. However, significant exposure to female humans is unlikely based on use pattern and low volatility.		47925309 48348201

[1] All data cited were submitted from the open scientific literature.
[2] Study conducted on an aerosol formulation containing 16-20% isopropyl myristate (nominal concentration of 33-41 mg/L).
[3] Refer below for discussion of results.

1. Acute Toxicity

All data cited from the registrant to satisfy the biochemical pesticide data requirements were submitted from the open scientific literature. Additional data were obtained using the Hazardous Substances Database (HSDB) from the National Library of Medicine. Isopropyl myristate is of low acute oral, acute dermal and acute inhalation toxicity. An additional acute inhalation toxicity study available in the HSDB (2011) indicated no mortality or significant adverse effects when rats were exposed to a aerosol formulation containing 4.7% isopropyl myristate (9.7 mg/L) for four 15-minutes periods. Several eye irritation studies conducted on rabbits indicate that the

chemical is nonirritating to minimally irritating. Studies on the dermal irritation of isopropyl myristate have yielded mixed results. The majority of these studies indicate that the chemical is minimally irritating when applied to rabbits. However, one study indicated severe irritation in rabbits, moderate irritation in guinea pigs and mild irritation in rats. The Agency has conservatively classified isopropyl myristate into toxicity category II for eye irritation based on the results of this study, although it is likely based on the results of the other studies that the chemical is only mildly irritating. The active ingredient is not considered to be a skin sensitizer.

A dermal pharmacokinetic, safety and tolerance study on the EP in humans was submitted in MRID 47925319. This study was not required and not reviewed.

2. Subchronic Toxicity

90-Day Oral

A 28-day non-guideline oral toxicity study was submitted on the EP (MRID 47925315) but is classified as unacceptable due to deficiencies in the study. Refer to the DER for more information.

In a 28-day non-guideline oral toxicity study, Wistar rats were exposed to isopropyl myristate via gavage once per day for five days a week at 0, 100, 500 or 1000 mg/kg bw. No treatment-related mortality or adverse effects were observed. Hyperplasia of the forestomach mucosa was recorded in all the test groups, including the control group. The injury was reversible following the 14-day recovery period. The NOAEL is ≥ 1000 mg/kg bw; the LOAEL could not be determined (no adverse effects at the highest dose tested). (HSDB, 2011)

Repeat human oral exposure is not expected based on the use pattern; the proposed use of isopropyl myristate is not food-use and will be applied dermally to cats and dogs to kill ticks.

90-Day Dermal

In a 28-day non-guideline dermal toxicity study, Landrace-Duroc pigs were exposed to the proposed product (Resultix) every three days. The applied doses were equivalent to 0, 20.31-33.89, 59.62-94.43, or 196.3-321.3 mg/kg bw. No mortality or adverse treatment related effects were observed. At the highest dose, there was a slight increase in male pituitary weights and there was an equivocal increase in female adrenal weights. These changes were not detected by the end of the 14-day recovery period. These observations may be treatment-related, but are not considered toxicologically significant due to the lack of associated findings or changes in the evaluated toxicological parameters. The NOAEL is ≥ 196.3-321.3 mg/kg bw and the LOAEL could not be determined (no adverse effects at the highest dose tested). Refer to the DER for more information.

Prolonged dermal exposure to the human skin is not expected as the proposed product is not purposely applied directly to the skin.

90-Day Inhalation

In a 13-week inhalation study, guinea pigs were exposed for three one-hour periods every day to an aerosol formulation containing 16-20% isopropyl myristate at 0, 63.3, or 224 mg/m^3. At four weeks, half of the animals were sacrificed. One female died during the course of the study from unknown causes. There was an increase in absolute and relative lung weights in the treated animals compared to the control animals. No other adverse treatment-related effects were observed during gross necropsy and histology in the animals that were sacrificed at four weeks and 13 weeks.

In a 13-week inhalation study, cynomolgus monkeys were exposed for three one-hour periods every day to the same formulation used in the guinea pig study (above) at 0, 5.3, 8.4, 33.6, or 37.0 mg/m^3. During the study, coughing and wheezing were observed and there was a bloody nasal discharge in two of the animals exposed to the 8.4 mg/m^3 dose. Accumulations of macrophages within the bronchiolar and alveolar walls were observed and were dose-related in treated monkeys. No other adverse treatment-related effects were noted.

Significant repeat inhalation exposure is unlikely based on the use pattern and low volatility of the active ingredient (<1 Torr at 20° C).

3. Developmental Toxicity

There are no developmental toxicity data for isopropyl myristate. However, significant exposure to female humans is not expected from the proposed product's use under widespread and commonly recognized practice. Oral exposure is not expected and would be incidental based on the proposed product's use pattern and significant inhalation exposure is not expected based on the low volatility of the chemical. Although dermal exposure may occur during application of the product and handling of animals post-application, significant exposure is not expected based on the proposed product's use pattern as a contact pesticide used to kill ticks. Additionally, female humans are already exposed to the chemical in cosmetic, personal care and pharmaceutical products.

4. Mutagenicity

Results were negative in an Ames mutagenicity assay with and without metabolic activation using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 at concentrations of 4, 20, 100, 500 and 2500 µg/plate. In a similar Ames assay, results were

negative using the same *S. typhimurium* strains with and without metabolic activation at a concentration of 50 mg/mL. Isopropyl myristate was non-mutagenic in these assays.

Data from an *in* vitro mammalian mutagenicity assay are unavailable. However, significant human exposure is unlikely; isopropyl myristate is not structurally related to a known mutagen and does not belong to a chemical class of compounds containing a known mutagen.

In a life-time dermal carcinogenicity study, 10%, 50% and 100% isopropyl myristate diluted in acetone applied to the backs of female Swill mice resulted in no difference in skin tumor frequency when compared to controls. Negative and positive controls were employed. In another dermal carcinogenicity study conducted in Swill albino mice, isopropyl myristate was applied once per week for 19 months at a concentration of 1% in acetone (42.5-56.6 mg.kg/wk-initially-dose decreased as mice grew). Negative and positive controls were employed. Of the 20 mice treated with isopropyl myristate, five escaped during treatment and four died before the end of the exposure period. No tumors were observed on the remaining 11 surviving mice or the four mice that died before the end of the exposure period.

B. Dose Response Assessment

No relevant toxicological endpoints were identified; therefore, a dose response assessment is not required.

C. Drinking Water Exposure and Risk Characterization

Based on the proposed use pattern of isopropyl myristate as a contact pesticide to kill ticks on dogs and cats, pesticide residues in drinking water are not expected when products are used according to label instructions. Pesticide application to pets is generally considered by the Agency to be an indoor use pattern; therefore, isopropyl myristate residues in drinking water are highly unlikely.

D. Occupational, Residential, School and Day Care Exposure and Risk Characterization

1. Occupational Exposure and Risk Characterization

An occupational exposure assessment was not conducted for isopropyl myristate. Based on the proposed use pattern and toxicity data available to the Agency, anticipated exposure is not likely to result in unreasonable risk to humans. No relevant toxicological endpoints were identified and significant exposure in an occupational setting is not expected.

2. Residential, School and Day Care Exposure and Risk Characterization

A residential, school and day care exposure assessment was not conducted for isopropyl myristate. Based on the use pattern, school and day care exposures are unlikely. Although the proposed product will be used in residential settings, based on the proposed use pattern and toxicity data available to the Agency, anticipated exposure is not likely to result in unreasonable risk to humans. No relevant toxicological endpoints were identified and significant exposure in a residential setting is not expected.

E. Risk Characterization

The Agency has considered isopropyl myristate in light of the relevant safety factors in FIFRA. A determination has been made that no unreasonable adverse effects to the U. S. population in general, and to infants and children in particular, will result from the use of this chemical when label instructions are followed.

STUDY SUMMARIES FOR RESULTIX™

Toxicology (MRIDs 47925309- 47925314)

All data requirements have been satisfied per 40 CFR 158.2050. The data presented in Table 2 below are a summary of the toxicity data and information submitted to support the EP, Resultix™. Refer to the DERs for more information.

Table 2. Mammalian Toxicology Data Requirements for *Resultix*™ (40 CFR § 158.2050)			
Study/OCSPP Guideline No.	**Results**	**Toxicity Category/Description**	**MRID**
Acute oral toxicity (rat) (870.1100)	No data were submitted for the EP. Based on reported LD_{50} values for the active and inert ingredients, the estimated LD_{50} > 4,800 mg/kg	III	47925309
Acute dermal toxicity (rat and rabbit) (870.1200)	LD_{50} > 5,050 mg/kg (rabbit) LD_{50} > 5,050 mg/kg (rat)	IV	47925310 47925311
Acute inhalation toxicity (rat) (870.1300)	No data were submitted for the EP. Based on reported LD_{50} values for the active and inert ingredients, the estimated LD_{50} = 2.7 mg/L	IV	47925309
Primary eye irritation (rabbit) (870.2400)	Minimally irritating	IV	47925312
Primary dermal irritation (rabbit) (870.2500)	Nonirritating	IV	47925313
Dermal sensitization (guinea pig) (870.2600)	Not a sensitizer		47925314
Hypersensitivity incidents (885.3400)	Must be reported		

The test substance utilized in some of the toxicity studies is referenced by different names, including "Resultix Tick Spray", "Pediculocide 100", "Piedmont Pediculocide 1" and "Piedmont Pediculocide 2". The registrant has verified in MRID 48348201 that the test substance in these studies is identical to the proposed product, "Resultix™".

REFERENCES

FDA Inactive Ingredients Database. 2011. "Isopropyl Myristate". U.S. Department of Health and Human Services. February 28, 2011. < http://www.accessdata.fda.gov/scripts/cder/iig/getiigWEB.cfm>

Household Products Database. 2010. "Isopropyl Myristate". U.S. Department of Health and Human Services, National Library of Medicine. February 28, 2011. < http://hpd.nlm.nih.gov/cgi-bin/household/search?queryx=110-27-0&tbl=TblChemicals&prodcat=all>

cc: Angela L. Gonzales, Cheryl Greene, BPPD Science Review File, IHAD/ARS
A. L. Gonzales, FT, PY-S: 3/28/11

DATA EVALUATION RECORD

RESULTIX TM

STUDY TYPE: Miscellaneous Toxicology Information to Satisfy Tier I Data Requirements

MRID 47925309

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37830
Task Order No. 10-026

Primary Reviewer: Cheryl B. Bast, Ph.D., D.A.B.T.	Signature:	Cheryl B Bast
	Date:	OCT 14 2010
Secondary Reviewers: Eric B. Lewis, M.S.	Signature:	Eric B. Lewis
	Date:	OCT 14 2010
Robert H. Ross, M.S., Group Leader	Signature:	Robert H. Ross
	Date:	OCT 14 2010
Quality Assurance: Lee Ann Wilson, M.A.	Signature:	L.A. Wilson
	Date:	OCT 14 2010

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA EVALUATION RECORD

EPA Secondary Reviewer:	**Angela L. Gonzales 3/28/11 /s/**
STUDY TYPE:	Miscellaneous Toxicology Information to Satisfy Tier I Data Requirements
MRID NO:	47925309
DECISION NO:	424225
DP BARCODE:	DP372778
TEST MATERIAL:	Resultix TM (EP). Isopropyl Myristate (AI)
PROJECT STUDY NO:	Not Applicable
SPONSOR:	Piedmont Animal Health, 204 Muirs Chapel Road, Suite 200, Greensboro, NC 27410.
TESTING FACILITY:	Not Applicable
TITLE OF REPORT:	Miscellaneous Toxicology Information
AUTHOR:	Phillips, S. and Barer, G. S.
STUDY COMPLETED:	Not Applicable
CONFIDENTIALITY CLAIMS:	A signed and dated Statement of No Data Confidentiality Claims was included.
GOOD LABORATORY PRACTICE:	A signed and dated GLP statement was included. The information is not a study by itself but consists of a compilation of data from various sources; therefore, it does not meet the requirements of 40 CFR Part 160.
CONCLUSION:	MRID 47925309 is a summary of studies submitted to fulfill the Tier I data requirements for Resultix TM (EP)/ Isopropyl Myristate (AI). It also includes justifications and rationales for use of alternate studies or for not conducting studies for some requirements. Guideline studies were submitted for acute dermal toxicity (870.1200), acute eye irritation (870.2400), acute dermal irritation (870.2500), skin sensitization (870.2600), 28-day oral toxicity (870.3050), 21/28-day dermal toxicity (870.3200), and companion animal safety (870.7200) on the EP. For all other data requirements for the EP and AI, other studies and/or information were submitted for the remaining Tier 1 requirements.
CLASSIFICATION:	Supplemental: additional data and information to support data requirements were provided in MRIDs 48348201-48348202.

CONTAINS CONFIDENTIAL BUSINESS INFORMATION

I. INTRODUCTION

MRID 47925309 is a summary of data submitted to fulfill the Tier I data requirements for Resultix TM (EP)/ Isopropyl Myristate (Active Ingredient). The EP, Resultix TM is a 50% w/w solution of Isopropyl Myristate (IPM) and [redacted] (Inert).

A. SUMMARY OF STUDIES

Acute Oral Toxicity (OPPTS 870.1100)

Inert ingredient information may be entitled to confidential treatment

Acute oral toxicity guideline studies were not included in the registration submission; however, other studies were substituted for this requirement. Oral rat LD_{50} values of >13.6 g/kg (Tox Category IV) and >4800 mg/kg (Tox. Category III) were reported for IPM (CIR, 1982) and [redacted] respectively. An oral rat LD_{Lo} of >16 g/kg has been reported for IPM (RTECS, 1997). The authors report that the two chemicals are not expected to react chemically with one another, and no toxicological potentiation is expected. Therefore, the classification is Toxicity Category III (LD_{50}>4800 mg/kg). A 28-day repeated-exposure rat oral toxicity study of Resultix is used to support this conclusion; minimal adverse effects noted at doses of 3-15 mL/kg, resolved after a 14-day recovery period (Volume 16 of submission; MRID 47925315).

Acute Dermal Toxicity (OPPTS 870.1200)

A dermal rabbit LD_{50} value of 5 g/kg (Tox Category III) was reported for IPM (CIR, 1982; RTECS, 1997; HSDB, 2003). A dermal LD_{50} value of >5050 mg/kg (Tox Category III) was reported for Resultix in both rabbits and rats (Volumes 11 and 12 of submission; MRIDs 47925310 & 47925311).

Acute Inhalation Toxicity (OPPTS 870.1300)

Acute inhalation toxicity guideline studies were not included in the registration submission; however, other studies were substituted for this requirement. An inhalation rat LC of >33 mg/L (Tox. Category IV) has been reported for IPM (CIR, 1982; RTECS, 1997). Inhalation rat LC_{50} values of 2.7 mg/L ([redacted]) (Tox Category III) and 8.7 mg/L [redacted]) (Tox. Category III) were reported for [redacted]. [redacted]) (Tox. Category IV). The authors report that IPM and [redacted] are not expected to react chemically with one another, and no toxicological potentiation is expected. Therefore, the classification is Toxicity Category IV (LC_{50} = 2.7 mg/L).

Acute Eye Irritation (OPPTS 870.2400)

A rabbit eye irritation test showed that IPM produced no irritation to mild irritation (PII = 0- 2.0 at 72 hours) (Tox. Category III) (CIR, 1982; RTECS, 1997; HSDB, 2003). A rabbit eye irritation test showed that Resultix produced no irritation (Tox. Category IV) (PII = 0 at 72 hours) (Volume 13 of submission; MRID 47925312).

Acute Dermal Irritation (OPPTS 870.2500)

Dermal irritation studies in rabbits showed that IPM produced minimal to no irritation (Tox. Category IV) (CIR, 1982) or mild irritation (Tox. Category III) (RTECS, 1997). However, one study indicated severe irritation in rabbits, moderate irritation in guinea pigs and mild irritation in rats. A rabbit dermal irritation test showed that Resultix produced no irritation (Tox. Caegory IV) (PII = 0 at 72 hours) (Volume 14 of submission; MRID 47925313).

Skin Sensitization (OPPTS 870.2600)

Inert ingredient information may be entitled to confidential treatment

In guinea pig dermal sensitization tests, neither IPM (CIR, 1982) nor Resultix (Volume 15 of submission; MRID 47925314) was a sensitizer.

28-Day Oral Toxicity (OPPTS 870.3050)

A 28-day repeated-exposure rat oral toxicity study of Resultix showed that minimal adverse effects at doses of 3-15 mL/kg resolved after a 14-day recovery period (Volume 16 of submission; MRID 47925315). This study was classified as unacceptable; refer to the DER for the study for more information.

90-Day Oral Toxicity (OPPTS 870.3100)

A 90-day oral toxicity guideline study was not included in the registration submission. The authors conclude that a study is not required because the use of Resultix will not result in repeated oral exposure of humans (40CFR Part § 158.2050).

28-Day Dermal Toxicity (OPPTS 870.3200)

In a 21/28-day dermal toxicity study of Resultix in pigs, a NOAEL of 10 mL/animal/day (highest dose tested) was established (Volume 17 of submission; MRID 47925316). Refer to the DER for this study for more information.

90-Day Dermal Toxicity (OPPTS 870.3250)

A 90-day dermal toxicity guideline study was not included in the registration submission; however, a 28-day dermal toxicity study was submitted on the proposed EP.

90-Day Inhalation Toxicity (OPPTS 870.3465)

A 90-day inhalation toxicity guideline study was not included in the registration submission. The authors conclude that a study is not required because the use of Resultix will not result in significant repeated inhalation exposure of humans. Examples of significant exposure include occupational exposure or repeated application of insect repellents directly to the skin (40CFR Part § 158.2050). The authors state that the use of Resultix to control ticks on domestic animals would not result in a significant inhalation exposure because the use is intermittent and often seasonal, the application is brief and only to observed ticks, and the applicator is not deliberately exposed to the product as would be the case for an insect repellent. Furthermore, Resultix is of low acute toxicity via the inhalation route.

Thirteen-week inhalation toxicity studies were conducted in guinea pigs (0, 63.3 or 224 mg/m^3) and cynomolgus monkeys (0, 5.3, 8.4, 33.6, or 37 mg/m^3) with an aerosol antiperspirant containing 16-20% IPM (CIR, 1982). Animals received three 1-hour exposures/day, seven days/week. Treatment-related effects in guinea pigs consisted of increased absolute and relative lung weights. Treated monkeys exhibited wheezing and coughing, and bloody nasal discharge was noted in two animals at 8.4 mg/m^3.

Concentrated-related accumulations of macrophages within the bronchiolar and alveolar walls were noted in treated monkeys.

Prenatal Developmental Toxicity (OPPTS 870.3700)

A prenatal developmental toxicity guideline study was not included in the registration submission. The authors conclude that a study is not required because the use of Resultix will not result in significant repeated inhalation exposure of female humans with regard to examples provided in 40CFR Part § 158.2050, occupational exposure or repeated application of insect repellents directly to the skin.

Bacterial Reverse Mutation Test (OPPTS 870.5100)

In a spot test with *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538, IPM was negative at a concentration of 50 µg/plate both with and without exogenous metabolic activation (S9) (Blevins and Taylor, 1982).

In vitro Mammalian cell Assay (OPPTS 870.5300, 5375)

In vitro mammalian cell guideline studies were not included in the registration submission. The authors conclude that these studies are not required because the use of Resultix will not result in significant repeated inhalation exposure of humans. Examples of significant exposure include occupational exposure or repeated application of insect repellents directly to the skin (40CFR Part § 158.2050). The authors state that the use of Resultix to control ticks on domestic animals would not result in a significant inhalation exposure because the use is intermittent and often seasonal, the application is brief and only to observed ticks, and the applicator is not deliberately exposed to the product as would be the case for an insect repellent. Also, IPM was negative in a bacterial reverse mutation assay (Blevins and Taylor, 1982), and IPM and its metabolites are not structurally related to known mutagens. Chronic application of undiluted IPM caused no systemic effects or tumors in rabbits or mice (Stenbaeck, 1977; Stenbaeck and Shubik, 1974).

B. REFERENCES

A list of references cited is available in Appendix A of MRID 47925309.

C. BPPD Reviewer's Conclusion

Regarding Isopropyl Myristate:

1. The registrant must provide the referenced 1997 study from RTECS that indicates that the active ingredient is mildly irritating via the dermal route.

2. Regarding the developmental (OCSPP 870.3700) and *in vitro* mammalian cell assay (OCSPP 870.5300 and 870.5375) data requirements, the registrant must provide more information regarding occupational exposure. Based on the available information, significant exposure to IPM may occur in an occupational setting (e.g.: veterinary office, grooming salon) through use of

the proposed product. Additionally, although the registrant states that significant exposure is not expected because application is often seasonal, application may occur more often in warmer climates where ticks may be prevalent year-round. Because toxicity data were not submitted and the rationale provided to support these data requirements is inadequate because it is based primarily on the lack of exposure, more information regarding occupational exposure and/or toxicity is required to support these data requirements.

Regarding Resultix™:

1. The test substance utilized in some of the toxicity studies is referenced by different names, including "Resultix Tick Spray", "Pediculocide 100", "Piedmont Pediculocide 1" and "Piedmont Pediculocide 2". The registrant must verify that the test substance in these studies is identical to the proposed product, "Resultix™".

DATA EVALUATION RECORD

ISOPROPYL MYRISTATE
(PIEDMONT PEDICULOCIDE 2)

STUDY TYPE: ACUTE DERMAL TOXICITY - RABBIT (870.1200)
MRID 47925310

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 10-026

Primary Reviewer:
Susan Chang, M.S.

Signature:
Date: OCT 14 2010

Secondary Reviewers:
H. Tim Borges, Ph.D., M.T.(A.S.C.P.), D.A.B.T.

Signature:
Date: OCT 14 2010

Robert H. Ross, M.S., Group Leader

Signature:
Date: OCT 14 2010

Quality Assurance:
Lee Ann Wilson, M.A.

Signature:
Date: OCT 14 2010

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

DATA EVALUATION RECORD

EPA Secondary Reviewer: ANGELA L GONZALES 3/2/11

STUDY TYPE:	Acute Dermal Toxicity - Rabbits (OPPTS 870.1200)
MRID NO:	47925310
DP BARCODE NO:	DP 372778
DECISION NO:	424225
SUBMISSION NO:	863571
TEST MATERIAL:	Piedmont Pediculocide 2 (EPA Reg. No. 86865-R)
PROJECT NO:	7205-02
SPONSOR:	Piedmont Pharmaceuticals, 204 Muirs Chapel Road, Greensboro, NC 27410
TESTING FACILITY:	Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478
TITLE OF REPORT:	Piedmont Pediculocide 2 - Acute Dermal Toxicity Study in Rabbits
AUTHOR:	Janice O. Kuhn
STUDY COMPLETED:	November 15, 2002
GOOD LABORATORY PRACTICE:	GLP Compliant with exception that Sec. 160.31(d), and 160.105 (a)(b)(e) characterization and stability information was not provided in a Certificate of Analysis.
CONCLUSION:	The dermal LD_{50} for males, females, and combined was greater than 5050 mg/kg.
CLASSIFICATION:	ACCEPTABLE -- TOXICITY CATEGORY IV

I. STUDY DESIGN:

1. **Test Material:** Piedmont Pediculocide 2; label: IPM Solution Lot No. 260902; measured density 0.9070 g/mL.

2. **Test Animals:** Ten male and ten female New Zealand White rabbits were received from Ray Nichols Rabbitry, Lumberton, TX, and weighed 2.000-2.625 kg (males) and 2.05-2.85 kg (females) on the day of treatment. The young adult animals, 12.5 weeks old, were housed individually in suspended stainless steel cages with wire bottoms. The animals were fed PMI Feeds Inc.™ Lab Rabbit Diet No. 5321 in measured amounts. Municipal water was available *ad libitum*. The environmental conditions of the animal room were as

follows: temperature, 20±3°C; relative humidity, 30-70%; air changes, 10-12 per hour; and photoperiod, 12 hour light/dark cycle.

3. **Methods**: Rabbits were identified by ear-tag: Test Group: Male – Nos. 4868-M, 4870-M, 4872-M, 4874-M, and 4876-M; Female – Nos. 4869-F, 4871-F, 4873-F, 4875-F, and 4877-F and Control Group: Male – Nos. 4878-M, 4880-M, 4882-M, 4886-M, and 4888-M; Female – Nos. 4879-F, 4881-F, 4883-F, 4885-F, and 4887- F. The rabbits were acclimated for 5 days. The test material (5050 mg/kg body weight) was applied evenly in a thin, uniform layer over the clipped dorsal trunk and covered with a 8 x 4 inch surgical gauze patch and secured with non-irritating adhesive tape. The gauze patch and entire trunk were wrapped with orthopedic stockinette and secured with non-irritating adhesive tape. The coverings and excess test material were removed after 24 hours. The test animals were observed at least three times on the day of treatment for mortality and clinical/behavioral signs of toxicity and at least once daily thereafter for 15 days. Dermal observation was made at approximately 60 minutes after removal of wrappings, and on days 4, 7, 11, and 14. The rabbits were weighed prior to treatment and on days 7 and 15. Serum from all animals was analyzed for ALT, AST, and ALP activity. The rabbits were euthanized on day 15 and necropsied. Histopathological examination of the lungs was performed by Colorado Pathology Services, Inc.

II. RESULTS:

1. **Mortality**: All rabbits survived the study.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg)	Males	Females	Combined
5050	0/5	0/5	0/10
0	0/5	0/5	0/10

Data taken from p. 11 and 12, MRID 47925310.

2. **Clinical Observations**: All rabbits appeared normal throughout the study.

3. **Body Weight**: One treated female did not gain weight during the first week and one treated female lost weight slightly during the second week. All other rabbits gained weight throughout the study.

4. **Gross Necropsy**: One male and one female in the treated group and one male and one female in the control group had pale lungs. No observable abnormalities were noted from the other animals at necropsy. Histopathological examination of the lungs was performed by Colorado Pathology Services, Inc. and the results showed that test material did not cause histomorphologic tissue alterations in the lungs examined.

5. **Liver Enzyme Measurements**: Serum ALT, AST, and ALP activity were generally within normal limits in all animals and no toxicological significance is attached to the findings.

III. DISCUSSION:

The acute dermal LD_{50} for males, females, and combined was greater than 5050 mg/kg. This places Piedmont Pediculocide 2 in TOXICITY CATEGORY IV. The packet classification is **ACCEPTABLE.**

DATA EVALUATION RECORD

ISOPROPYL MYRISTATE
(PIEDMONT PEDICULOCIDE 2)

STUDY TYPE: ACUTE DERMAL TOXICITY - RAT (870.1200)
MRID 47925311

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 10-026

Primary Reviewer:
Susan Chang, M.S.

Signature:
Date: OCT 14 2010

Secondary Reviewers:
H. Tim Borges, Ph.D., M.T.(A.S.C.P.), D.A.B.T.

Signature:
Date: OCT 14 2010

Robert H. Ross, M.S., Group Leader

Signature:
Date: OCT 14 2010

Quality Assurance:
Lee Ann Wilson, M.A.

Signature:
Date: OCT 14 2010

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA EVALUATION RECORD

EPA Secondary Reviewer: ANGELA L GONZALES 3/2/11

STUDY TYPE:	Acute Dermal Toxicity - Rats (OPPTS 870.1200)
MRID NO:	47925311
DP BARCODE NO:	DP 372778
DECISION NO:	424225
SUBMISSION NO:	863571
TEST MATERIAL:	Piedmont Pediculocide 2 (EPA Reg. No. 86865-R)
PROJECT NO:	7204-02
SPONSOR:	Piedmont Pharmaceuticals, 204 Muirs Chapel Road, Greensboro, NC 27410
TESTING FACILITY:	Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478
TITLE OF REPORT:	Piedmont Pediculocide 2 - Acute Dermal Toxicity Study in Rats
AUTHOR:	Janice O. Kuhn
STUDY COMPLETED:	November 15, 2002
GOOD LABORATORY PRACTICE:	GLP Compliant with exception that Sec. 160.31(d), and 160.105 (a)(b)(c) characterization and stability information was not provided in a Certificate of Analysis.
CONCLUSION:	The dermal LD_{50} for males, females, and combined was greater than 5050 mg/kg.
CLASSIFICATION:	ACCEPTABLE -- TOXICITY CATEGORY IV

I. STUDY DESIGN:

1. **Test Material:** Piedmont Pediculocide 2; label: IPM Solution Lot No. 260902; measured density 0.9070 g/mL.

2. **Test Animals:** Ten male and ten female Sprague-Dawley rats were received from Texas Animal Specialties, Humble, TX, and weighed 233-286 g (males) and 170-202 g (females) on the day of treatment. The young adult animals, 8.5 weeks old, were housed individually in suspended stainless steel cages with wire bottoms. The animals were fed PMI Feeds Inc.™ Formulab No. 5008, *ad libitum*. Municipal water was available *ad libitum*. The environmental conditions of the animal room were as follows: temperature, 22±3°C; relative humidity, 30-70%; air changes, 10-12 per hour; and photoperiod, 12 hour light/dark cycle.

3. **Methods:** The rats were identified by ear punch: Test Group: Male – Nos. 171-M to 175-M; Female – Nos. 176-F to 180-F and Control Group: Male – Nos. 181-M to 185-M; Female – Nos. 186-F to 190-F. The rats were acclimated for 5 days. The test material (5050 mg/kg body weight) was applied evenly in a thin, uniform layer over the clipped dorsal trunk and covered with a 2 x 4 inch surgical gauze patch and secured with non-irritating adhesive tape. The gauze patch and entire trunk were wrapped with vet wrap and secured with non-irritating adhesive tape. The coverings and excess test material were removed after 24 hours. The test animals were observed at least three times on the day of treatment for mortality and clinical/behavioral signs of toxicity and at least once daily thereafter for 15 days. Dermal observation was made at approximately 60 minutes after removal of wrappings, and on days 4, 7, 11, and 14. The rats were weighed prior to treatment and on days 7 and 15. Blood serum of all animals was analyzed for ALT, AST, and ALP activity. The rats were euthanized on day 15 and necropsied. Histopathological examination of the lungs, liver, and small intestines (harvested and fixed in 10% buffered formalin) was performed by Colorado Pathology Services, Inc.

II. RESULTS:

1. **Mortality:** All rats survived the study.

TABLE 1. Doses, mortality/animals treated

Dose (mg/kg)	Males	Females	Combined
5050	0/5	0/5	0/10
0	0/5	0/5	0/10

Data taken from p. 11 and 12, MRID 47925311.

2. **Clinical Observations:** All rats appeared normal throughout the study.

3. **Body Weight:** One control female did not gain weight during the first week. One treated male lost weight during the first week and one treated female lost weight during the second week. All other rats gained weight throughout the study.

4. **Gross Necropsy:** All control rats and all males and four females in the treated group had white spots on the small intestines. Two treated females had pale lungs. Histopathological examination was performed by Colorado Pathology Services, Inc. and the results showed that test material did not cause histomorphologic tissue alterations in the lungs, liver, or small intestines examined.

5. **Liver Enzyme Measurements:** Serum ALT, AST, and ALP activity were generally within normal limits in all animals and no toxicological significance was noted between control and treated groups.

III. DISCUSSION:

The acute dermal LD_{50} for males, females, and combined was greater than 5050 mg/kg. This places Piedmont Pediculocide 2 in TOXICITY CATEGORY IV. The packet classification is **ACCEPTABLE.**

DATA EVALUATION RECORD

ISOPROPYL MYRISTATE
(PIEDMONT PEDICULOCIDE 1)

STUDY TYPE: PRIMARY EYE IRRITATION - RABBIT (870.2400)
MRID 47925312

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 10-026

Primary Reviewer: Susan Chang, M.S.	Signature: Date:	OCT 14 2010
Secondary Reviewers: H. Tim Borges, Ph.D., M.T.(A.S.C.P.), D.A.B.T.	Signature: Date:	OCT 14 2010
Robert H. Ross, M.S., Group Leader	Signature: Date:	OCT 14 2010
Quality Assurance: Lee Ann Wilson, M.A.	Signature: Date:	OCT 14 2010

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

DATA EVALUATION RECORD

EPA Secondary Reviewer: ANGELA L GONZALES 3/2/11

STUDY TYPE:	Acute Eye Irritation - Rabbits (OPPTS 870.2400)
MRID NO:	47925312
DP BARCODE NO:	DP 372778
DECISION NO:	424225
SUBMISSION NO:	863571
TEST MATERIAL:	Piedmont Pediculocide 2 (EPA Reg. No. 86865-R)
PROJECT NO:	7089-02
SPONSOR:	Piedmont Pharmaceuticals, 204 Muirs Chapel Road, Greensboro, NC 27410
TESTING FACILITY:	Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478
TITLE OF REPORT:	Piedmont Pediculocide 1 – Acute Eye Irritation Study in Rabbits
AUTHOR:	Janice O. Kuhn
STUDY COMPLETED:	August 2, 2002
GOOD LABORATORY PRACTICE:	GLP Compliant with exception that Sec. 160.31(d), and 160.105 (a)(b)(e) characterization and stability information was not provided in a Certificate of Analysis.
CONCLUSION:	No corneal opacity, iritis, or positive conjunctival irritation was noted on any rabbit. Slight dulling of normal luster on the cornea was noted on two rabbits one hour after test material instillation with clearance on one rabbit by 24 hours and on another rabbit by 48 hours. A constricted pupil was noted on one male at one hour. The maximum average score was 2.0 at one hour after test material instillation. Piedmont Pediculocide 1 was minimally irritating.
CLASSIFICATION:	ACCEPTABLE -- TOXICITY CATEGORY IV

I. STUDY DESIGN:

1. **Test Material:** Piedmont Pediculocide 1; label: IPM Solution Lot No. 170602A; pH 5.68

2. **Test Animals:** Two male and one female young adult New Zealand White rabbits were received from Nichols Rabbitry Inc., Lumberton, TX. The animals were housed

individually in suspended stainless steel cages with wire bottoms. The animals were fed PMI Feed, Inc.™ Lab Rabbit Diet No. 5321, in measured amounts. Municipal water was available *ad libitum*. The environmental conditions of the animal room were as follows: temperature, 20±3°C; relative humidity, 30-70%; air changes, 10-12 per hour; and photoperiod, 12 hour light/dark cycle.

3. **Methods:** The rabbits were ear-tagged: Nos. 4626-M and 4632-M (males) and 4625-F (female) and were acclimated for 5 days. The undiluted test material (0.1 mL/eye/animal) was applied in the conjunctival sac of the right eye, and the eye held closed for approximately one second. The untreated left eye served as control. The eyes were examined and scored 1, 24, 48 and 72 hours after test material instillation. All treated eyes were washed with room temperature deionized water for one minute immediately after the 24 hour observation.

II. RESULTS:

1. **Mortality:** All rabbits survived the study.

2. **Ocular Lesions:** No corneal opacity, iritis, or positive conjunctival irritation was noted on any rabbit (Table 1). Slight dulling of normal luster on the cornea was noted on two rabbits one hour after test material instillation with clearance on one rabbit by 24 hours and on another rabbit by 48 hours. A constricted pupil was noted on one male at one hour. The maximum average score was 2.0 at one hour after test material instillation (Table 2).

TABLE 1. Summary of Eye Irritation Scores with Time: Conjunctiva and Iris

Score Conditions	1 hour	24 hours	48 hours	72 hours
Conjunctiva				
Erythema	0 to 1	0 to 1	0	0
Chemosis	0 to 1	0	0	0
Discharge	0	0	0	0
Iris	0	0	0	0

Irritation score is based on Draize Method

Scale for Scoring Ocular Lesions

Cornea

A. Opacity-degree of density (area most dense taken for reading)
- No opacity 0
- Slight dulling of normal luster ..... +
- Scattered or diffuse areas of opacity (other than slight dulling of normal luster), details of iris clearly visible 1*
- Easily discernible translucent areas, details of iris slightly obscured 2*
- Nacreous areas, no details of iris visible, size of pupil barely discernible 3*
- Opaque cornea, iris not discernible through the opacity 4*

B. Area of cornea involved
- One quarter (or less), but not zero ....
- Greater than one quarter, but less than half 2
- Greater than half, but less than three quarters 3
- Greater than three quarters, up to whole area 4

Score = A x B x 5 Total Maximum Score = 80

Iris

A. Grades

Normal 0

Marked deepened rugae, congestion, swelling, moderate circumcorneal hyperemia or injection (any of these or combination thereof), iris still reacting to light (sluggish reaction is positive) 1*

No reaction to light, hemorrhage, gross destruction (any or all of these) 2*

Score = A x 5 Total Maximum Score = 10

Conjunctive

A. Redness: (refers to palpebral and bulbar conjunctive excluding cornea and iris)

Blood vessels normal 0

Some blood vessels definitely hyperemic (injected) 1

Diffuse, crimson color, individual vessels not easily discernible 2*

Diffuse beefy red 3*

B. Chemosis: lids and/or nictating membranes

No swelling 0

Any swelling above normal (includes nictitating membrane) 1

Obvious swelling with partial eversion of lids 2*

Swelling with lids about half closed 3*

Swelling with lids more than half closed 4*

C. Discharge

No discharge 0

Any amount different from normal (does not include small amounts observed in inner canthus of normal animals) 1

Discharge with moistening of the lids and hairs just adjacent to lids 2

Discharge with moistening of the lids and hairs, and considerable area around the eye 3

Score = (A + B + C) x 2 Total Maximum Score = 20

* Reaction indicates a positive effect.

TABLE 2. Summary of Total[a] and Primary Eye Irritation Scores with Time

Animal #	1 h	24 h	48 h	72 h
4625-F	2	0	0	0
4626-M	4	2	0	0
4632-M	0	0	0	0
Average scores[b]	2.0	0.7	0.0	0.0

[a]Formula: Total Irritation Score = I + II + III, where,
I = Corneal Score = [Density (A) x Area (B)] x 5
II = Iris Score = Severity x 5
III = Conjunctival Score = [Erythema (A) + Chemosis (B) + Discharge (C)] x 2
[b]Average Primary Irritation = Sum of Total Irritation Scores ÷ 3

III. DISCUSSION:

No corneal opacity, iritis, or positive conjunctival irritation was noted on any rabbit. Slight dulling of normal luster on the cornea was noted on two rabbits one hour after test material instillation with clearance on one rabbit by 24 hours and on another rabbit by 48 hours. Constricted pupil was noted on one male at one hour. The maximum average score was 2.0 at one hour after test material instillation. The reviewer agrees with the study author that Piedmont Pediculocide 1 was minimally irritating and is in TOXICITY CATEGORY IV. The packet classification is **ACCEPTABLE.**

DATA EVALUATION RECORD

ISOPROPYL MYRISTATE
(PIEDMONT PEDICULOCIDE 1)

STUDY TYPE: PRIMARY DERMAL IRRITATION - RABBIT (870.2500)
MRID 47925313

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 10-026

Primary Reviewer:
Susan Chang, M.S.

Signature: S. S. Chang
Date: OCT 14 2010

Secondary Reviewers:
H. Tim Borges, Ph.D., M.T.(A.S.C.P.), D.A.B.T.

Signature: Tim Borges
Date: OCT 14 2010

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date: OCT 14 2010

Quality Assurance:
Lee Ann Wilson, M.A.

Signature: L.A. Wilson
Date: OCT 14 2010

Disclaimer

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DATA EVALUATION RECORD

EPA Secondary Reviewer: ANGELA L GONZALES 3/2/11

STUDY TYPE:	Primary Dermal Irritation - Rabbits (OPPTS 870.2500)
MRID NO:	47925313
DP BARCODE NO:	DP 372778
DECISION NO:	424225
SUBMISSION NO:	863571
TEST MATERIAL:	Piedmont Pediculocide 2 (EPA Reg. No. 86865-R)
PROJECT NO:	7090-02
SPONSOR:	Piedmont Pharmaceuticals, 204 Muirs Chapel Road, Greensboro, NC 27410
TESTING FACILITY:	Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478
TITLE OF REPORT:	Piedmont Pediculocide 1 – Acute Dermal Irritation Study in Rabbits
AUTHOR:	Janice O. Kuhn
STUDY COMPLETED:	August 8, 2002
GOOD LABORATORY PRACTICE:	GLP Compliant with the exception that Sec. 160.31(d), and 160.105 (a)(b)(e) characterization and stability information was not provided in a Certificate of Analysis.
CONCLUSION:	No dermal irritation was noted on any rabbit. The primary irritation index was 0.0. Piedmont Pediculocide 1 was not irritating.
CLASSIFICATION:	ACCEPTABLE -- TOXICITY CATEGORY IV

I. STUDY DESIGN:

1. **Test Material:** Piedmont Pediculocide 1; label: IPM Solution Lot No. 170602A; pH 5.68.

2. **Test Animals:** One female and two male young adult New Zealand White rabbits were received from Nichols Rabbitry Inc., Lumberton, TX. The animals were housed individually in suspended stainless steel cages with wire bottoms. The animals were fed PMI Feed, Inc.™ Lab Rabbit Diet No. 5321, in measured amounts and municipal water was available *ad libitum*. The environmental conditions of the animal room were as follows: temperature, 20±3°C; relative humidity, 30-70%; air changes, 10-12 per hour; and photoperiod, 12 hour light/dark cycle.

3. **Methods:** The rabbits were ear-tagged: Nos. 4636-M and 4638-M (males) and 4641-F (female) and acclimated for 5 days. The fur on the dorsal trunk of each rabbit was clipped on the day prior to treatment. The rabbits were treated with 0.5 mL of undiluted test material applied on a clipped intact dose site, and the site covered with a 2.5 cm x 2.5 cm gauze patch. The patch and entire trunk were wrapped with a semi-permeable dressing tape. The covering was removed 4 hours later and the site cleansed to remove any residual test material. Dermal examination was recorded at 1, 24, 48, and 72 hours after removal of the patch.

II. RESULTS:

1. **Mortality:** All rabbits survived the study.

2. **Dermal responses:** No dermal irritation was noted on any rabbit. The primary irritation index was 0.0.

Irritation Scores:

TABLE 1. Summary of individual rabbit's dermal irritation scores with time

	Hours			
Animal Nos.	1	24	48	72
4636-M	0/0[a]	0/0	0/0	0/0
4638-M	0/0	0/0	0/0	0/0
4641-F	0/0	0/0	0/0	0/0

Data taken from Table 1, p. 11, MRID 47925313.
[a]Erythema/Edema

DESCRIPTION OF RATING METHOD

Evaluation of Skin Reaction:	Score
Erythema formation:	
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Edema Formation:	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Severe edema (raised by more than 1 mm extending beyond the area of exposure)	4

III. DISCUSSION:

No dermal irritation was noted on any rabbit. The primary irritation index was 0.0. The reviewer agrees with the study author that Piedmont Pediculocide 1 was not irritating and is in TOXICITY CATEGORY IV. The packet classification is **ACCEPTABLE.**

DATA EVALUATION RECORD

ISOPROPYL MYRISTATE
(RESULTIX TICK SPRAY)

STUDY TYPE: SKIN SENSITIZATION - GUINEA PIG (870.2600)
MRID 47925314

Prepared for
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by
Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 10-026

Primary Reviewer: Susan Chang, M.S.	Signature:	
	Date:	OCT 14 2010
Secondary Reviewers: H. Tim Borges, Ph.D., M.T.(A.S.C.P.), D.A.B.T.	Signature:	
	Date:	OCT 14 2010
Robert H. Ross, M.S., Group Leader	Signature:	
	Date:	OCT 14 2010
Quality Assurance: Lee Ann Wilson, M.A.	Signature:	
	Date:	OCT 14 2010

Disclaimer

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DATA EVALUATION RECORD

EPA Secondary Reviewer:	**Angela L. Gonzales 3/28/11**
STUDY TYPE:	Skin Sensitization - Guinea Pigs (OPPTS 870.2600)
MRID NO:	47925314
DP BARCODE NO:	DP 372778
DECISION NO:	424225
SUBMISSION NO:	863571
TEST MATERIAL:	Resultix Tick Spray (EPA Reg. No. 86865-R)
PROJECT NO:	13304-09
SPONSOR:	Piedmont Pharmaceuticals, 204 Muirs Chapel Road, Greensboro, NC 27410
TESTING FACILITY:	Stillmeadow, Inc., 12852 Park One Drive, Sugar Land, TX 77478
TITLE OF REPORT:	Resultix Tick Spray - Skin Sensitization Study in Guinea Pigs
AUTHOR:	Janice O. Kuhn
STUDY COMPLETED:	November 6, 2009
GOOD LABORATORY PRACTICE:	GLP Compliant with exception that Sec. 160.31(d), and 160.105 (a)(b)(e) characterization and stability information was not provided in a Certificate of Analysis.
CONCLUSION:	After three consecutive weekly inductions, the test and naive control animals showed no signs of reactivity at 24 and 48 hours after challenge. The study included an α-hexylcinnamaldehyde positive control study which was carried out within six months of the study and the results were appropriate. Piedmont Pediculocide 2 was not a dermal sensitizer.
CLASSIFICATION:	ACCEPTABLE

I. STUDY DESIGN:

1. **Test material:** Resultix Tick Spray; label identification: Resultz®, DIN 02279592, head lice treatment, Lot No. C6102711.

2. **Test animals:** Seventeen male and seventeen female Hartley guinea pigs received from Charles River Laboratories, Wilmington, MA were assigned to groups and weighed 330-378 g (males) and 317-394 g (females) at experiment start. The young adult animals were housed in suspended stainless steel cages with wire bottoms. The animals were fed PMI Feeds, Inc.™, Guinea Pig Diet No. 5025, *ad libitum*. Municipal water was available *ad libitum*. The environmental conditions of the animal room were as follows: temperature, 19-21°C; relative humidity, 47-94% (Humidity outside the protocol range but did not affect the study outcome); air changes, 10-12 per hour; and photoperiod, 12 hour light/dark cycle.

3. **Methods:** Male and female guinea pigs were identified by ear punch and grouped: Preliminary irritation testing – Nos. 1-M and 2-M (males) and 3-F and 4-F (females); Test – Nos. 201-M to 205-M and 211-M to 215-M (males) and Nos. 206-F to 210-F and 216-F to 220-F (females); Naive Control – Nos. 191-M to 195-M (males) and Nos. 196-F to 200-F (females). The guinea pigs were acclimated for 5 days. The animals were induced and challenged according to the method of Buehler. The results of the preliminary irritation testing determined that the undiluted test material was to be used for induction and challenge. The back of the trunks of 20 test and 10 naive control guinea pigs were clipped prior to each treatment. For the induction, 0.4 mL undiluted test material was applied beneath a 2.5 x 2.5 cm surgical gauze patch and secured with non-irritating adhesive tape. A strip of clear polyethylene film was placed over the patch and securely taped. After six hours, the coverings and excess test material were removed. The procedure was repeated once each week for three consecutive weeks. After a two-week rest period, the test animals were challenged with 0.4 mL undiluted test material under occlusion to naive sites. At challenge, a naive control group (10 animals) was treated with 0.4 mL undiluted test material. Reactions were scored at approximately 24 hours following induction and challenge application and at 48 hours following the first induction and challenge.

II. RESULTS:

1. **Mortality:** All animals survived the study.

2. **Body Weight:** All animals gained weight during the study.

3. **Skin Effects:** No dermal reaction was noted on any test animal after inductions. No dermal reaction was noted on any test or naive control animal after challenge.

TABLE 1. Summary of Individual Erythema Challenge Scores with Time [a]

	24 hours				48 hours			
Erythema Score	0	0.5	1.0	2.0	0	0.5	1.0	2.0
Treated	20	0	0	0	20	0	0	0
Naive Control	10	0	0	0	20	0	0	0

[a]Number of animals affected
Evaluation score is based on Buehler Grading Scale.

SCALE FOR SCORING SKIN REACTION

Buehler sensitization scoring scale

Erythema	Score
No reaction	
Very faint, usually nonconfluent	0.5
Faint, usually confluent	1
Moderate	2
Severe with or without edema	3

III. DISCUSSION:

After three consecutive weekly inductions, the test and naive control animals showed no signs of reactivity at 24 and 48 hours after challenge. The study included an alpha-hexylcinnamaldehyde positive control study which was carried out within six months of the current study and the results were appropriate. Resultix Tick Spray was not a dermal sensitizer. The packet is classified as **ACCEPTABLE.**

DATA EVALUATION RECORD

ISOPROPYL MYRISTATE [RESULTIX™]
NON-GUIDELINE
STUDY TYPE: 28-DAY ORAL TOXICITY - RAT
MRID 47925315

Prepared for

Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by

Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
BPPD Work Assignment No. 10-026

Primary Reviewer:
Donna L. Fefee, D.V.M.

Signature: Robert H. Ross for D.L. Fefee
Date:

Secondary Reviewers:
H.T. Borges, Ph.D., MT(ASCP), D.A.B.T.

Signature: Tim Borges
Date:

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date:

Quality Assurance:
Eric Lewis, M.S.

Signature: Eric B. Lewis
Date:

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

EPA Work Assignment Manager: Cheryl Greene, Ph.D. (7511C) **Signature:** _____
ANGELA L GONZALES 3/28/11 **Date:** _____

TXR#:

DATA EVALUATION RECORD

STUDY TYPE: 28-Day Oral [Gavage] Toxicity - Rat; Non-guideline

PC CODE: 000207 **DP BARCODE:** 372778

TEST MATERIAL (PURITY): Pediculocide 100 [Isopropyl Myristate Solution 50% w/w] (50.95% a.i., lot #C0163A001)

SYNONYMS: Resultix™

CITATION: Goldenthal, E. (2003) 28-Day oral toxicity study in rats with a 14-day recovery. MPI Research, Inc., 54943 N. Main Street, Mattawan, Michigan. Laboratory study number 1016-001, November 20, 2003. MRID 47925315. Unpublished.

SPONSOR: Piedmont Pharmaceuticals, Greensboro, North Carolina.

EXECUTIVE SUMMARY:

In a 28-day oral toxicity study (MRID 47925315), undiluted Pediculocide 100 [Isopropyl Myristate Solution 50% w/w] (50.95% a.i., lot #C0163A001) was administered by gavage every three days to ten CD® [Crl:CD® (SD)IGS BR] rats/sex/dose at volumes of 3, 7.5, or 15 mL/kg, and a control group of ten animals/sex was treated in a similar manner with 15 mL/kg of deionized water. Four "recovery" groups of five animals/sex/dose were treated according to the same schedule and at the same dose volumes described above, followed by a 14-day recovery period with no further treatments. Three additional groups of ten animals/sex/dose were given the test material by gavage every three days at a dose volume of 3, 7.5, or 15 mL/kg and used for toxicokinetic determinations. Dosing took place on days 1, 4, 7, 10, 13, 16, 19, 22, 25, and 28 of the study, and the doses were equivalent to 0, 1407, 3518, or 7036 mg/kg bw/*dose* (every three days).

One high-dose main study female was found dead on day 8, and one high-dose recovery female was found dead on day 42; the causes of these deaths could not be determined. Two high-dose females were observed to be "hypersensitive to touch": one during weeks 2-4, and the other during week 5. The remaining treatment-related clinical signs were dermatological in nature and included the following: oily hair, sparse hair, dry skin, scabbed areas, red discoloration of the skin, and scaling of the tail. During the main study, 4, 11, and 15 males from each of the low-, mid-, and high-dose groups, respectively, and 1, 3, 12, and 14 females from the control, low-, mid-, and high-dose groups, respectively, had some combination of these signs, which increased in distribution, severity, and duration with increasing dose. In general, the first sign to appear was oily hair in the anogenital region, and the last sign to appear was scaling or dry skin and

scabbing of the tail. Some of the low- and mid-dose animals had their initial onset of dermatological signs during recovery or had a recurrence and worsening of signs that had resolved before week 4.

High-dose males had decreased weight gain during the first three weeks, lost more weight than controls during the fourth week of the main study, and had decreased cumulative body weight gain over the main study interval (41% less than controls). High-dose females had decreased body weight gain during the first two weeks of the main study, with a resultant decrease in cumulative body weight gain over the main study interval (64% less than controls). Absolute body weight was not significantly affected by treatment. Mid- and high-dose females had increased liver weights on day 28 (relative to body weights: 38% and 48% greater than controls, respectively), which had largely resolved by the end of recovery (relative to body weights: 13% and 25% greater than controls, respectively). These correlated with histopathological observations of minimal to mild panlobular hepatocyte hypertrophy, which was seen on day 28 only and which is considered an adaptive, physiological response to a xenobiotic agent, rather than an adverse effect. The high-dose recovery females had markedly increased pituitary and thyroid/parathyroid weights (relative to body weights were 42% and 33% greater than controls); because these organs were only examined microscopically in the main study animals, the significance of these increases is unknown.

For the reasons given below, the results of this study cannot be used to determine a subchronic (28-day) oral toxicity LOAEL and NOAEL.

Because the investigators neglected to perform histopathology on tissues and organs identified as showing effects in the treated groups, and failure to use a consistent dosing volume and vehicle for all treatment groups, this 28-day oral toxicity study in the rat is **Unacceptable / Non-guideline**. Due to use of an incorrect dosing regimen, this study *does not satisfy* the guideline requirement for a 28-day oral toxicity study (OPPTS 870.3050; OECD 407) in a rodent species, although it may provide useful supplemental information.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS:

A. MATERIALS:

1. Test material: Pediculocide 100

Description:	Clear, viscous liquid; specific gravity: 0.9207
Lot:	C0163A001 or C0163001 (different lot numbers given on analytical release forms
Purity:	50.95% a.i.; water content 0.0000%
Compound stability:	Expected to be stable for the duration of the study
CAS # of TGAI:	Not available
Structure:	Not available

2. Vehicle and/or positive control: The vehicle was deionized water supplied by the Test Material Control Department. No positive control was used.

3. Test animals:

Species:	Rat
Strain:	CD® [Crl:CD® (SD)IGS BR]
Age/weight at study initiation:	Approximately 10 weeks/males: 327-413 g; females: 199-284 g
Source:	Charles River Laboratories, Portage, Michigan
Housing:	Individually in suspended, stainless-steel, wire-mesh cages
Diet:	Meal Lab Diet® Certified Rodent Diet® #5002 (PMI Nutrition International, Inc.), *ad libitum*
Water:	Tap water, *ad libitum*
Environmental conditions:	**Temperature:** 69-79°F **Humidity:** 32-68% **Air changes:** not reported **Photoperiod:** 12 hrs dark/12 hrs light
Acclimation period:	Approximately two weeks

B. STUDY DESIGN:

1. In life dates: Start: June 19, 2003; End: July 31, 2003.

2. Animal assignment: Animal assignment is given in Table 1. Animals were assigned to the test groups based on body weight using a standard block randomization procedure. The first five animals per sex in the main study groups were designated for further evaluation over a 14-day recovery period.

TABLE 1: Study design

Test group	Dosing volume (mL/kg) every 3 days	Estimated dose to animal (mg/kg) every 3 days [a]	# Assigned					
			Main Study		Recovery		Toxicokinetic	
			Males	Females	Males	Females	Males	Females
Control	15	0	10	10	5	5	0	0
Low-dose	3	1407	10	10	5	5	10	10
Mid-dose	7.5	3518	10	10	5	5	10	10
High-dose	15	7036	10	10	5	5	10	10

Data from pp. 11-12 and 585, MRID 47925315.

[a] Calculated by reviewer as dosing volume in mL times 0.9207 g/mL times % a.i. times 1000 mg/g.

3. **Dose selection rationale:** The dose levels were selected by the sponsor, based on previous studies. No further information was provided.

4. **Dose administration:** Doses of the control article or undiluted test material were administered once every three days (on days 1, 4, 7, 10, 13, 16, 19, 22, 25, and 28), in the volumes given in Table 1, based on the most recent body weights. Although not explicitly stated in the study report, it is assumed that dosing was by gavage.

5. **Statistics:** Mean body and organ weights, hematology values, and all clinical chemistry results except for creatine kinase activity were analyzed using Levene's test followed by either Dunnett's test (for data with homogeneous variances) or Welch's t-test with a Bonferroni correction (for data with non-homogeneous variances). Total and differential leukocyte counts were log-transformed prior to analysis. Creatine kinase data were rank-transformed and then analyzed using Dunnett's test. All endpoints were analyzed using two-tailed tests, and the results were reported at the 0.05 and 0.01 significance levels.

   The Reviewer considers the analyses to be appropriate.

6. **Historical control data:** The study report included the following historical control data:
   - Historical control data for clinical pathology (hematology and clinical chemistry) for male and female Sprague-Dawley rats, aged 9 to 14 weeks, and sampled by orbital sinus collection between August 1998 and July 2003.
   - Historical control data for clinical pathology (hematology and clinical chemistry) for male and female Sprague-Dawley rats, aged 14 to 18 weeks, and sampled by orbital sinus collection between August 1998 and October 2002.
   - Historical control data for clinical pathology (urinalysis) for male and female Sprague-Dawley rats, aged 14 to 18 weeks, and sampled by orbital sinus collection [sic] between August 1998 and October 2002.

   These were presented as overall means and standard deviations, ranges of the mean ± two standard deviations, and individual animal range. The numbers of animals ranged from twenty to thirty.

C. METHODS:

1. Observations:

a. **Cageside observations:** All animals were observed at least twice daily for mortality, morbidity, signs of toxicity, or injury.

b. **Clinical examinations:** Detailed clinical examinations were conducted weekly. Only the main study and recovery animals received these examinations.

c. **Neurological evaluations:** Neurological evaluations were not done as part of the current study. No explanation was provided for the omission.

2. **Body weight:** Animals were weighed the day after arrival, prior to randomization (day -1), and daily during treatment and recovery, except for days 31 and 32 (of recovery), when the measurements were inadvertently omitted.

3. **Food consumption:** Individual food consumption was measured daily during the treatment and recovery intervals, except for days 31 and 32 (of recovery), when the measurements were inadvertently omitted. Food consumption by the animals used for toxicokinetic analyses was not measured.

4. **Ophthalmoscopic examination:** All animals were given eye examinations prior to exposure and on day 26. The examinations were done by a board-certified veterinary ophthalmologist. Eyes were dilated with tropicamide, and an indirect ophthalmoscope was used.

5. **Hematology and clinical chemistry:** On day 28 (main study and recovery animals) and at the end of recovery (for recovery animals) and following an overnight fast of food only, blood for hematology, coagulation, and clinical chemistry evaluations was collected from all surviving animals of these groups. Samples were taken from the orbital sinus plexus under carbon dioxide anesthesia. The CHECKED (X) parameters were examined. Although not stated explicitly in the study report, it is assumed that the recovery samples were collected on day 42.

   a. **Hematology:**

X	Hematocrit (HCT)*	X	Leukocyte differential count*
X	Hemoglobin (HGB)*	X	Mean corpuscular HGB (MCH)*
X	Leukocyte count (WBC)*	X	Mean corpusc. HGB conc.(MCHC)*
X	Erythrocyte count (RBC)*	X	Mean corpusc. volume (MCV)*
X	Platelet count*	X	Reticulocyte count
	Blood clotting measurements*		
X	(Thromboplastin time)		
	(Clotting time)		
X	(Prothrombin time)		

* Recommended for 28-day oral rodent studies based on Guideline 870.3050

b. **Clinical chemistry:**

X	ELECTROLYTES	X	OTHER
X	Calcium	X	Albumin*
X	Chloride	X	Creatinine*
	Magnesium	X	Urea nitrogen*
X	Phosphorus	X	Total Cholesterol*
X	Potassium*	X	Globulins
X	Sodium*	X	Glucose*
	ENZYMES (more than 2 hepatic enzymes eg., *)	X	Total bilirubin
X	Alkaline phosphatase (ALK)*	X	Total protein (TP)*
	Cholinesterase (ChE)	X	Triglycerides
X	Creatine phosphokinase (CK)		Serum protein electrophoresis
	Lactic acid dehydrogenase (LDH)		
X	Alanine aminotransferase (ALT/also SGPT)*		
X	Aspartate aminotransferase (AST/also SGOT)*		
	Sorbitol dehydrogenase*		
X	Gamma glutamyl transferase (GGT)*		
	Glutamate dehydrogenase		

* Recommended for 28-day oral rodent studies based on Guideline 870.3050

6. **Urinalysis***: Following blood collection, the main study and/or recovery animals were transferred to metabolism cages for an approximately 16-hour urine collection. The CHECKED (X) parameters were examined.

X	Appearance*	X	Glucose
X	Volume*	X	Ketones
X	Specific gravity/osmolality*	X	Bilirubin
X	pH*	X	Blood/blood cells*
X	Sediment (microscopic)		Nitrate
X	Protein*	X	Urobilinogen

* Optional for 28-day oral rodent studies

7. **Plasma concentration determinations:** On days 1-2 and 28-29, blood samples were collected from the animals of the toxicokinetic groups, prior to dosing (i.e. 0 hours after dosing) and 1, 2, 4, 8, and 24 hours after dosing for determinations of the plasma concentration of the test material. Samples were collected from cohorts of three unfasted animals/sex/group at each time point from the orbital sinus under carbon dioxide anesthesia, such that one cohort was evaluated at 0 and 4 hours post-dosing, one cohort was evaluated at 1 and 8 hours post-dosing, and one cohort was evaluated at 2 and 24 hours post-dosing. Following blood collection on day 29, the animals of the toxicokinetic groups were sacrificed by carbon dioxide asphyxiation and discarded without further evaluation.

The blood samples were placed on ice after collection. The separated plasma was later aliquoted into pre-labeled plastic tubes or vials, and stored at –70°C. The analytical assay was conducted by KAR Laboratories, Inc., Kalamazoo, Michigan, using a sponsor-supplied, validated analytical method, which was not otherwise specified or described in the protocol or the study report.

8. **Sacrifice and pathology:** Surviving animals from the main study and recovery groups were sacrificed by exsanguination from the abdominal vena cava under carbon dioxide anesthesia on day 29 (main study animals) or on day 43 (recovery animals). All were subjected to a gross necropsy, which included external examination including palpable masses and internal examination of the contents of the abdominal, thoracic, and cranial cavities. Bone marrow smears were collected and retained for potential future examination. The CHECKED (X) organs or tissues, or representative samples thereof, were collected and fixed in neutral buffered formalin or Davidson's fixative (for eyes with optic nerve and contiguous Harderian gland). Histopathological examination was conducted on the full complement of collected tissues from animals of the main study control and high-dose groups, as well as the livers and all gross lesions and masses from the main study animals of the lower dose groups and the recovery animals from all groups. The INDICATED (XX) organs, in addition, were weighed, with the paired organs weighed together.

Complete necropsies were also conducted for any main study or recovery animals that were found dead or sacrificed moribund. These were done in a similar manner to that described above, including collection and subsequent microscopic evaluation of the full complement of tissues, where practical.

X	DIGESTIVE SYSTEM	X	CARDIOVASC./HEMAT.	X	NEUROLOGIC
X	Tongue	X	Aorta*	XX	Brain*+
X	Salivary glands*	XX	Heart*+	X	Peripheral nerve (sciatic)*
X	Esophagus*	X	Bone marrow*	X	Spinal cord (3 levels)*
X	Stomach*	X	Lymph nodes*	XX	Pituitary*#
X	Duodenum*	XX	Spleen*+	X	Eyes (optic nerve)*
X	Jejunum*	X	Thymus*+	X	GLANDULAR
X	Ileum*			XX	Adrenal gland*+
X	Cecum*	X	UROGENITAL	X	Lacrimal gland
X	Colon*	XX	Kidneys*+	XX	Parathyroid*#^
X	Rectum*	X	Urinary bladder*	XX	Thyroid*#^
XX	Liver*+	XX	Testes*+	X	Harderian gland
	Gall bladder (not rat)*	X	Epididymides*+	X	OTHER
	Bile duct (rat)	X	Prostate*	X	Bone (sternum and/or femur)
X	Pancreas*	X	Seminal vesicles*	X	Skeletal muscle (biceps femoris)
X	RESPIRATORY	XX	Ovaries*+	X	Skin*
X	Trachea*	X	Uterus with cervix*+	X	All gross lesions and masses*
X	Lung*	X	Mammary gland*‡		
	Nose*	X	Vagina		
	Pharynx*				
	Larynx*				

* Recommended for 28-day oral rodent studies based on Guideline 870.3050
\+ Organ weights required for rodent studies.
\# Weighed following fixation.
^ Thyroid and parathyroids were weighed together.
‡ Females only.

II. RESULTS:

A. OBSERVATIONS:

1. **Clinical signs of toxicity:** Cageside observations either were not reported or were reported together with the observations from the weekly detailed clinical examinations, as "clinical findings." Treatment-related or potentially treatment-related clinical findings are given in Table 2.

   Two high-dose females were observed to be "hypersensitive to touch": one during weeks 2-4, and the other during week 5; the significance of this finding is unclear, as it could be an indication of neurotoxicity, but it also could be related to pain or discomfort. The remaining treatment-related clinical signs were dermatological in nature and somewhat distinctive with respect to their regional distribution and time course. Affected main study low-dose animals had oily and/or sparse hair in the anogenital region and/or rarely the inguinal regions during weeks 2 or 2-3, which resolved by week 4. With increasing dose, the lesions persisted longer, and the oily and/or sparse hair spread cranially, over the ventral surface of the animal and/or over the sacrum, over the rear legs, and possibly over the entire body. In general, the last sign to appear was scaling or dry skin and scabbing of the tail. Some of the low- and mid-dose animals had their initial onset of dermatological signs during recovery or had a recurrence and worsening of signs that had resolved before week 4.

2. **Mortality:** One high-dose main study female was found dead on day 8 and had an abnormal gross necropsy finding of red discoloration of the lung with no histopathological correlates. One high-dose recovery female was found dead on day 42, with no abnormal gross necropsy findings. The causes of these deaths could not be determined.

TABLE 2. Clinical findings (number of times observed/number of affected animals) [a]

Observation	Dose (mL/kg bw/every three days)							
	Males				Females			
	Control	3	7.5	15	Control	3	7.5	15
Weeks 1 to 4 (Main study)								
[Number of animals]	[15]	[15]	[15]	[15]	[15]	[15]	[15]	[14-15]
Hypersensitive to touch	0/0	0/0	0/0	0/0	0/0	0/0	0/0	3/1
Hair oily	0/0	5/4	54/11	58/15	0/0	5/3	15/7	41/13
Hair sparse	0/0	0/0	0/0	98/14	2/1	1/1	66/11	109/14
Skin dry	0/0	0/0	0/0	17/6	0/0	0/0	0/0	30/8
Scabbed area	0/0	0/0	0/0	8/3	1/1	0/0	0/0	41/9
Scaling of the tail	0/0	0/0	1/1	3/3	0/0	0/0	0/0	5/5
Skin discolored, red	0/0	0/0	0/0	14/2	0/0	0/0	0/0	16/4
Weeks 5 to 6 (Recovery)								
[Number of animals]	[5]	[5]	[4]	[5]	[5]	[5]	[5]	[3-4]
Hypersensitive to touch	0/0	0/0	0/0	0/0	0/0	0/0	0/0	1/1
Hair oily	0/0	26/5	10/4	13/5	0/0	21/5	9/5	5/3
Hair sparse	2/1	0/0	5/4	30/3	0/0	1/1	25/5	25/4
Skin dry	0/0	0/0	4/2	10/4	0/0	2/1	6/4	11/4
Scabbed area	0/0	0/0	0/0	12/3	0/0	0/0	4/1	5/2
Scaling of the tail	0/0	0/0	0/0	2/1	0/0	0/0	0/0	1/1
Skin discolored, red	0/0	0/0	0/0	3/2	0/0	0/0	0/0	2/2

Data from Table 1, pp. 42-45, MRID 47925315.

B. BODY WEIGHT AND WEIGHT GAIN: Selected body weight data are given in Tables 3a and 3b. High-dose males gained less weight than controls during the first three weeks and lost more weight than controls during the fourth week of the main study, and this group's cumulative body weight gain over the main study interval was 41% less than controls. This was followed by a slight compensatory increase in weight gain by high-dose recovery males during the first week of recovery. High-dose females had decreased body weight gain during the first two weeks of the main study and had similar weight gain (or weight loss) to controls over the remaining two weeks of the main study. This resulted in a cumulative body weight gain over the main study interval that was 64% less than controls, which was followed by a 66% increase in weight gain (relative to controls) by the high-dose recovery females during the first week of recovery.

The decreased body weight gains of high-dose males and females were not reflected in the groups' mean absolute body weights, which remained within ±7% of the control values throughout treatment.

TABLE 3a. Body weight data for male rats treated for 28 days with or without 14 days of recovery (g) [a]

Parameter/Study day or interval		Dose (mL/kg/every three days)			
		Control	3	7.5	15
Main Study [n = 15, all groups]					
Absolute body weight:	Day -1	360.7 ± 22.29	358.9 ± 12.29	359.4 ± 14.95	358.3 ± 22.65
	Day 7	373.6 ± 28.87	373.5 ± 15.47	374.3 ± 23.54	369.4 ± 25.90
	Day 14	398.0 ± 34.59	401.7 ± 21.39	407.3 ± 30.22	383.7 ± 34.11
	Day 21	427.9 ± 34.47	426.7 ± 27.41	435.7 ± 33.17	406.6 ± 34.94
	Day 28	424.8 ± 36.65	412.8 ± 29.93	421.5 ± 36.65	396.0 ± 36.64
Body weight changes [b]:	Days -1 to 7	12.9	14.6	14.9	11.1 (-14)[c]
	Days 7 to 14	24.4	28.2	33.0	14.3 (-41)
	Days 14 to 21	29.9	25.0	28.4	22.9 (-23)
	Days 21 to 28	-3.1	-13.9	-14.2	-10.6
Cumulative change	Days -1 to 28	64.1	53.9	62.1	37.7 (-41)
Recovery [n = 5, all groups]					
Absolute body weight:	Day 28	416.4 ± 18.47	416.6 ± 38.99	415.2 ± 26.07	397.2 ± 48.80
	Day 36	453.6 ± 24.12	462.8 ± 40.94	454.2 ± 27.03	439.2 ± 41.71
	Day 43	457.0 ± 25.13	467.4 ± 37.69	454.4 ± 28.97	441.0 ± 38.01
Body weight changes[b]:	Days 28 to 36	37.2	46.2	39.0	42.0 (+13)
	Days 36 to 43	3.4	4.6	0.2	1.8
Cumulative change	Days 28 to 43	40.6	50.8	39.2	43.8

Data from Table 2, pp. 47-48 and 51, MRID 47925315.

[a] Values are Mean ± Standard Deviation with group sizes as indicated.

[b] Calculated by reviewer, using group means; not analyzed statistically.

[c] Numbers in parentheses equal percent different from control; calculated by reviewer.

* p <0.05; **p <0.01

TABLE 3b. Body weight data for female rats treated for 28 days with or without 14 days of recovery (g) [a]

Parameter/Study day or interval		Dose (mL/kg/every three days)			
		Control	3	7.5	15
Main Study [n = 15, 15, 15, and 14-15, in ascending group order] [b]					
Absolute body weight:	Day -1	231.5 ± 10.74	235.0 ± 16.26	237.4 ± 17.48	229.7 ± 13.05
	Day 7	235.4 ± 14.17	240.1 ± 17.37	245.3 ± 18.13	230.2 ± 16.04
	Day 14	247.3 ± 14.92	256.8 ± 20.31	259.7 ± 18.29	236.8 ± 13.89
	Day 21	255.0 ± 18.52	265.8 ± 22.21	266.8 ± 17.69	245.4 ± 18.23
	Day 28	246.5 ± 18.56	252.5 ± 23.45	253.1 ± 19.15	235.1 ± 16.90
Body weight changes [c]:	Days -1 to 7	3.9	5.1	7.9	0.5 (-87) [d]
	Days 7 to 14	11.9	16.7	14.4	6.6 (-45)
	Days 14 to 21	7.7	9.0	7.1	8.6
	Days 21 to 28	-8.5	-13.3	-13.7	-10.3
Cumulative change	Days -1 to 28	15.0	17.5	15.7	5.4 (-64)
Recovery [n = 5, 5, 5, and 3-4, in ascending group order] [e]					
Absolute body weight:	Day 28	237.6 ± 15.76	271.4* ± 9.37	256.0 ± 25.67	243.0 ± 18.97
	Day 36	253.6 ± 18.06	293.4* ± 13.37	278.2 ± 33.30	269.5 ± 16.74
	Day 43	248.2 ± 21.42	286.8* ± 5.22	280.6 ± 32.62	269.7 ± 14.36
Body weight changes [c]:	Days 28 to 36	16.0	22.0	22.1	26.5 (+66)
	Days 36 to 43	-5.4	-6.6	2.4	0.2
Cumulative change	Days 28 to 43	10.6	15.4	24.6	26.7 (+152)

Data from Table 2, pp. 49-50 and 52, MRID 47925315.

[a] Values are given as Mean ± Standard Deviation with group sizes as indicated.

[b] There were 15 high-dose females on days -1 through 7 and 14 thereafter.

[c] Calculated by reviewer, using group means; not analyzed statistically.

[d] Numbers in parentheses equal percent different from control; calculated by reviewer.

[e] There were 4 high-dose females on days 28 through 42, and 3 on day 43.

* $p < 0.05$; ** $p < 0.01$

C. **FOOD CONSUMPTION:** For the first three weeks of the study, mean daily food consumption of the high-dose animals of both sexes followed a pattern, in which food consumption was decreased on the days the animals were dosed, increased on the day prior to dosing, and at an "intermediate" level on the day after dosing, and on numerous occasions the decreases or increases relative to controls were statistically significant. These differences are attributable to the 15-mL dosing volume used for these animals, which exceeded the recommendation to use a dosing volume no greater than 1 mL per 100 g body weight when using non-aqueous solutions. Although these differences are related to treatment, they are due to mechanical overfilling of the stomach rather than systemic toxicity, and the time-weighted average weekly food consumption values of the high-dose animals were similar to those of controls throughout the treatment interval for males or during weeks 2-4 of treatment for females. Nevertheless, high-dose animals of both sexes had a compensatory increase in food consumption during the first week of recovery.

TABLE 4. Food consumption of rats treated 28 days with or without 14 days of recovery (g/animal/day) [a]

Parameter/Study day or interval		Dose (mL/kg/every three days)			
		Control	3	7.5	15
Males [n = 15 for all groups during main study, and n = 5 for all groups during recovery]					
Main Study:	Day 1	25.2 ± 3.10	24.2 ± 2.34	22.2* ± 2.01 (-12) [b]	20.3** ± 2.13 (-19)
	Week 1	25.2	24.9	24.4	23.8
	Week 2	24.7	25.6	26.5	25.5
	Week 3	26.2	26.5	27.6	28.1
	Week 4	24.8	22.8	23.2	24.7
Recovery:	Week 5 [c]	28.6	27.8	28.7	33.2 (16)
	Week 6	25.5	24.9	24.3	27.4
Females [n = 15, 15, 15, and 14-15 during main study and n = 5, 5, 5, and 3-4 during recovery, in ascending group order] [d]					
Main Study:	Day 1	17.1 ± 2.19	16.1 ± 3.41	15.4 ± 3.62	11.7** ± 2.63 (-32)
	Week 1	17.7	17.9	18.1	14.9 (-15)
	Week 2	18.2	19.9	19.8	17.9
	Week 3	18.4	19.7	19.8	19.7
	Week 4	16.7	16.7	17.1	16.6
Recovery:	Week 5 [c]	18.7	21.2 (13)	22.5 (20)	24.9 (33)
	Week 6	16.4	18.9 (15)	20.4 (25)	18.0 (10)

Data taken or derived from Table 3, pp. 58-64, MRID 47925315.

[a] Values are given as Mean ± Standard Deviation with group sizes as indicated or as a time weighted mean of means, calculated by reviewer and not analyzed statistically.

[b] Numbers in parentheses equal percent different from control; calculated by reviewer.

[c] The values reported for day 30 were a mean of days 30-32. The mean of means was calculated using this value for the whole three days rather than just once.

[d] During main study there were 15 high-dose females on days -1 through 7 and 14 thereafter. During recovery there were 4 high-dose females on days 28 through 42, and 3 on day 43.

* $p < 0.05$; ** $p < 0.01$

D. OPHTHALMOSCOPIC EXAMINATION: The only recorded abnormality was conjunctivitis in the left eye of one mid-dose male. This finding was not considered treatment-related.

E. BLOOD ANALYSES:

1. **Hematology:** Selected hematology data are given in Table 5. On day 28, both sexes had slight, but statistically significant, dose- and treatment-related decreases in mean erythrocyte counts (RBC), hemoglobin concentration (HGB), and hematocrit (HCT) without co-occuring changes in the erythrocyte indices (MCV, MCH, MCHC). These changes are not considered adverse because almost all of the mean values remained within the provided historical control ranges; the exception was the mean HCT for high-dose females, which fell just below the range for 14- to 18-week old animals (41.7-47.9%). On day 42, the mean values of the treated groups were similar to those of controls.

TABLE 5. Hematology data of male and female rats treated for 28 days with or without 14 days of recovery [a]					
Parameter/Study day		Dose (mL/kg/every third day)			
		Control	3	7.5	15
Males [n = 15 for all groups on day 28, and n = 5 for all groups on day 42]					
Erythrocytes (10^6/µL):	Day 28	8.412 ± 0.523	7.915* ± 0.410	7.665** ± 0.631	7.477** ± 0.649
	Day 42	7.982 ± 0.324	7.490 ± 0.392	7.616 ± 0.327	7.650 ± 0.355
Hemoglobin (g/dL):	Day 28	15.25 ± 0.853	14.42* ± 0.923	13.93** ± 0.979	13.67** ± 1.011
	Day 42	14.72 ± 0.507	14.20 ± 0.704	14.34 ± 0.695	14.62 ± 1.291
Hematocrit (%):	Day 28	49.08 ± 2.557	46.48* ± 2.382	44.89** ± 3.278	44.07** ± 3.194
	Day 42	47.22 ± 1.639	45.66 ± 2.158	45.40 ± 1.471	46.96 ± 3.260
Females [n = 15, 15, 15, and 14 on day 28, and n = 5, 5, 5, and 4 on day 42, in ascending group order]					
Erythrocytes (10^6/µL):	Day 28	7.980 ± 0.233	7.478 ± 0.635	7.303** ± 0.496	7.113** ± 0.507
	Day 42	7.352 ± 0.390	6.898 ± 0.453	6.848 ± 0.478	7.280 ± 0.412
Hemoglobin (g/dL):	Day 28	14.55 ± 1.378	14.05 ± 1.021	13.59* ± 0.852	13.17** ± 0.945
	Day 42	14.54 ± 0.808	13.34 ± 0.865	13.50 ± 1.002	13.88 ± 0.957
Hematocrit (%):	Day 28	47.15 ± 1.515	44.15** ± 2.758	42.55** ± 2.323	41.58** ± 3.076
	Day 42	45.68 ± 2.095	41.74 ± 1.932	42.32 ± 3.193	43.25 ± 2.265

Data from Table 4, pp. 65-80, MRID 47925315.

[a] Values are given as Mean ± Standard Deviation with group sizes as indicated.

* p <0.05; **p <0.01

2. **Clinical chemistry:** Selected clinical chemistry data are given in Table 6. On day 28, both sexes had slight, but statistically significant, dose- and treatment-related decreases in albumin with increased globulin and decreased albumin/globulin ratio, which is a pattern of change consistent with inflammation. On day 42, the mean globulin levels of high-dose males and females were at the top of their respective historical control ranges, although statistical significance was no longer attained, and the albumin/globulin ratios of both sexes remained statistically significantly decreased, with the mean value of the high-dose males right at the bottom of the historical control range. High-dose males and females also had small but statistically significant decreases in triglyceride concentration on day 28, which were close to or below the lower limit of the provided reference ranges. These differences are not considered adverse or toxicologically significant due to small magnitude.

TABLE 6. Clinical chemistry data from male and female rats treated for 28 days with or without 14 days of recovery [a]

Parameter/Study day		Dose (mL/kg/every third day)				Historical control ranges [b]
		Control	3	7.5	15	
Males [n = 15 for all groups on day 28, and n = 5 for all groups on day 42]						
Albumin (g/dL):	Day 28	3.61 ± 0.106	3.55 ± 0.146	3.40** ± 0.125	3.29** ± 0.153	3.0-3.6
	Day 42	3.58 ± 0.110	3.48 ± 0.110	3.48 ± 0.130	3.32* ± 0.179	2.9-3.5
Globulin (g/dL):	Day 28	3.03 ± 0.228	3.17 ± 0.162	3.17 ± 0.261	3.35** ± 0.125	2.6-3.8
	Day 42	3.18 ± 0.266	3.28 ± 0.228	3.34 ± 0.114	3.40 ± 0.122	2.8-3.4
A/G ratio:	Day 28	1.21 ± 0.083	1.14* ± 0.070	1.09** ± 0.099	0.98** ± 0.068	0.8-1.3
	Day 42	1.14 ± 0.055	1.06 ± 0.055	1.04* ± 0.055	0.96** ± 0.055	1.0-1.1
Triglycerides (mg/dL):	Day 28	41.3 ± 10.72	32.9* ± 9.66	26.9** ± 8.06	22.1** ± 3.99	25-63
	Day 42	36.4 ± 14.57	37.8 ± 10.80	23.8 ± 4.60	26.8 ± 8.29	21-87
Females [n = 15, 15, 15, and 14 on day 28, and n = 5, 5, 5, and 4 on day 42, in ascending group order]						
Albumin (g/dL):	Day 28	4.15 ± 0.247	3.99 ± 0.295	3.85* ± 0.267	3.76** ± 0.341	3.2-4.0
	Day 42	4.12 ± 0.228	3.94 ± 0.313	4.04 ± 0.261	3.90 ± 0.141	2.7-4.6
Globulin (g/dL):	Day 28	3.34 ± 0.150	3.65** ± 0.223	3.73** ± 0.179	3.89** ± 0.188	2.8-4.2
	Day 42	3.38 ± 0.148	3.46 ± 0.397	3.66 ± 0.207	3.88 ± 0.377	2.6-3.8
A/G ratio:	Day 28	1.23 ± 0.072	1.10** ± 0.100	1.03** ± 0.088	0.96** ± 0.101	0.9-1.3
	Day 42	1.22 ± 0.110	1.14 ± 0.134	1.14 ± 0.089	1.03* ± 0.096	0.9-1.3
Triglycerides (mg/dL):	Day 28	29.9 ± 6.55	25.8 ± 4.02	25.1 ± 6.90	22.9** ± 5.35	19-98
	Day 42	21.4 ± 5.03	25.6 ± 3.29	27.2 ± 6.38	23.0 ± 3.46	24-47

Data from pp. 82-93 and pp. 570-573, MRID 47925315.

[a] Values are given as Mean ± Standard Deviation with group sizes as indicated.

[b] The ranges provided for day 28 are for animals 9-14 weeks of age, and the ranges provided for day 42 are for animals 14-18 weeks of age.

* $p < 0.05$; ** $p < 0.01$

F. **URINALYSIS:** Mean urine pH of the high-dose males was significantly decreased on day 28 relative to controls (6.77 ± 0.32 vs. 7.67 ± 0 for controls; $p<0.01$) but was similar to that of controls on day 42 (7.10 ± 0.22 vs. 7.10 ± 0.42). The mean pH values of both groups on day 28 did fall within the provided historical control range of 6.5-8.0; however, one high-dose animal and two controls had urine pH values outside of this range (6.0 for the control male and ≥9.0 for both controls). Although the difference is considered potentially treatment-related, in the absence of correlated clinical signs, alterations in clinical chemistry parameters, or histopathological changes, it is not considered toxicologically significant.

There were other statistically significant increases or decreases for some urinalysis parameters relative to control values, but these were not considered treatment-related due to the absence of a dose-response pattern.

G. **SACRIFICE AND PATHOLOGY:**

1. **Organ weight:** Selected organ weight data are given in Table 7. Mid- and high-dose females had treatment-related, biologically and statistically significant increases in liver weight on day 28. The changes in liver weight had almost entirely resolved by the end of the

recovery interval, but at this time the high-dose females had marked, statistically significant increases in pituitary and thyroid/parathyroid weights.

TABLE 7. Organ weight data from female rats treated for 28 days with or without 14 days of recovery [a]

Parameter	Dose (mL/kg/every third day)			
	Control	3	7.5	15
Main Study [n = 10 for all groups]				
Body weight (g)	259 ± 21	253 ± 24	264 ± 19	238 ± 18
Brain weight (g)	1.787 ± 0.136	1.807 ± 0.143	1.860 ± 0.135	1.826 ± 0.126
Liver:				
Absolute weight (g)	9.446 ± 1.090	11.353 ± 2.301	13.259** ± 1.516 (+40) [b]	12.862** ± 2.289 (+36)
Organ/body weight (%)	3.636 ± 0.219	4.448** ± 0.464 (+22)	5.0223** ± 0.408 (+38)	5.389** ± 0.754 (+48)
Organ/brain weight (ratio)	5.288 ± 0.486	6.335 ± 1.498	7.137** ± 0.726 (+35)	7.072** ± 1.372 (+34)
Recovery [n = 5, 5, 5, and 3, in ascending group order]				
Body weight (g)	247 ± 20	285* ± 6 (+15)	274 ± 31	265 ± 16
Brain weight (g)	1.844 ± 0.095	1.964 ± 0.075	1.960 ± 0.156	2.006 ± 0.172
Liver:				
Absolute weight (g)	8.452 ± 0.618	10.772** ± 0.514 (+27)	10.567** ± 1.307 (+25)	11.337** ± 1.292 (+11)
Organ/body weight (%)	3.428 ± 0.208	3.783* ± 0.179 (+10)	3.864* ± 0.205 (+13)	4.270** ± 0.236 (+25)
Organ/brain weight (ratio)	4.584 ± 0.260	5.490# ± 0.307 (+20)	5.433# ± 0.927 (+19)	5.655# ± 0.470 (+23)
Pituitary:				
Absolute weight (g)	0.0164 ± 0.0019	0.0219* ± 0.0032 (+34)	0.0192 ± 0.0018	0.0248** ± 0.0014 (+51)
Organ/body weight (%)	0.0066 ± 0.0012	0.0077 ± 0.0011	0.0071 ± 0.0003	0.0094** ± 0.0002 (+42)
Organ/brain weight (ratio)	0.0088 ± 0.0011	0.0111 ± 0.0015	0.0099 ± 0.0015	0.0124** ± 0.0009 (+41)
Thyroid/parathyroid:				
Absolute weight (g)	0.0173 ± 0.0016	0.0208 ± 0.0028	0.0194 ± 0.0021	0.0246** ± 0.0050 (+42)
Organ/body weight (%)	0.0070 ± 0.0007	0.0073 ± 0.0010	0.0072 ± 0.0011	0.0083* ± 0.0020 (+33)
Organ/brain weight (ratio)	0.0094 ± 0.0005	0.0106 ± 0.0014	0.0099 ± 0.0009	0.0122* ± 0.0021 (+30)

Data from Table 8, pp. 108-109 and 114-115, MRID 47925315.

[a] Values are given as Mean ± Standard Deviation with group sizes as indicated.

[b] Numbers in parentheses equal percent different from control; calculated by reviewer.

* $p < 0.05$; ** $p < 0.01$

# $p < 0.05$; Dunnett's test performed by reviewer.

2. **Gross pathology:** One high-dose main study male had chronic dermatitis of the tail as a correlate to treatment-related in-life findings. Other gross lesions noted at the scheduled necropsies included sporadic observations of small epididymides or testes, red discoloration of the epididymides, enlargement or red discoloration of the mandibular lymph node, white focus in the nonglandular stomach, distended urinary bladder, ovarian cyst, mild dilatation of the renal pelvis, and absence of the left kidney and left uterine horn (both in the same animal). All were present at single incidences and were not considered treatment-related.

3. **Microscopic pathology:** Selected histopathology observations are given in Table 8. Treatment-related effects were noted in main-study females of all dose levels and consisted

of minimal to mild panlobular hepatocyte hypertrophy, characterized by cell enlargement and increased homogenous eosinophilic staining of cytoplasm. No similar findings were noted at the end of the two-week recovery interval. All of the examined pituitary, thyroid, and parathyroid glands were found to be within normal limits; however, these organs were only evaluated in control and high-dose main-study animals and the high-dose recovery female that was found dead on day 42.

All other microscopic observations were sporadic single occurrences and/or present at similar incidences in the control and high-dose groups and generally consisted of common findings in rats of this strain and age, such as thymic atrophy, cardiomyopathy and chronic progressive nephropathy.

TABLE 8. Liver histopathology from surviving female rats treated for 28 days with or without 14 days of recovery [a]

Observation	Dose (mL/kg/every third day)			
	Control	3	7.5	15
Main Study				
[Number examined]	[10]	[10]	[10[	[10]
Panlobular hepatocyte hypertrophy:				
Minimal	0	2	6	7
Mild	0	1	3	2
Total	0	3	9	9
Focal necrosis	0	1	0	0
Subacute inflammation (minimal)	9	9	10	9
Within normal limits	1	1	0	0
Recovery				
[Number examined[	[5]	[5[	[5[	[3]
Panlobular hepatocyte hypertrophy:	0	0	0	0
Subacute inflammation (minimal)	5	5	5	3
Within normal limits	0	0	0	0

Data from Table 9, pp. 127 and 135, MRID 47925315.

H. TEST MATERIAL CONCENTRATION IN PLASMA: Selected results of the plasma analyses are given in Table 9. The active ingredient was not found above the detectable limit (0.5 µg/mL or 0.5 ppm) in any of the samples taken pre-dosing (at 0 hours), and the active ingredient was not detected at any time point in low-dose males on any day, in mid-dose males on day 1-2, or in mid-dose females on day 28-29. One or more samples taken from high-dose animals of both sexes on both days, from mid-dose females on day 1-2, or from mid-dose males on day 28-29, did contain detectable concentrations of the test material at one or more time points between 1 and 24 hours after dosing. However, the available data were insufficient to establish a toxicokinetic time course or pattern.

TABLE 9. Mean [and individual] detectable plasma levels of active ingredient following dosing on days 1 and 28 (µg/mL)

Treatment group/ Study day		Hours post-dosing				
		1	2	4	8	24
Males						
Low-dose	Day 1	Not detected	Not detected	Not detected	Not detected	Not detected
	Day 28	Not detected	Not detected	Not detected	Not detected	Not detected
Mid-dose	Day 1	Not detected	Not detected	Not detected	Not detected	Not detected
	Day 28	Not detected	0.30 [0.90, 0.00, 0.00]	Not detected	Not detected	Not detected
High-dose	Day 1	0.22 [0.66, 0.00, 0.00]	0.42 [0.64, 0.62, 0.00]	0.49 [0.68, 0.00, 0.79]	Not detected	Not detected
	Day 28	0.18 [0.00, 0.00, 0.53]	0.43 [0.00, 0.00, 1.30]	Not detected	Not detected	Not detected
Females						
Low-dose	Day 1	Not detected	0.35 [1.06, 0.00, 0.00]	0.48 [0.00, 1.43, 0.00]	Not detected	Not detected
	Day 28	Not detected	Not detected	Not detected	Not detected	Not detected
Mid-dose	Day 1	Not detected	0.51 [0.79, 0.00, 0.74]	0.20 [0.00, 0.00, 0.59]	0.97 [2.03, 0.00, 0.87]	1.19 [1.87, 0.00, 1.71]
	Day 28	Not detected	Not detected	Not detected	Not detected	Not detected
High-dose	Day 1	0.53 [0.00, 0.67, 0.91]	0.57 [0.00, 0.00, 1.72]	1.41 [1.09, 3.14, 0.00]	Not detected	0.81 [0.00, 1.16, 1.28]
	Day 28	0.24 [0.72, 0.00, 0.00]	0.27 [0.80, 0.00, 0.00]	0.00 [0.00, 0.00, 0.00]	0.60 [0.00, 0.00, 1.80]	0.42 [0.00, 0.68, 0.58]

Data from pp. 406-407, MRID 47925315.

III. DISCUSSION AND CONCLUSIONS:

A. INVESTIGATOR'S CONCLUSIONS: The study author concluded that oral administration of the test material to rats every three days at dose levels of 3, 7.5, and 15 mL/kg was well tolerated and resulted in minor changes in hematology and clinical chemistry parameters in both sexes, along with increased liver weights in females, which corresponded to hepatocellular hypertrophy. The study author noted that the hepatocellular hypertrophy most likely represented an adaptive, physiological response of the liver to the presence of a xenobiotic agent rather than an adverse effect. The study author also noted that most of the treatment-related changes had resolved by the conclusion of the 14-day recovery interval.

B. REVIEWER COMMENTS:
In the opinion of the reviewer, there were other biologically significant treatment-related effects in addition to the reversible, marginally significant hematological changes in high-dose animals of both sexes (slight normocytic, normochromic reduction in erythroid mass)

and reversible hepatocellular hypertrophy in mid- and high-dose females that were mentioned by the author of the study report. It is unknown whether the decreased body weight gains of the high-dose males and females were entirely attributable to the cyclic increases and reductions in food consumption related to the timing of dosing and the large volume of the doses; therefore, these must be considered potentially treatment-related. They could have resulted from systemic toxicity or impaired absorption of nutrients due to the physical characteristics of the test material.

The observations of "hypersensitive to touch" in two high-dose females are also considered treatment-related, although the significance of this finding is unclear, as it could be an indication of neurotoxicity, but it also could be related to pain or discomfort. The treatment-related dermatological clinical signs are of unknown significance but are considered potentially adverse.

The reviewer agrees that the hepatocellular hypertrophy and resultant increased liver weights most likely were an adaptive, physiological response to a xenobiotic agent, rather than an adverse effect. There were no concurrent lesions indicative of hepatic tissue or organ toxicity, coagulation was unaltered, and there were no increases in enzyme activity indicative of hepatocellular injury or impaired hepatobiliary function. Albumin was trending downward, but total protein, globulin, cholesterol, and urea (BUN) were not.

However, in light of the marked increases in pituitary and thyroid/parathyroid glands of the high-dose females during recovery, it *is* possible that the altered hepatic metabolism resulted in secondary, extrahepatic toxicity, such as altered levels of thyroid hormones or a disruption of the hypothalamic-pituitary-thyroid axis, which went undetected during the treatment interval. It is therefore very disappointing that the investigators did not perform histopathology on these "delayed" target organs.

C. STUDY DEFICIENCIES:

OPPTS 870.3050 states that the animals are to be dosed with the test substance daily, seven days each week, for a period of 28 days, although the use of a 5-day-per-week dosing regimen is acceptable if adequate justification is provided. In this study, doses were administered once every three days (on days 1, 4, 7, 10, 13, 16, 19, 22, 25, and 28); therefore, this study *does not satisfy* the guideline requirement for a 28-day oral toxicity study (OPPTS 870.3050; OECD 407) in a rodent species.

This study is therefore classified as a non-guideline study.

An additional major deficiency is that the pituitary, thyroid, and parathyroid glands of the recovery females were not examined under light microscopy despite showing marked weight increases in just two weeks time. Although these changes occurred during recovery, further investigation was very much warranted in order to identify and further characterize an undetected but potentially serious treatment-related effect and determine whether further, in-depth investigation of this aspect is necessary. Because the investigators neglected to do histopathology on tissues and organs identified as showing effects in the treated groups, this study is unacceptable.

The following deficiencies were also noted:

- Functional neurological observations (assessment of sensory reactivity to stimuli of different types, grip strength measurement, and motor activity assessments) were not performed and have not been conducted in conjunction with any other study available to the reviewer.
- Clinical signs data did not include accurate description of time of onset or duration, as the individual data only indicated that a particular animal exhibited a particular clinical sign during a particular week.
- The nature of a clinical observation "hypersensitive to touch" was not adequately described. This is of special concern because the hypersensitivity could have a neurological basis or be due to pain or discomfort from skin lesions.
- The dosing volume of the high-dose group exceeded the recommended 1 mL/100 g limit for non-aqueous solutions.
- The animals were approximately 10 weeks of age at the initiation of dosing, rather than less than 9 weeks old, as specified in the guideline.
- The following organs were not weighed: thymus, uterus, and epidiymus.
- The following organs and tissues, or representative samples thereof, were not collected and preserved for possible future histopathology: nose, pharynx, and larynx.
- A uniform dosing volume that employed the vehicle found in the test material should have been used for all treatment groups to differentiate toxicities due to vehicle, and effects to the animals from the large dosing volume.

DATA EVALUATION RECORD

ISOPROPYL MYRISTATE [RESULTIX™]
OPPTS 870.3200
STUDY TYPE: 28-DAY DERMAL TOXICITY - PIG
MRID 47925316

Prepared for

Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202

Prepared by

Toxicology and Hazard Assessment Group
Environmental Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
BPPD Work Assignment No. 10-026

Primary Reviewer:
Donna L. Fefee, D.V.M.

Signature: Robert H. Ross for D. L. Fefee
Date:

Secondary Reviewers:
H.T. Borges, Ph.D., MT(ASCP), D.A.B.T.

Signature: Tein Borges
Date:

Robert H. Ross, M.S., Group Leader

Signature: Robert H. Ross
Date:

Quality Assurance:
Eric Lewis, M.S.

Signature: Eric B. Lewis
Date:

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

EPA Work Assignment Manager: Cheryl Greene, Ph.D. **Signature:** _____
ANGELA L. GONZALES 3/20/11 **Date:** _____

TXR#:

DATA EVALUATION RECORD

STUDY TYPE: 28-Day Dermal Toxicity - Pig; Non-guideline

PC CODE: 000207 **DP BARCODE:** 372778

TEST MATERIAL (PURITY): Pediculocide 100 [Isopropyl Myristate Solution 50% w/w] (50.95% a.i., Lot #C0163A001)

SYNONYMS: Resultix™

CITATION: Goldenthal, E. (2003) 28-Day toxicity study in pigs with a 14-day recovery. MPI Research, Inc., 54943 N. Main Street, Mattawan, Michigan. Laboratory study number 1016-002, November 20, 2003. MRID 47925316. Unpublished.

SPONSOR: Piedmont Pharmaceuticals, Greensboro, North Carolina.

EXECUTIVE SUMMARY:

In a 28-day dermal toxicity study (MRID 47925316), groups of four Landrace-Duroc pigs/sex/dose were dermally exposed to undiluted Pediculocide 100 [Isopropyl Myristate Solution 50% w/w] (50.95% a.i., lot #C0163A001) applied topically, every three days, at dose volumes of 1, 3, or 10 mL/animal, to clipped 20 cm by 40 cm application sites on the back. A control group of four animals/sex was treated in a similar manner with 10 mL of deionized water. Additional "recovery" groups of two animals/sex/dose were treated with 10 mL volumes of either deionized water or test material according to the regimen described above, followed by a 14-day recovery period with no further treatments. Dosing took place on days 1, 4, 7, 10, 13, 16, 19, 22, 25, and 28 of the study, and the applied doses were equivalent to 0, 20.31-33.89 mg/kg bw, 59.62-94.43 mg/kg bw, or 196.3-321.3 mg/kg bw.

There were no adverse treatment-related effects on survival, clinical signs, dermal irritation, body weight, hematology, clinical chemistry, or gross and histologic pathology. At the highest dose level tested, males had slightly increased pituitary weights, relative to controls (absolute: 26%, relative to body: 50%, and relative to brain 33%; $p<0.05$ or 0.01 for all), and females had equivocally increased adrenal weights (absolute: 18%, relative to body: 21%, and relative to brain: 24%; 0.01 for organ/brain, only). These changes were not detected at the conclusion of the recovery period. These findings may be treatment-related but were not considered toxicologically significant, as there were no correlated microscopic findings or potentially associated changes in any of the evaluated clinical pathology parameters.

Under the conditions of this study, the dermal toxicity LOAEL for every-third-day application of Pediculocide 100 [Isopropyl Myristate Solution 50% w/w] to Landrace-Duroc pigs has not been identified, and the NOAEL is greater than or equal to 10 mL (or 196.3-321.3 mg/kg bw).

This 28-day dermal toxicity study in the pig is **Acceptable / Non-guideline**. Due to use of an incorrect dosing regimen and inappropriate dose selection, this study *does not satisfy* the guideline requirement for a 28-day dermal toxicity study (OPPTS 870.3200; OECD 410). See deficiency section.

COMPLIANCE: Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

I. MATERIALS AND METHODS:

A. MATERIALS:

1. **Test material:** Pediculocide 100 [Isopropyl Myristate Solution 50% w/w]

Description:	Clear, viscous liquid
Lot #:	C0163A001 (also C01630001)
Purity:	50.95% a.i.
Compound stability:	Expected to be stable for the duration of the study
CAS #:	Not available
Structure:	Not available

2. **Vehicle and/or positive control:** The vehicle was deionized water supplied by the Test Material Control Department. No positive control was used.

3. **Test animals:**

Species:	Porcine	
Strain:	Landrace-Duroc Cross	
Age/weight at study initiation:	Approximately six weeks/males: 12.6-16.1 kg; females: 14.0-18.0 kg.	
Source:	Bailey Terra Nova Farms, Schoolcraft, Michigan	
Housing:	Individually, in large animal runs with aspen wood shavings.	
Diet:	Lab Minipig Diet (Grower) #5081 (PMI Nutrition International, Inc.), at 0.75 kg/animal/day	
Water:	Unspecified drinking water, *ad libitum*	
Environmental conditions:	**Temperature:**	69-81°F
	Humidity:	32-68%
	Air changes:	Not reported
	Photoperiod:	Approximately 12 hrs dark/12 hrs light
Acclimation period:	Two weeks	

B. STUDY DESIGN:

1. **In life dates:** Start: July 17, 2003; End: August 29, 2003.

2. **Animal assignment:** Animal assignment is given in Table 1. Animals were assigned to the test groups based on body weight using a standard block randomization procedure. The first two animals per sex in the control and high-dose groups were designated for further evaluation over a 14-day recovery period.

TABLE 1: Study design

Test group	Application volume (mL/animal) every 3 days	Dose to animal (mg/animal) every 3 days [a]	Dose range (mg/kg bw) every 3 days [b]	Main Study		Recovery	
				# Male	# Female	# Male	# Female
1. Control	10	0	0	4	4	2	2
2. Low-dose	1	469.1	20.31-33.89	4	4	0	0
3. Mid-dose	3	1407	59.62-94.43	4	4	0	0
4. High-dose	10	4691	196.3-321.3	4	4	2	2

Data taken from p. 11, MRID 47925316.

[a] Calculated by reviewer as dosing volume in mL times 0.9207 g/mL times % a.i. times 1000 mg/g.

[b] Calculated by reviewer, using individual body weights.

3. **Dose selection rationale:** The doses were selected based on the results of a preliminary study conducted at the testing facility. No further information or data from the study were provided.

4. **Preparation and treatment of animal skin:** Approximately one day before the first application and approximately every two weeks thereafter (or as needed to demarcate the application site), the hair was clipped from an area measuring at least 20 cm by 40 cm on the back of each test animal, using electric clippers. The appropriate dosing volume of the test substance or vehicle control was evenly distributed over the designated application site using a spatula. No dressings or occlusive coverings were used. The study protocol stated that, prior to each application, any residual test article would be removed by gently wiping the dose site with tepid tap water and a cotton or paper towel (p. 423), but there was no mention of this in the "Material and Methods" section of the study report (p. 12). Doses were administered once every three days (on days 1, 4, 7, 10, 13, 16, 19, 22, 25, and 28), in the application volumes given in Table 1.

5. **Statistics:** Mean body and organ weights, hematology and all clinical chemistry parameters except for creatine kinase activity were analyzed using Levene's test followed by either Dunnett's test (for data with homogeneous variances) or Welch's t-test with a Bonferroni correction (for data with non-homogeneous variances). Total and differential leukocyte counts were log-transformed prior to analysis. Creatine kinase data were rank-transformed and then analyzed using Dunnett's test. All endpoints were analyzed using two-tailed tests, and the results were reported at the 0.05 and 0.01 significance levels. Data from the recovery portion of the study were not subjected to statistical analysis.

C. METHODS:

1. Observations:

a. **Cageside observations:** The animals were observed at least twice daily for mortality, morbidity, signs of toxicity, or injury.

b. **Clinical examinations:** Detailed clinical examinations were conducted weekly.

c. **Neurological evaluations:** Neurological evaluations were not done as part of the current study.

d. **Skin reactions:** Once daily throughout the study, the application site of each animal was examined for signs of local skin irritation and scored for erythema and edema according to the Draize method. On treatment days, this was done prior to application of the test or control substance.

2. **Body weight:** Animals were weighed prior to randomization on day -1 and weekly during the study.

3. **Food consumption:** Food consumption was not recorded.

4. **Ophthalmoscopic examination:** All animals were given eye examinations prior to exposure and on day 25. The examinations were conducted by a board-certified veterinary ophthalmologist. The eyes were dilated with tropicamide, and an indirect ophthalmoscope was used.

5. **Hematology and clinical chemistry:** Blood for hematology, coagulation, and clinical chemistry evaluations was collected following an overnight fast from all surviving animals pre-test, on day 27, and at the end of recovery (for recovery animals). Samples were taken from the jugular vein. The CHECKED (X) parameters were examined.

a. **Hematology:**

X	Hematocrit (HCT)*	X	Leukocyte differential count*
X	Hemoglobin (HGB)*	X	Mean corpuscular HGB (MCH)*
X	Leukocyte count (WBC)*	X	Mean corpusc. HGB conc.(MCHC)*
X	Erythrocyte count (RBC)*	X	Mean corpusc. volume (MCV)*
X	Platelet count*	X	Reticulocyte count (absolute and percentage)
	Blood clotting measurements*		
X	(Thromboplastin time)		
	(Clotting time)		
X	(Prothrombin time)		

* Recommended for 28-day dermal toxicity studies based on Guideline 870.3200

b. **Clinical chemistry:**

X	ELECTROLYTES	X	OTHER
X	Calcium	X	Albumin*
X	Chloride	X	Creatinine*
	Magnesium	X	Urea nitrogen*
X	Phosphorus	X	Total Cholesterol*
X	Potassium* (K)	X	Globulins
X	Sodium* (NA)	X	Glucose*
X	**ENZYMES** (more than 2 hepatic enzymes, eg., *)	X	Total bilirubin
X	Alkaline phosphatase (AP)*	X	Total protein*
	Cholinesterase (ChE)	X	Triglycerides
X	Creatine phosphokinase (CK)		Serum protein electrophoresis
	Lactic acid dehydrogenase (LDH)		
X	Alanine aminotransferase (ALT/also SGPT)*		
X	Aspartate aminotransferase (AST/also SGOT)*		
X	Gamma glutamyl transferase (GGT)*		
	Glutamate dehydrogenase		
	Sorbitol dehydrogenase*		

* Recommended for 28-day dermal toxicity studies based on Guideline 870.3200

6. **Urinalysis:** Urinalysis is optional for 28-day dermal toxicity studies and was not carried out as part of the current study.

7. **Plasma test material concentration:** On days 1-2 and 28-29, blood samples were collected from all animals of the low-, mid-, and high-dose groups, prior to dosing and 1, 2, 4, 8, and 24 hours after dosing for determinations of the plasma concentration of the test material. Samples were taken from the jugular vein, and except for the 24-hour post-dosing sample, taken on day 29 (prior to necropsy), the animals were not fasted prior to collection. According to the study protocol, the analytical assay was conducted by KAR Laboratories, Inc., Kalamazoo, Michigan, using a sponsor-supplied, validated analytical method, which was not otherwise specified or described in the study report.

8. **Sacrifice and pathology:** On day 29 (main study animals) or at the end of recovery, the surviving animals were sedated with Telazol and sacrificed via intravenous or intracardiac injection of sodium pentobarbital followed by exsanguination through the femoral vessels. All were subjected to a gross necropsy, which included external examination including palpable masses and internal examination of the contents of the abdominal, thoracic, and cranial cavities. Bone marrow smears were collected and retained for potential future examination. The CHECKED (X) organs or tissues, or representative samples thereof, were collected, fixed in neutral buffered formalin or Davidson's fixative (for eyes with optic nerve and contiguous Harderian gland), processed, stained with hematoxylin and eosin, and subjected to histological examination. The INDICATED (XX) organs, in addition, were weighed.

X	DIGESTIVE SYSTEM	X	CARDIOVASC./HEMAT.	X	NEUROLOGIC
X	Tongue	X	Aorta, thoracic*	XX	Brain*+
X	Salivary glands*	XX	Heart*+	X	Peripheral nerve* (sciatic)
X	Esophagus*	X	Bone marrow*	X	Spinal cord (3 levels)*
X	Stomach*	X	Lymph nodes*	XX	Pituitary*
X	Duodenum*	XX	Spleen*+	X	Eyes (optic nerve)*
X	Jejunum*	X	Thymus*+	X	GLANDULAR
X	Ileum*			XX	Adrenal gland*+
X	Cecum*	X	UROGENITAL		Lacrimal gland
X	Colon*	XX	Kidneys*+	X	Harderian gland
X	Rectum*	X	Urinary bladder*	XX	Parathyroid*#
XX	Liver*+	XX	Testes*+	XX	Thyroid*#
X	Gall bladder* (not rat)	X	Epididymides*+	X	OTHER
	Bile duct* (rat)	X	Prostate*	X	Bone (sternum and femur)
X	Pancreas*	X	Seminal vesicles*	X	Skeletal muscle (biceps femoris)
X	RESPIRATORY	XX	Ovaries*+	X	Skin* (treated & untreated areas)
X	Trachea*	X	Uterus*+ (with cervix)	X	All gross lesions and masses*
X	Lung*	X	Vagina		
	Nose*	X	Mammary gland*^		
	Pharynx*				
	Larynx*				

* Recommended for 28-day dermal toxicity studies based on Guideline 870.3200
\+ Organ weights required.
\# Thyroid and parathyroid were weighed together.
^ Females only.

II. RESULTS:

A. OBSERVATIONS:

1. **Clinical signs of toxicity:** Cageside observations either were not reported or were reported together with the observations from the weekly detailed clinical examinations, as "clinical findings." No abnormal clinical findings were reported. In both the summary and individual tables, all observations were recorded simply as "no abnormalities detected" along with study week(s). The summary tables and "deviations" section of the study report indicated that the detailed clinical observations were not conducted for some animals during week 5 of the study (apparently at the end of the treatment interval).

2. **Mortality:** There were no deaths or moribund sacrifices during the main study or recovery intervals.

3. **Dermal irritation:** The application sites of some of the animals were not scored on days 26, 29, or 30. These included the following: on day 26, three animals per sex from the control and high-dose groups and 1 animal per sex from the low-, and mid-dose groups; on day 29, one high-dose female; and one day 30 one animal per sex from the control and high-dose groups.

   The application site of one high-dose female had very slight erythema (grade 1) on day 29 and very slight edema (grade 1) on days 28 and 29. There were no observations of erythema

and/or edema on this animal at any other time point, and the application sites of all of the other animals were normal on all of the occasions on which scores were recorded.

B. BODY WEIGHT AND WEIGHT GAIN: Body weight data are given in Table 2. Mean absolute body weights of the treated groups were similar to those of controls throughout treatment. Weekly body weight gain was highly variable, both within and between groups, as well as for individual animals from one interval to the next.

Although all treated groups did have decreased body weight gain during the first week of the study, these differences cannot be definitively attributed to treatment. An additional confounder is that the treated animals (but not the controls) were subjected to six blood draws within a 24-hour time at the beginning of the study. Stress is known to decrease growth rates, decrease efficiency of food utilization, and cause uneven growth in weanling and grower pigs. No other clear, consistent patterns were seen.

TABLE 2. Body weight data (kg)[a]

Parameter/Study week or interval	Dose (mL/animal/every three days)			
	Control	1	3	10
Males				
Main study body weight:				
Week -1	15.75 ± 1.39	15.50 ± 1.12	16.08 ± 1.27	16.52 ± 1.35
Week 1	17.74 ± 1.42	16.66 ± 1.44	16.56 ± 1.06	17.89 ± 1.00
Week 2	18.81 ± 1.38	17.16 ± 2.17	17.95 ± 1.14	18.63 ± 1.63
Week 3	20.11 ± 1.07	18.68 ± 2.02	18.71 ± 1.15	19.95 ± 1.70
Week 4	21.94 ± 1.10	20.68 ± 1.75	21.24 ± 1.65	21.97 ± 1.59
Recovery body weight[c]:				
Week 4	21.55 ± 1.06	Not applicable, or NA	NA	22.65 ± 1.77
Week 5	21.75 ± 0.50	NA	NA	22.25 ± 1.06
Week 6	22.45 ± 0.21	NA	NA	23.13 ± 0.25
Body weight changes[bc]:				
Weeks -1 to 1	1.99 ± 1.13	1.17 ± 1.07 (-42)[d]	0.48 ± 0.69 (-76)	1.37 ± 0.65 (-31)
Weeks 1 to 2	1.07 ± 0.33	0.50 ± 0.87 (-53)	1.39 ± 0.80 (+30)	0.74 ± 1.24 (-31)
Weeks 2 to 3	1.30 ± 0.69	1.51 ± 0.31 (+17)	0.76 ± 0.60 (-41)	1.33 ± 1.12 (+2)
Weeks 3 to 4	1.83 ± 0.52	2.00 ± 0.38 (+9)	2.53 ± 0.82 (+38)	2.02 ± 0.71 (+10)
Weeks -1 to 4, in kg	6.19 ± 0.90	5.18 ± 01.42 (-16.4)	5.16 ± 01.76 (-17)	5.45 ± 0.93 (-12.0)
[and % initial BW[	[39.3%]	[33.4%]	[32.1%]	[33.0%]
Recovery (Weeks 4-6)	0.90 ± 0.85	NA	NA	0.48 ± 1.52 (-47)
Females				
Main study body weight:				
Week -1	16.97 ± 1.91	16.72 ± 1.85	16.88 ± 1.62	17.11 ± 0.98
Week 1	18.86 ± 1.61	17.97 ± 1.00	17.85 ± 1.18	17.82 ± 0.75
Week 2	19.28 ± 1.37	19.17 ± 0.63	18.36 ± 0.34	19.06 ± 1.07
Week 3	20.84 ± 1.50	20.01 ± 2.04	20.14 ± 1.19	20.06 ± 0.84
Week 4	22.87 ± 1.47	22.25 ± 0.66	21.96 ± 1.24	22.15 ± 1.00
Recovery body weight[c]:				
Week 4	22.60 ± 2.12	NA	NA	21.98 ± 2.02
Week 5	22.85 ± 2.90	NA	NA	22.25 ± 0.92
Week 6	24.70 ± 3.39	NA	NA	21.75 ± 3.46
Body weight changes[bc]:				
Weeks -1 to 1	1.89 ± 0.93	1.25 ± 1.13 (-34)	0.97 ± 1.48 (-49)	0.72 ± 0.45 (-62)
Weeks 1 to 2	0.41 ± 0.25	1.20 ± 0.71 (+192)	0.52 ± 0.94 (+26)	1.07 ± 0.84 (+160)
Weeks 2 to 3	1.57 ± 0.78	0.85 ± 2.0 (-46)	1.78 ± 0.97 (+13)	1.17 ± 1.47 (-26)
Weeks 3 to 4	2.03 ± 0.42	2.24 ± 1.54 (+11)	1.83 ± 0.57 (-10)	2.09 ± 0.91
Weeks -1 to 4, in kg	5.90 ± 1.34	5.53 ± 1.91	5.09 ± 1.16 (-14)	5.05 ± 0.40 (-14)
[and % initial BW[	[35%]	[33%[	[30%[	[29%]
Recovery (Weeks 4-6)	2.10 ± 1.27	NA	NA	-0.23 ± 1.45

Data from Table 2, pp. 33-36, MRID 47925316.

[a] Values are given as Mean ± Standard Deviation. Group sizes (n) during Main Study were 6, 4, 4, and 6 in ascending group order; during Recovery n = 2 for both control and high-dose groups.

[b] Calculated by reviewer.

[c] Not analyzed statistically.

[d] Numbers in parentheses are percent difference from control; calculated by reviewer.

C. **TEST MATERIAL CONCENTRATIONS IN PLASMA:** The active ingredient was not found above the detectable limit (0.5 µg/mL or 0.5 ppm) in any of the samples from the low- and mid-dose animals. Three high-dose males and four high-dose females had detectable plasma levels of the active ingredient at one or more time points between one and eight hours after dosing on day 1 and/or day 28. These results are given in Table 3.

TABLE 3. Plasma concentration (µg/mL) of active ingredient in high-dose animals on Day 1 and Day 28

Animal number/Study day		Hours post-dosing			
		1	2	4	8
Males					
130:	Day 1	1.29	-- [a]	1.43	--
	Day 28	--	--	--	--
133:	Day 1	1.71	--	--	--
	Day 28	--	--	--	--
134:	Day 1	--	--	--	--
	Day 28	1.62	0.602	--	0.571
Females					
135:	Day 1	--	--	0.757	--
	Day 28	0.613	0.614	0.524	2.73
137:	Day 1	0.799	0.608	--	--
	Day 28	1.71	2.4	0.689	--
138:	Day 1	1.1	--	--	--
	Day 28	--	--	--	--
140:	Day 1	--	1.28	--	--
	Day 28	0.892	--	--	--

Data from Appendix J, pp. 290-291, MRID 47925316.
[a] Active ingredient was not detected.

D. **OPHTHALMOSCOPIC EXAMINATION:** There were no abnormal ophthalmological findings.

E. **BLOOD ANALYSES:**

1. **Hematology:** There were no treatment-related effects on hematology or coagulation parameters. A statistically significant decrease in the percentage reticulocytes in high-dose males on day 27 (relative to the control value) was not considered toxicologically relevant in the absence of correlated changes in hematocrit, erythrocyte count, and/or hemoglobin.

2. **Clinical chemistry:** There were no biologically or toxicologically significant treatment-related effects on the evaluated clinical chemistry parameters. There were statistical increases or decreases for some parameters relative to control values, but in all cases the changes were minimal, did not exhibit a dose response, and/or the values fell within two standard deviations of the mean control value.

F. SACRIFICE AND PATHOLOGY:

1. **Organ weight:** High-dose main study males had slightly increased pituitary weights, and high-dose females had equivocally increased adrenal weights (Table 4). These findings may be treatment-related but are not considered toxicologically significant, as there were no correlated microscopic findings or potentially associated changes in any of the evaluated clinical pathology parameters.

TABLE 4. Organ weight data from male pigs treated for 28 days[a]

Parameter	Dose (mL/kg/every third day)			
	Control	1	3	10
Main study males [n = 4 for all groups[				
Body weight (kg)	21.03 ± 0.60	19.71 ± 1.82	20.15 ± 1.34	20.18 ± 1.60
Brain weight (g)	73.48 ± 2.848	69.64 ± 2.599	65.07** ± 4.014 (-11)[b]	70.40 ± 3.137
Pituitary gland: [# examined[	[3]	[4]	[4]	[3]
Absolute weight (g)	0.088 ± 0.007	0.088 ± 0.007	0.098 ± 0.009	0.111* ± 0.008 (+26)
Organ/body weight (%)	0.0004 ± 0.0000	0.0004 ± 0.0001	0.0005 ± 0.0001	0.0006* ± 0.0001 (+50)
Organ/brain weight (ratio)	0.0012 ± 0.0000	0.0013 ± 0.0001	0.0015** ± 0.0001 (+25)	0.0016** ± 0.0000 (+33)
Main study females [n = 4 for all groups[				
Body weight (kg)	21.86 ± 0.94	21.40 ± 1.32	20.64 ± 1.20	21.11 ± 0.19
Brain weight (g)	70.923 ± 4.044	67.810 ± 1.136	68.050 ± 5.271	67.332 ± 5.868
Adrenal gland: [# examined[	[4]	[4]	[4]	[4]
Absolute weight (g)	2.088 ± 0.218	2.000 ± 0.116	2.278 ± 0.366	2.458 ± 0.043 (+18)
Organ/body weight (%)	0.0096 ± 0.0013	0.0094 ± 0.0004	0.0110 ± 0.0013	0.0116 ± 0.0002 (+21)
Organ/brain weight (ratio)	0.0295 ± 0.0032	0.0295 ± 0.0013	0.0334 ± 0.0035	0.0367** ± 0.0028 (+24)

Data from Table 7, pp. 102-103, MRID 47925316.

[a] Values given as Mean ± Standard Deviation, with group sizes as indicated.

[b] Numbers in parentheses equal percent difference from control; calculated by reviewer.

*p<0.05; **p<0.01

2. **Gross pathology:** The only abnormal gross findings were a mild adhesion of the urinary bladder in one control female and a moderate abscess of the subcutis in the anogenital region of one high-dose female.

3. **Microscopic pathology:** There were no treatment-related microscopic changes, and all pituitary and adrenal glands were found to be within normal limits. The most common observations were lymphocytic infiltration of the kidneys and lungs, which were both noted in all or most animals. Other findings included lymphocytic infiltration of mandibular salivary gland, liver, testes, epididymides, or vagina, vulvar abscess, subacute inflammation of the heart, tongue or lungs, and regeneration in the pyloric region of the stomach. These were noted sporadically in single animals and/or without a dose response.

III. DISCUSSION AND CONCLUSIONS:

A. INVESTIGATORS' CONCLUSIONS: The study author concluded that dermal application of the test material every three days at volumes of 1, 3, or 10 mL/animal was very well tolerated and did not affect any of the evaluated parameters. Accordingly, the study author set a No-Observed-Effect-Level (NOEL) of 10 mL/animal.

B. REVIEWER COMMENTS:

The reviewer agrees that there were no adverse treatment-related effects on survival, clinical signs, dermal irritation, body weight, hematology, clinical chemistry, organ weight, or gross and microscopic pathology. The reviewer does consider the increased pituitary weights in high-dose males and the increased adrenal weights in high-dose females potentially treatment-related, although non-adverse in the absence of correlated microscopic findings or potentially associated changes in any of the evaluated clinical pathology parameters. Had dosing been carried out on a seven-day-per-week basis and at dose levels where a range of toxic effects were expected to occur (or at the limit dose), correlated changes might have been noted in the gross and microscopic evaluations or clinical pathology parameters.

The dermal toxicity LOAEL for every-third-day application of Pediculocide 100 [Isopropyl Myristate Solution 50% w/w] to Landrace-Duroc pigs has not been identified, and the NOAEL is greater than or equal to 10 mL (or 196.3-321.3 mg/kg bw).

C. STUDY DEFICIENCIES: OPPTS 870.3200 states that the animals should be treated with test substance at least six hours per day, seven days per week, although application five days per week is acceptable when based on practical considerations. In this study, doses were administered once every three days; therefore, this study *does not satisfy* the guideline requirement for a 28-day dermal toxicity study (OPPTS 870.3200; OECD 410).

The guideline states that the dose is to be applied to approximately ten percent of the body surface and provides an anatomical description [the area starting at the scapulae (shoulders) to the wing of the ileum (hipbone) and half way down the flank on each side of the animal]. It should be noted, the guideline suggests the use of rats, rabbits, or guinea pigs and likely was not intended for porcine use.

Moreover, the doses selected for use in the study were not appropriate, as the highest dose level was less than the "limit" dose, no adverse effects were seen, and there was no provision of data (or a summary) from a range-finding study to indicate that a range of toxic effects was expected to occur at the dose levels that were used.

For these reasons, this study is classified as a non-guideline study.

Additional deficiencies included the following:

- The study report did not provide justification for use of a species other than the rat, rabbit, or guinea pig.

- Animals in the control group were not handled in an identical manner to the test group in that they were not subjected to the additional blood draws for determination of the concentration of the test material in plasma.
- Group size was four per sex rather than ten animals per sex per dose or five animals per sex per dose, as specified in the guideline (for full studies and screening studies, respectively). Again, the guideline recommends rats, rabbits or guinea pigs for the study and likely did not account for the use of pigs.
- Food consumption was not measured.
- The following organs were not weighed: thymus, uterus, and epidiymus.
- The following organs and tissues, or representative samples thereof, were not collected and preserved for possible future histopathology: nose, pharynx, and larynx.

DATA EVALUATION RECORD

RESULTZ™
NONGUIDELINE
STUDY TYPE: DERMAL PHARMACOKINETIC, SAFETY AND TOLERANCE
MRID 47925319

Prepared for

Biopesticides and Pollution Prevention
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202

Prepared by

Toxicology and Hazard Assessment Group
Life Sciences Division
Oak Ridge National Laboratory
Oak Ridge, TN 37831
Task Order No. 10-026

Primary Reviewer: H.T. Borges, Ph.D., MT(ASCP), D.A.B.T.	Signature: Terri Borges Date: OCT 1 1 2010
Secondary Reviewers: R.A. Young, Ph.D., D.A.B.T.	Signature: Robert A. Young Date: OCT 1 1 2010
Robert H. Ross, M.S., Group Leader	Signature: Robert H. Ross Date: OCT 1 1 2010
Quality Assurance: Lee Ann Wilson, M.A.	Signature: L.A. Wilson Date: OCT 1 1 2010

Disclaimer

This review may have been altered subsequent to the contractor's signatures above.

Oak Ridge National Laboratory managed and operated by UT-Battelle, LLC., for the U.S. Department of Energy under Contract No. DE-AC05-00OR22725.

Inert ingredient information may be entitled to confidential treatment

EPA Reviewer: C. Greene, Ph.D. **Signature:** _____
Date: _____

Angela L. Gonzales 3/28/11

DATA EVALUATION RECORD

STUDY TYPE: Dermal Pharmacokinetic, Safety, and Tolerance – Human Nonguideline

DECISION: 424225 **DP BARCODE:** 372778
SUBMISSION: 863571

TEST MATERIAL: RESULTZ™ (50% isopropyl myristate (ai), 50% [redacted])

CITATION: Garg, D. (2005) Pharmacokinetic, safety, and tolerance study of RESULTZ™; Pediculicide rinse in pediatric subjects with *Pediculosis capitis*. Hill Top Research, Inc., 900 Osceola Drive, West Palm Beach, FL 33409. Study Number 04-123941-108. June 4, 2005. MRID 47925319. Unpublished.

SPONSOR: Piedmont Pharmaceuticals, 204 Muirs Chapel Road, Greensboro, NC 27410

EXECUTIVE SUMMARY:

In a dermal penetration study (MRID 47925319), 120 mL of RESULTZ™ (50% isopropyl myristate and 50% [redacted] Lot Number C4F00931) was applied to the hair and scalp of 12 children infested with *Pediculosis capitis*. Following a 10-minute shampoo, blood samples were drawn pretreatment and at 1, 2, 4, 6 (children ≥ 8 years), 8, and 12 (children ≥ 8 years) hours post-treatment to determine the pharmacokinetics of the active ingredient and its carrier. The scalp was also evaluated for erythema and edema just prior to treatment, one-hour post-treatment, and at the end of the study. The children were also monitored for treatment-related ill effects.

No severe treatment-related clinical signs of toxicity were found, although one child developed a moderate headache during the study. The headache may not have been treatment-related, however, since the child had a history of headaches and the mother failed to disclose this before the start of the study. No increased erythema or edema was observed on the scalp of any treated subject one hour after treatment or at study termination. The active ingredient, isopropyl myristate, showed no detectable absorption, while the carrier, [redacted] showed minimal absorption. Pharmacokinetic calculations of [redacted] provided a C_{max} of 0.06 μg/g, a T_{max} of 1.1 hours to yield an AUC of 0.11 μg/g · hour.

– **BPPD Reviewer Comment: this study was not required and was not reviewed by BPPD.** –

COMPLIANCE: A Quality Assurance statement was not provided. Signed and dated Data Confidentiality and GLP statements were provided. The study followed FDA guidelines (21 CFR 312.21).

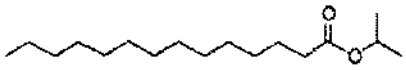
Inert ingredient information may be entitled to confidential treatment

I. MATERIALS AND METHODS:

A. MATERIALS:

1. **Test material:** **RESULTZ™ (50% isopropyl myristate, 50% [redacted]**

Description: Liquid
Label Information: IND# 66651; Lot C4F00931
Storage: Room temperature
Composition: **Isopropyl myristate**
CAS # 110-27-0
Structure:



Function: Dissolves the exoskeleton wax covering of lice to induce dehydration

[redacted]

2. **Relevance of test material to proposed formulation:** The end-use product was used for the study.

3. **Test Subjects:** Thirteen children between the ages of 4 and 13 were recruited and twelve completed the study (11 girls, one boy; ages 6-13). Subjects completed the study were composed of one Hispanic, 9 Caucasian, and 2 of other races (not reported). All subjects had active cases of *Pediculosis capitis* which included the observance of at least three viable adults, viable nits or eggs, and scalp irritation induced by prolonged lice infestation. One four year old female withdrew from the study when blood could not be drawn pre-treatment and parental consent was withdrawn.

B. STUDY DESIGN:

1. **Subject Selection:** Prior to the conduct of the study, the Hill Top Research Investigational Review Board (IRB) (Miamiville, OH) reviewed and approved the protocol, screening and study consent forms, screening and study assent forms, subject instructions, safety information, Form FDA -1572, and advertisement and recruiting packages. The IRB was constituted under Title 21 CFR 50 and 60.

Inert ingredient information may be entitled to confidential treatment

Children between the ages of 2 and 18 were eligible for the study. All had to be in good general health and free from systemic or dermatologic disorders. Each had to have an active *Pediculosis capitis* infestation that included the observance of at least three viable adults, viable nits or eggs, and scalp irritation induced by prolonged lice infestation. A consenting parent or legal guardian had to sign a consent form before acceptance into the study. All subjects were screened for suitable veins for drawing blood and all had to be able to stay for the duration of the study (up to 12 hours).

Potential participants were excluded if: they had a history of irritation or sensitivity to pediculicide or hair care products; a history of ragweed allergy; a history of systemic diseases that could interfere with interpretation of study results; the participant had been treated for head lice in the preceding four-weeks; a history of hair dyes, bleaches, permanent wave or relaxing solution use within the preceding two-weeks; any condition or illness that would interfere with interpretation of the results; a history of antibiotics or other systemic medication use within the preceding two-weeks; participation in a previous drug study within the preceding 30 days; pregnant or nursing females (participating subjects of childbearing age were given a pregnancy test before the start of the study); individuals with any skin/scalp conditions at the treatment site; individuals or guardians who did not understand the requirements of the study; participants wearing makeup, skin creams/lotions, deodorants, or suntan lotion on the day of treatment; and if two members of the household were already entered into the study.

2. **Treatment:** The test material was used as supplied by the Study Sponsor and was applied directly to the scalp (dry hair) by study personnel wearing gloves. The test material (120 mL ≅ 120 g) was distributed over all of the hair and allowed to remain for 10 minutes. The gloves and container containing the test material were weighed before and after use to ensure adequate dosage and determine loss of test material.

   After treatment, the hair and scalp were rinsed with warm water for at least three minutes with the face and eyes shielded using a suitably sized clean towel. The hair was then shampooed with Johnson & Johnson's Baby Shampoo®, rinsed, and dried.

3. **Pharmacokinetic Sampling:** Approximately 3 mL of blood was collected from each participant into heparinized tubes at the following intervals:

   Subjects < 8 years of age (1 male, 5 females): pre-treatment, and 1, 2, 4, and 8 hours post-treatment; and

   Subjects ≥ 8 years of age (6 females): pre-treatment, and 1, 2, 4, 6, 8, and 12 hours post-treatment.

   Plasma was obtained from all samples and stored frozen until time of assay. Gas chromatography-Mass spectrometry was used to determine plasma concentrations of isopropyl myristate and [redacted] The calibration range used for both constituents was 0.5 - 50 µg/g which provided a limit of detection of 0.104 µg/g for isopropyl myristate and 0.036 µg/g for [redacted]

Inert ingredient information may be entitled to confidential treatment

4. **Skin Irritation:** The scalps of all subjects were evaluated for erythema and edema one hour after test material application and after the final blood draw. The method used for scoring irritation was according to the Draize Scale Method of Grading Responses.

5. **Statistical Analyses:** Pharmacokinetic parameters were calculated when possible by WinNonLin (version 4.1, PharSight Corp., Inc.) Separate analyses were done for subjects < 8 years and for those ≥ 8 years of age. Missing data from subjects included in the study were not included in the analysis of pharmacokinetic parameters. ANOVA was used to determine if differences existed in variables for subjects between the groups.

II. RESULTS:

A. SIGNS AND SYMPTOMS OF TOXICITY:

One 10 year old Caucasian female complained of a headache on the day of treatment. The symptoms were considered moderate, no action was taken, and the symptoms resolved on the day of onset. It was later learned that the subject frequently complained of headaches at least once or twice/week; however, the mother of the subject did not inform the study staff of the frequency or occurrence. Relationship to treatment is unknown, but is considered doubtful. No other treatment-related effects were reported.

B. PHARMACOKINETICS:

Isopropyl myristate was below the limit of detection (0.104 μg/g) in all plasma samples indicating no dermal absorption occurred. Pharmacokinetic parameters could not be calculated.

Since no statistically significant differences were found in dermal pharmacokinetic parameters for [redacted] the two age classes were combined for analysis. Very low plasma concentrations of [redacted] were found in the test subjects with a C_{max} of 0.064 ± 0.05 μg/g at a T_{max} of 1.11 ± 0.33 hours. The area under the curve for the course of the study was 0.11 ± 0.11 μg/g ·hr indicating that very low concentrations of [redacted] were absorbed, and rapidly eliminated. Individual subject results for the concentration of [redacted] found in the plasma are shown in Table 1.

Inert ingredient information may be entitled to confidential treatment

TABLE 1. Individual plasma concentrations of [redacted]							
Age	Concentration (µg/g) hours after treatment						
	0	1	2	4	6	8	12
10	BLQ	0.074	BLQ	BLQ	BLQ	BLQ	BLQ
10	BLQ	0.146	0.057	BLQ	BLQ	BLQ	BLQ
10	BLQ	0.132	0.061	BLQ	BLQ	BLQ	BLQ
6	BLQ	0.043	BLQ	BLQ	NS	BLQ	NS
13	BLQ	0.087	0.076	0.053	BLQ	BLQ	BLQ
8	BLQ	0.058	0.059	BLQ	BLQ	0.046[2]	BLQ
9	BLQ	BLQ	BLQ	BLQ	MS	BLQ	BLQ
6	BLQ	BLQ	BLQ	BLQ	NS	BLQ	NS
7	BLQ	0.108	0.065	0.055	NS	BLQ	NS
7	BLQ	0.083	0.059	0.049	NS	BLQ	NS
6	BLQ	MS	BLQ	BLQ	NS	BLQ	NS
6	BLQ	.041	MS	BLQ	NS	MS	NS
Avg. Conc.[1]	BLQ	0.086	0.063	0.052	BLQ	0.046	BLQ

Data from page 24 of MRID 47925319
[1]Average concentration for those results above limit of detection calculated by reviewer
[2]Considered aberrant as preceding samples were BLQ and close to BLQ
BLQ = Below limit of quantitation (0.036 µg/g); MS = Missing sample, unable to collect; NS = No sample collected as per protocol

C. SKIN IRRITATION:

No significant changes in scalp erythema or edema from baseline to 1-hour post-treatment or the final evaluation were found.

III. DISCUSSION AND CONCLUSIONS:

A. INVESTIGATORS' CONCLUSIONS:

The study author stated that the active ingredient, isopropyl myristate, showed no detectable absorption, while the carrier, [redacted], showed minimal absorption. Pharmacokinetic calculations of [redacted] provided a C_{max} of 0.06 µg/g and a T_{max} of 1.1 hours to yield an AUC of 0.11 µg/g ·hour. No severe adverse treatment reactions were found, although one subject complained of a headache that may have been related to treatment. Treatment did not induce erythema or edema.

B. REVIEWER COMMENTS:

Thirteen children between the ages of 4 and 13 with active cases of *Pediculosis capitis* were recruited to evaluate the pharmacokinetic properties of RESULTZ™ containing the active ingredient isopropyl myristate and its carrier, [redacted]. One child withdrew from the study and 12 completed it. Following a 10-minute shampoo with the test material, blood samples were drawn pretreatment and at 1, 2, 4, 6 (children ≥ 8 years), 8, and 12 (children ≥ 8 years) hours post-treatment to determine the pharmacokinetics of the active ingredient and its carrier. The scalp was also evaluated for erythema and edema just prior to treatment, one-

hour post-treatment, and at the end of the study. The children were also monitored for treatment-related ill effects.

No severe treatment-related clinical signs of toxicity were found, although one child developed a moderate headache during the study. The headache may not have been treatment-related, however, since the child had a history of headaches and the mother failed to disclose this before the start of the study. No increased erythema or edema was observed on the scalp of treated subjects one hour after treatment or at study termination. The active ingredient, isopropyl myristate, showed no detectable absorption, while the carrier, [redacted] showed minimal absorption. Pharmacokinetic calculations of [redacted] provided a C_{max} of 0.06 μg/g, and a T_{max} of 1.1 hours to yield an AUC of 0.11 μg/g ·hour.

C. STUDY DEFICIENCIES:

None that would preclude interpretation of the study results.

Inert ingredient information may be entitled to confidential treatment

entry for IHAD/ARS, e-copy for Cheryl
Angela Gonzales to: Cheryl Greene 03/28/2011 03:15 PM
Cc: Manying Xue

86865-R [Resultix (isopropyl myristate)(Response to Deficiencies-Tox) 3-28-11].doc

47925309.der.v2.doc 47925310.der.v2.doc 47925311.der.v2.doc 47925312.der.v2.doc 47925313.der.v2.doc

47925314.der.v2.doc 47925315.der.v2.doc 47925316.der.v2.doc 47925319.der.v2.doc

Angela L. Gonzales
Environmental Protection Specialist
U.S. Environmental Protection Agency
Biopesticides & Pollution Prevention Division (7511P)
1200 Pennsylvania Ave, NW
Washington, DC 20460
gonzales.angela@epa.gov
703-308-0460

Decision #: 424225
DP #: (386086)
PRIA
Parent DP #:
Submission #: 888652

DATA PACKAGE BEAN SHEET

Date: 21-Jan-2011

* * * Registration Information * * *

Registration: 86865-R - RESULTIX TM

Company: 86865 - PIEDMONT ANIMAL HEALTH

Risk Manager: RM 91 - Linda Hollis - (703) 308-8733 Room# PYt S-8761

Risk Manager Reviewer: Leonard Cole LCDLE02

Sent Date: 11-Jan-2011 Calculated Due Date: 25-Aug-2011 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: (B600) NEW AI;NON-FOOD USE;MICROBIAL/BIOCHEMICAL;

Ingredients: 000207, Isopropyl myristate[redacted]

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 21-Jan-2011 Due Back:

DP Ingredient: 000207, Isopropyl myristate

DP Title:

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

	Assigned To	Date In	Date Out		
Organization:	BPPD / BPB			Last Possible Science Due Date:	30-Aug-2010
Team Name:	RM 91			Science Due Date:	
Reviewer Name:				Sub Data Package Due Date:	
Contractor Name:					

* * * Studies Sent for Review * * *

Printed on Page 2

* * * Additional Data Package for this Decision * * *

Can be printed on its own page

* * * Data Package Instructions * * *

Attention Russell Jones, Ph.D.: Russ, would you forward this data package to your reviewer for evaluation. This is information submitted in response to a deficiency letter sent to Piedmont Animal Health. The product is Resultix with the new active ingredient is Isopropyl myristate. The Phase IV due date is MAY 25, 201 t.

Product ingredient source information may be entitled to confidential treatment

DP#: (386086) *** Studies Sent for Review *** Decision#: (424225)

MRID	MRID Status	Citation Reference	Guideline
48348202		Phillips, S.; Barer, G. (2011) Published Articles Concerning the Safety of Myristic Acid and its Derivatives, Including Isopropyl Myristate. Unpublished study prepared by Piedmont Animal Health. 123 p.	870.7200/Companion animal safety
48348204		Young, D. (2011) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray Against Rhipicephalus sanguineus and Dermacentor variabilis on Cats: Amended Final Report. Project Number: PAH/09/0065. Unpublished study prepared by Young Veterinary Research Services. 85 p.	870.7200/Companion animal safety
48348202		Phillips, S.; Barer, G. (2011) Published Articles Concerning the Safety of Myristic Acid and its Derivatives, Including Isopropyl Myristate. Unpublished study prepared by Piedmont Animal Health. 123 p.	870.5300/In vitro mammalian cell gene mutation test
48348201		Phillips, S.; Barer, G. (2011) Discussion of Submitted Information: (RESULTIX End-Use Product). Unpublished study prepared by Piedmont Animal Health. 67 p.	870.5375/In vitro mammalian chromosome aberration test
48348202		Phillips, S.; Barer, G. (2011) Published Articles Concerning the Safety of Myristic Acid and its Derivatives, Including Isopropyl Myristate. Unpublished study prepared by Piedmont Animal Health. 123 p.	870.5375/In vitro mammalian chromosome aberration test
48348201		Phillips, S.; Barer, G. (2011) Discussion of Submitted Information: (RESULTIX End-Use Product). Unpublished study prepared by Piedmont Animal Health. 67 p.	870.3700/Prenatal developmental toxicity study
48348204		Young, D. (2011) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray Against Rhipicephalus sanguineus and Dermacentor variabilis on Cats: Amended Final Report. Project Number: PAH/09/0065. Unpublished study prepared by Young Veterinary Research Services. 85 p.	810.3300/Treatments to control pests of humans and pets
48348201		Phillips, S.; Barer, G. (2011) Discussion of Submitted Information: (RESULTIX End-Use Product). Unpublished study prepared by Piedmont Animal Health. 67 p.	870.5300/In vitro mammalian cell gene mutation test
48348201		Phillips, S.; Barer, G. (2011) Discussion of Submitted Information: (RESULTIX End-Use Product). Unpublished study prepared by Piedmont Animal Health. 67 p.	870.7200/Companion animal safety
48348203		Young, D. (2011) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanguineus and Dermacentor variabilis on Dogs: Amended Final Report. Project Number: PAH/09/0036. Unpublished study prepared by Young Veterinary Research Services. 83 p.	810.3300/Treatments to control pests of humans and pets
48348202		Phillips, S.; Barer, G. (2011) Published Articles Concerning the Safety of Myristic Acid and its Derivatives, Including Isopropyl Myristate. Unpublished study prepared by Piedmont Animal Health. 123 p.	870.3700/Prenatal developmental toxicity study
48348203		Young, D. (2011) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanguineus and Dermacentor variabilis on Dogs: Amended Final Report. Project Number: PAH/09/0036. Unpublished study prepared by Young Veterinary Research Services. 83 p.	870.7200/Companion animal safety

Explore Registrations

Reg Number: 86865-R Reg. Type: Product Registration - Section 3 Status: Under Review (04-Dec-2009)

Name: RESULTIX TM <View Registration Details>

(No New Receipts)

S.	Submission Type	OPP Rec'vd Date	Resubmission	Description

- ...Decisions...
  - Data Requirements
  - D: Closed; 424226; 86865-R;W075;SMALL BUSI
  - D: Pending; 424225; 86865-R;B600;NEW AI;ND
    - 75-Day Letters
    - DP 383262;BPPD / BPB; Last Possible Scie
    - (ALERT) S: 888652 1/10/2011; New Registr
    - S: 877175 6/24/2010; New Registration; 86
    - S: 863571 12/3/2009; New Registration; 86

S: 863571 Reg #: 86865-R

Submission Type: New Registration

Resubmission?: Yes No

Decision #: 424225; B600;NEW AI;NON-FOOD USE;MICROBIAL/BIOCHEM

Submitter Company: PIEDMONT ANIMAL HEALTH

Application Date: 03-Dec-2009

OPP Received Date: 03-Dec-2009 Date Sent to Risk manager: 07-Dec-2009

Studies Included?: Yes No Fast Track?: Yes No

Form A Signed?: Yes No None Date:

Form B Signed?: Yes No None Date:

Reviewer: Greene, Cheryl

Received DT: Editable Due DT:

Submission Due DT: 25-Aug-2011 Response: 0 , 03-Dec-2009

Priority Weight: Priority Points:

Comments: New a.i. section 3 application

Please read instructions on reverse before co. eting form. Form Appro . OMB No. 2070-0060. Approval expires 2-28-95

EPA United States Environmental Protection Agency Washington, DC 20460

☐ Registration ☐ Amendment ☑ Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number: 86865-R
2. EPA Product Manager: L. Hollis
3. Proposed Classification: ☐ None ☐ Restricted
4. Company/Product (Name): ResultixTM
PM#: 91
5. Name and Address of Applicant *(Include ZIP Code)*
Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410
☐ *Check if this is a new address*
6. **Expedited Reveiw.** (In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to:
EPA Reg. No. _____
Product Name _____

Section - II

☐ Amendment - Explain below.
☑ Resubmission in response to Agency letter dated DEC 09 2010
☐ Notification - Explain below.
☐ Final printed labels in rapsonse to Agency letter dated Aug
☐ "Me Too" Application.
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)
Submission of requested and additional information in support of the registration of ResultixTM.

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes ☐ No	☐ Yes ☑ No	☐ Yes ☑ No	☐ Metal ☑ Plastic ☐ Glass ☐ Paper ☐ Other (Specify)
* *Certification must be submitted*	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information: ☑ Label ☐ Container
4. Size(s) Retail Container: 20 mL (0.65 fl oz)
5. Location of Label Directions: ☐ Container
6. Manner in Which Label is Affixed to Product: ☑ Lithograph Paper glued Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Kathleen G. Palma, Ph.D.	VP Research & Development	336-544-0320 x 202

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowlingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature: Kathleen G. Palma, Ph.D.
3. Title: VP Research & Development
4. Typed Name: Kathleen G. Palma, Ph.D.
5. Date: JAN 9, 2011

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

VOLUME 1

Administrative Portion
for the
Registration of RESULTIX™
Pesticide End-Use Product
Submission of Requested and Additional Information

FRONT PANEL

RESULTIX™

End-Use Product
Kills Ticks on Dogs and Cats

ACTIVE INGREDIENT	
Isopropyl Myristate	50.0%
OTHER INGREDIENT	50.0%
TOTAL	100.0%

KEEP OUT OF REACH OF CHILDREN

CAUTION

See Side/Back Panel for First Aid

STOP - READ LABEL BEFORE USE

EPA Reg. No. 86865-R

EPA Est. No. 71979-SC-001

Manufactured for
Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

NET CONTENTS
20 mL (0.65 oz.)

SIDE PANEL

FIRST AID

Hot Line Number

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-222-1222 for emergency medical treatment information.

If on skin:	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor immediately for treatment advice.
If in eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. • Call a poison control center or doctor immediately for treatment advice.
If inhaled:	• Move person to fresh air. • If person is not breathing, call 911 or an ambulance; then give artificial respiration, preferably mouth-to-mouth if possible. • Call a poison control center or doctor immediately for treatment advice.
If swallowed:	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by a poison control center or doctor. • Do not give anything by mouth to an unconscious person.

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION. May cause eye and dermal irritation. Avoid contact with eyes, skin, or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet. Remove contaminated clothing and wash clothing before reuse. Wear appropriate protective equipment, such as protective eyewear, rubber gloves, and long-sleeved shirts.

ENVIRONMENTAL HAZARDS

This pesticide is toxic to invertebrates and fish. Do not discharge this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage authority. For guidance, contact your State Water Board or Regional Office of the EPA.

BACK PANEL

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

For the treatment of ticks on dogs and cats.

- Use when you see a tick or ticks on your dog or cat.
- Remove cap and hold pump bottle upright, direct nozzle at tick and spray until tick is covered with solution (2 sprays).
- Dispose of dead ticks.

For external use only.

Wash hands after use.

Do not use near dog's or cat's eyes.

Stop and ask a vet if skin irritation or infection is present or develops during use of product.

Keep away from open flames

Store at 59° F – 86° F (15° C – 30° C)

STORAGE AND DISPOSAL

Do not contaminate water, food, or feed by storage and disposal.

Pesticide Storage:

Store in a dry place away from extreme heat and cold (tightly closed at or below +30°C). Keep container closed when not in use. Always store pesticide in the original container. Store away from food and pet food.

In case of fire or other emergency, report at once by toll-free telephone to CHEMTREC (800-424-9300).

Pesticide Disposal and Container Handling:

Nonrefillable container. Do not reuse or refill this container.

If empty: place in trash or offer for recycling if available.

If partly filled: call your local solid waste agency for disposal instructions.

Never place unused product down any indoor or outdoor drain.

NOTICE: Seller warrants that the product conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use. Neither this warranty nor any other warranty of merchantability or fitness for a particular purpose, express or implied, extends to the use of this product contrary to label instructions, or under abnormal conditions, or under conditions not reasonably foreseeable to Seller, and Buyer assumes the risk of any such use.

ANY PANEL (Do not substitute these for required statements)

Label Claims (one or more in various combinations, located in various places throughout the box and bottle/insert labels)

Breakthrough in tick treatments

Clinically proven

Convenient and easy to apply as soon as you see a tick on your pet

Even kills "super ticks", the ones that have built up resistance to traditional pesticide treatments

For the Treatment of Ticks on Dogs and Cats

Free of conventional pesticides

Guaranteed effective

Kills ticks on pets

No conventional pesticides

Patented spray formula softens the waterproof outer waxy layer of the tick's body, resulting in rapid dehydration

Recommended to use on its own or in conjunction with other flea and tick control medications

Safe for you and your family

Safe to use on pets

Simple way to kill more than 90% of ticks on your pet that's completely non-toxic to animals, odorless and pesticide-free

Tick Killing Solution™

Works to reduce human exposure to tick-borne diseases (when used in conjunction with safe tick removal practices)

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

January 20, 2011

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

KATHLEEN G. PALMA, PH.D.
PIEDMONT ANIMAL HEALTH
204 MUIRS CHAPEL ROAD, SUITE 200
GREENSBORO, NC 27410-

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your submittal of 10-JAN-11. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your submittal was found to be in full compliance with the standards for submission of data contained in PR Notice 86-5. A copy of your bibliography is enclosed, annotated with Master Record ID's (MRIDs) assigned to each document submitted. Please use these numbers in all future references to these documents. Thank you for your cooperation. If you have any questions concerning this data submission, please raise them with the cognizant Product Manager, to whom the data have been released.

Receipt for Section 3

S: 888652

Regulatory Type: Product Registration - Section 3

Fee For Service: Yes No

Application Type: New Registration

Billable: Yes No

Company: 86865 PIEDMONT ANIMAL HEALTH

Print Letter

Enter More Information

Tracking

Risk Manager: Biologicals & Pollution Prevention Division, PM Team 91

Product #: 86865-R Product Name: RESULTIX TM

Overridea:

Me Too Section3: Me Too Product Name:

Application Date: 10-Jan-2011 OPP Rec'vd Date: 10-Jan-2011

Front End Date: 11-Jan-2011 Risk Manager Send Date: 11-Jan-2011

FFS Due Date: Negotiated Due Date:

OPP Target Date:

Receipt Content	Des
Study	

Fast Track: New Ingredient:

View/Edit

Receipt Description:

requested & additional information

New Ingredient Request Date:

New Ingredient Received Date:

Form A: Signature Date: Form B: Signature Date:

GSB

WASHINGTON, D.C. OFFICE
fifth floor
flour mill building
1000 potomac street nw
washington, d.c. 20007-3501
TEL 202 965 7880 FAX 202 965 1729

OTHER OFFICES
beijing, china
new york, new york
portland, oregon
seattle, washington
GSBLAW.COM

GARVEY SCHUBERT BARER

483482-00

Please reply to SUSAN PHILLIPS
sphillips@gsblaw.com TEL EXT 1785

January 10, 2011

Linda A. Hollis
Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division
U.S. EPA – OPPTS **(Mail Code 7511P)**
Ariel Rios Building
1200 Pennsylvania Avenue NW
Washington, DC 20460

Re: Submission of Requested and Additional Information in Support of the Pesticide Registration Submission for RESULTIX™ End-Use Product (EPA Registration No. 86865-R)

Dear Ms. Hollis:

On behalf Piedmont Animal Health LLC (Piedmont), we are submitting requested and new information in support of the pesticide registration application for RESULTIX™ End-Use Product (EPA Registration No. 86865-R). This submission is in response to your letter dated December 9, 2010 that described deficiencies in the original pesticide registration submission of December 3, 2009.

In addition, the responses to the deficiency letter are moderated by the results of the teleconference between EPA personnel, Dr. Kathy Palma and GSB personnel on Tuesday December 14, 2010. The EPA personnel indicated during this teleconference that because the registration is only for the end-use product (EP) and not also for the active ingredient/manufacturing-use product (TGAI/MP), the submission of a Confidential Statement of Formula (CSF) for the TGAI/MP is not necessary. Consequently, any deficiencies noted for the draft TGAI/MP label in the above referenced EPA letter are also not of concern. Thus, chemistry and label deficiencies pertaining to TGAI/MP noted in the December 9, 2010 letter are not addressed in this submission.

Included in this submission package are the following items:

- Volume 1 Administrative Materials, including 8570-1 application form, revised EPA Form 8570-4 (CSF) for the EP, and a revised draft label for the EP;

Product ingredient source information may be entitled to confidential treatment

- Volume 2, a discussion of the safety and toxicology of isopropyl myristate (IPM) as it pertains to the deficiencies noted in the above referenced EPA letter;
- Volume 3, three published articles, one requested by the EPA in the above referenced EPA letter and two additional articles on the safety of IPM as determined by the Cosmetic Ingredient Review (CIR) Expert Panels;
- Volumes 4 and 5, revised safety and efficacy studies in dogs and cats, respectively, containing additional information addressing deficiencies noted in the above referenced EPA letter.

Following are the deficiencies noted in the December 9, 2010 letter and the location of the information addressing these deficiencies.

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The product chemistry data submission (MRIDs 479253-01 to 479253-08) is unacceptable as noted below and must be successfully addressed.

1. Piedmont submitted two Confidential Statements of Formula (CSF) in support of the referenced application. Both CSFs are dated 12/02/09.
   a. The following deficiencies apply to the CSF submitted for the technical grade active ingredient (TGAI) [redacted] (Isopropyl Myristate):

   As per the teleconference on Tuesday December 14 2010, only the end-use product CSF is included in Volume 1 of this submission.

   b. The following deficiencies apply to the CSF for the end-use product (RESULTIX).
      i. Column 13(b) - The nominal concentration of the active ingredient (isopropyl myristate) must match the label, which currently reads 50.0%.
      ii. Column 10 - The source of the active ingredient is not noted on the CSF. Piedmont must list the source of [redacted] Isopropyl Myristate, [redacted] alongside the name of the active ingredient (isopropyl myristate).

   The changes were made on the revised draft CSF included in Volume 1 of this submission.

Product Performance/Efficacy

MRID 479253-17 - Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate Tick Spray against *Rhipicephalus sanguineus* and *Dermacentor variabilis* on Dogs.

1. The amount of product applied to each dog was not reported. Companion Animal Safety Guideline (OCSPP 870.7200) recommends that animals be treated with 1, 3 and 5 times the recommended dose. In the submitted study only one dose (2 sprays) was applied to each animal. Based on labeling instructions for RESULTIX and the proposed use pattern, the amount of product applied to each dog will vary depending on the number of ticks found on the dogs. As such, the study fails to investigate the effect that increased doses of the proposed product will have on the health of dogs treated. Data/information demonstrating the effect of increased doses

of the proposed product on dogs must be submitted before the Agency can proceed with its review.

Additional information has been included in the Revised Safety and Efficacy Study on Dogs in Volume 4 of this submission. A discussion of potential exposures is in Volume 2 of this submission.

2. The submitted label for the proposed product states that RESULTIX "starts killing ticks in seconds." Since the submitted data shows that death only occurs six 6 hours after treatment, the statement "starts killing ticks in seconds is false and misleading because the user is not informed that it will take the treated ticks six (6) hours to actually die. Therefore, Piedmont must either submit new data that validates the claim that the product kills ticks in seconds or remove the statement from the product label or add language to the label that fully explains the time it will take a tick to die once it is treated.

   A revised Draft Label was amended and is included in Volume 1 of this submission.

3. The submitted label claims 100% efficacy. However, the submitted data records efficacy at less than 100%. The Agency therefore views the state 100% efficacy as false and misleading. Piedmont must either submit new data/information that validates the claim that RESULTIX is 100% efficacious or remove the statement from the product label.

   A revised Draft Label was amended and is included in Volume 1 of this submission.

4. The submitted data did not contain a discussion of food consumption and body weight of the test animals. As described in OCSPP Guideline 870.7200 (p6.-7) data from Companion animal Safety studies should include the test animal(s) individual body weights (measured at specific intervals throughout the study) and the measures of individual food consumption of test animals on a daily basis. These data are critical markers of the health of the test animals as well as the effect of the product on the animal(s). This information must be submitted before the Agency can proceed with its review.

   Additional information has been included in the Revised Safety and Efficacy Study on Dogs in Volume 4 of this submission. Additional discussion of animal health is in Volume 2 of this submission.

5. The Agency's review has determined that the submitted data/information is missing certain individual data parameters for hematology and clinical chemistry analysis. Specifically, the following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC). This information must be submitted before the Agency can proceed with its review.

   Additional information has been included in the Revised Safety and Efficacy Study on Dogs in Volume 4 of this submission. Additional discussion of hematological parameters is in Volume 2 of this submission.

6. The Agency's review has determined that some clinical pathology values [CK (U/L; GGT (U/L); Cholesterol (mg/dL); Total CO2 (MeQ/l); Chloride (mEq/L), and Potassium (mEq/L)] were outside of the reference range prior to treatment. Based on these values, the Agency questions

whether the dogs in the study were healthy prior to and during the study (Refer to MRID 479253-17 page 16, Table 2, Summary Clinical Chemistry Data). Piedmont must submit data/information that successfully demonstrates the health of the studied animal(s) before the Agency can proceed with its review.

Additional information has been included in the Revised Safety and Efficacy Study on Dogs in Volume 4 of this submission. Additional discussion of clinical chemistry parameters is in Volume 2 of this submission.

MRID 479253-18 - Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate Tick Spray against Rhipicephalus sanuineus and Dermacentor variabilis on Cats.

1. The amount of product applied to each cat was not reported. Companion Animal Safety Guideline OCSPP 870.7200 recommends that animals be treated with 1, 3 and 5 times the recommended dose. In the submitted study only one dose (2 sprays) was applied to each animal. Based on labeling instructions and the proposed use pattern, the amount of product applied to each cat will vary depending on the number of ticks found on the cats. As such, the study fails to investigate the effect that increased doses of the proposed product will have on the health of cats treated. Data/information demonstrating the effect of increased doses of the proposed product on cats must be submitted before the Agency can proceed with its review.

   Additional information has been included in the Revised Safety and Efficacy Study on Cats in Volume 5 of this submission. A discussion of potential exposures is in Volume 2 of this submission.

2. The submitted data did not contain a discussion of food consumption and body weight of the test animals. As described in OCSPP Guideline 870.7200 (pages 6 and 7) data from Companion animal Safety studies should include the test animal(s) individual body weights (measured at specific intervals throughout the study) and the measures of individual food consumption of test animals on a daily basis. These data are critical markers of the health of the test animals as well as the effect of the product on the animal(s). This information must be submitted before the Agency can proceed with its review.

   Additional information has been included in the Revised Safety and Efficacy Study on Cats in Volume 5 of this submission. Additional discussion of animal health is in Volume 2 of this submission.

3. The submitted label for the proposed product claims that the product starts killing ticks in seconds. Since the submitted data shows that death only occurs six 6 hours after treatment the statement "starts killing ticks in seconds: is false and misleading because the user is not informed that it will take the treated ticks six (6) hours to actually die. Therefore, Piedmont must either submit new data that validates the claim that the product kills ticks in seconds or remove the statement from the product label or add language to the label that fully explains the time it will take a tick to die once it is treated.

   A Revised Draft Label was amended and is included in Volume 1 of this submission.

4. The submitted label claims 100% efficacy. However, the submitted data records efficacy at less than 100%. The Agency therefore views the statement 100% efficacy as false and misleading.

Piedmont must either submit new data/information validating the claim that RESULTIX is 100% efficacious or remove the statement from the product label.

A Revised Draft Label was amended and is included in Volume 1 of this submission.

5. The Agency's review has determined that individual data parameters for hematology and clinical chemistry analysis were under reported. Specifically, the following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC).

   Additional information has been included in the Revised Safety and Efficacy Study on Cats in Volume 5 of this submission. Additional discussion of hematological parameters is in Volume 2 of this submission.

6. Some of the clinical pathology values [Alk Phos (U/L); CK(U/L); GGT (U/L); UN (mg/dL), and phosphorous (mg/dL)] were outside of the reference range prior to treatment, which leads to the question of whether the cats in the study were healthy prior to and during the study (Refer to page 15, Table 2, Summary Clinical Chemistry Data; Pre and Post Treatment in MRID 479253-18). Piedmont must submit data/information that successfully demonstrates the health of the studied animal(s) before the Agency can proceed with its review.

   Additional information has been included in the Revised Safety and Efficacy Study on Cats in Volume 5 of this submission. Additional discussion of clinical chemistry parameters is in Volume 2 of this submission.

Toxicology

Certain data submitted to address toxicology is deficient and unacceptable. The deficiencies identified below must be successfully addressed before the Agency can proceed with its review of the referenced application. The deficiencies are:

The following deficiencies apply to the active ingredient (isopropyl myristate)

a. Regarding the dermal irritation data requirement (OCSPP 870.2500) – The referenced 1997 study from RTECS that indicates that the active ingredient is mildly irritating was not included in your application (Refer to MRID 47925309). The Agency cannot make a determination on the data submitted for dermal irritation until a review of the RTECS study has been reviewed. Piedmont must submit this study before the Agency can proceed.

The cited article is included in Volume 3 of this submission.

b. Regarding the developmental (OCSPP 870.3700) and *in vitro* mammalian cell assay (OCSPP 870.5300 and 870.5375) data requirements – The data/rationale submitted to fulfill these data requirements is insufficient. Piedmont states that significant occupational exposure is not expected because application is often seasonal. However, this rationale fails to consider that applications may occur more often in warmer climates where ticks may be prevalent year-round. Moreover, based on the available information, significant exposure to isopropyl myristate may occur in an occupational setting (e.g.: veterinary office, grooming salon) through use of the

proposed product. The data/information submitted to satisfy occupational exposure also does not address either of these exposure scenarios. Piedmont must submit data/information that addresses both of these exposure scenarios before the Agency can proceed with its review.

Additional information is presented in Volume 3 of this submission and further discussion and rationales are addressed in Volume 2 of this submission.

***The following deficiency applies to the* end-use product(RESULTIX)**

c. The test substance utilized in the submitted studies is interchangeably referenced by different names, including "Resultix Tick Spray", "Pediculocide 100", "Piedmont Pediculocide 1" and "Piedmont Pediculocide 2". Piedmont must submit data/information verifying that the test substance(s) referred to in the studies is identical to the proposed product, "RESULTIX".

This is addressed in Volume 2 of this submission.

If you have any questions or need additional information, please do not hesitate to contact me. My telephone number is 202-298-1785 and my email address is sphillips@gsblaw.com.

Regards,

Susan D. Phillips

Susan D. Phillips, M.S.
Science Advisor

Attachment

TRANSMITTAL DOCUMENT

1. Name and Address of Submitter

Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

Agent

Kathleen G. Palma, Ph.D.
Vice President of Research & Development
Email: kpalma@piedmontpharma.com
Telephone: 336-544-0320 x 202

2. Regulatory Action for which this Package is Submitted

Pesticide Registration Submission
RESULTIX™
EPA File Symbol No. 86865-R
Registration for the End-Use Product

3. Transmittal Date

January 10, 2011

4. List of Submitted Documents

Volume 1 Administrative Materials

- Transmittal Document
- EPA Form 8570-1 (Application for Pesticide Registration)
- EPA Form 8570-4 (Confidential Statement of Formula) for EP
- Draft label for EP, 5 copiees

48348201 Volume 2 Discussion of Submitted Information

48348202 Volume 3 Published Articles Concerning the Safety of Myristic Acid and its Derivatives, Including Isopropyl Myristate

48348203 Volume 4 Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against *Rhipicephalus sanguineus* and *Dermacentor variabilis* on Dogs (Study No. PAH-09-0036). AMENDED FINAL REPORT

✓

48348204 Volume 5 Pivotal Study to Determine 5afety and Efficacy of Isopropyl Myristate (IPM) Tick Spray Against *Rhipicephalus sanguineus* and *Dermacentor voriabilis* on Cats

Memorandum

Date: 01 / 21 / 11

To: PM 91, Regulatory Manager

From: Information Services Branch, ITRMD

Your receipt of this data submission is not an indication that MRIDs for the enclosed studies have been posted to OPPIN.

We expect that it will be approximately 5 days from the above date before the study-level data is available in OPPIN.

If you have any questions about this process, please contact Teresa Downs (305-5363).

This is a:
- ☑ fully accepted submission
- ☐ partially accepted submission
- ☐ rejected submission

GSB

WASHINGTON, D.C. OFFICE
fifth floor
flour mill building
1000 potomac street nw
washington, d.c. 20007-3501
TEL 202 965 7880 FAX 202 965 1729

OTHER OFFICES
beijing, china
new york, new york
portland, oregon
seattle, washington
GSBLAW.COM

GARVEY SCHUBERT BARER

483482-00

Please reply to SUSAN PHILLIPS
sphillips@gsblaw.com TEL EXT 1785

January 10, 2011

Linda A. Hollis
Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division
U.S. EPA – OPPTS **(Mail Code 7511P)**
Ariel Rios Building
1200 Pennsylvania Avenue NW
Washington, DC 20460

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   Additional information has been included in the Revised Safety and Efficacy Study on Cats in Volume 5 of this submission. A discussion of potential exposures is in Volume 2 of this submission.

2. The submitted data did not contain a discussion of food consumption and body weight of the test animals. As described in OCSPP Guideline 870.7200 (pages 6 and 7) data from Companion animal Safety studies should include the test animal(s) individual body weights (measured at specific intervals throughout the study) and the measures of individual food consumption of test animals on a daily basis. These data are critical markers of the health of the test animals as well as the effect of the product on the animal(s). This information must be submitted before the Agency can proceed with its review.

   Additional information has been included in the Revised Safety and Efficacy Study on Cats in Volume 5 of this submission. Additional discussion of animal health is in Volume 2 of this submission.

3. The submitted label for the proposed product claims that the product starts killing ticks in seconds. Since the submitted data shows that death only occurs six 6 hours after treatment the statement "starts killing ticks in seconds: is false and misleading because the user is not informed that it will take the treated ticks six (6) hours to actually die. Therefore, Piedmont must either submit new data that validates the claim that the product kills ticks in seconds or remove the statement from the product label or add language to the label that fully explains the time it will take a tick to die once it is treated.

   A Revised Draft Label was amended and is included in Volume 1 of this submission.

4. The submitted label claims 100% efficacy. However, the submitted data records efficacy at less than 100%. The Agency therefore views the statement 100% efficacy as false and misleading.

Piedmont must either submit new data/information validating the claim that RESULTIX is 100% efficacious or remove the statement from the product label.

A Revised Draft Label was amended and is included in Volume 1 of this submission.

5. The Agency's review has determined that individual data parameters for hematology and clinical chemistry analysis were under reported. Specifically, the following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC).

   Additional information has been included in the Revised Safety and Efficacy Study on Cats in Volume 5 of this submission. Additional discussion of hematological parameters is in Volume 2 of this submission.

6. Some of the clinical pathology values [Alk Phos (U/L); CK(U/L); GGT (U/L); UN (mg/dL), and phosphorous (mg/dL)] were outside of the reference range prior to treatment, which leads to the question of whether the cats in the study were healthy prior to and during the study (Refer to page 15, Table 2, Summary Clinical Chemistry Data; Pre and Post Treatment in MRID 479253-18). Piedmont must submit data/information that successfully demonstrates the health of the studied animal(s) before the Agency can proceed with its review.

   Additional information has been included in the Revised Safety and Efficacy Study on Cats in Volume 5 of this submission. Additional discussion of clinical chemistry parameters is in Volume 2 of this submission.

<u>Toxicology</u>

Certain data submitted to address toxicology is deficient and unacceptable. The deficiencies identified below must be successfully addressed before the Agency can proceed with its review of the referenced application. The deficiencies are:

<u>The following deficiencies apply to the active ingredient (isopropyl myristate)</u>

a. Regarding the dermal irritation data requirement (OCSPP 870.2500) – The referenced 1997 study from RTECS that indicates that the active ingredient is mildly irritating was not included in your application (Refer to MRID 47925309). The Agency cannot make a determination on the data submitted for dermal irritation until a review of the RTECS study has been reviewed. Piedmont must submit this study before the Agency can proceed.

The cited article is included in Volume 3 of this submission.

b. Regarding the developmental (OCSPP 870.3700) and *in vitro* mammalian cell assay (OCSPP 870.5300 and 870.5375) data requirements – The data/rationale submitted to fulfill these data requirements is insufficient. Piedmont states that significant occupational exposure is not expected because application is often seasonal. However, this rationale fails to consider that applications may occur more often in warmer climates where ticks may be prevalent year-round. Moreover, based on the available information, significant exposure to isopropyl myristate may occur in an occupational setting (e.g.: veterinary office, grooming salon) through use of the

proposed product. The data/information submitted to satisfy occupational exposure also does not address either of these exposure scenarios. Piedmont must submit data/information that addresses both of these exposure scenarios before the Agency can proceed with its review.

Additional information is presented in Volume 3 of this submission and further discussion and rationales are addressed in Volume 2 of this submission.

***The following deficiency applies to the* end-use product(RESULTIX)**

c. The test substance utilized in the submitted studies is interchangeably referenced by different names, including "Resultix Tick Spray", "Pediculocide 100", "Piedmont Pediculocide 1" and "Piedmont Pediculocide 2". Piedmont must submit data/information verifying that the test substance(s) referred to in the studies is identical to the proposed product, "RESULTIX".

This is addressed in Volume 2 of this submission.

If you have any questions or need additional information, please do not hesitate to contact me. My telephone number is 202-298-1785 and my email address is sphillips@gsblaw.com.

Regards,

Susan D. Phillips

Susan D. Phillips, M.S.
Science Advisor

Attachment

TRANSMITTAL DOCUMENT

1. Name and Address of Submitter

Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

Agent

Kathleen G. Palma, Ph.D.
Vice President of Research & Development
Email: kpalma@piedmontpharma.com
Telephone: 336-544-0320 x 202

2. Regulatory Action for which this Package is Submitted

Pesticide Registration Submission
RESULTIX™
EPA File Symbol No. 86865-R
Registration for the End-Use Product

3. Transmittal Date

January 10, 2011

4. List of Submitted Documents

Volume 1 Administrative Materials

- Transmittal Document
- EPA Form 8570-1 (Application for Pesticide Registration)
- EPA Form 8570-4 (Confidential Statement of Formula) for EP
- Draft label for EP, 5 copiees

48348201 Volume 2 Discussion of Submitted Information

48348202 Volume 3 Published Articles Concerning the Safety of Myristic Acid and its Derivatives, Including Isopropyl Myristate

48348203 Volume 4 Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against *Rhipicephalus sanguineus* and *Dermacentor variabilis* on Dogs (Study No. PAH-09-0036). AMENDED FINAL REPORT

48348204 Volume 5 Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray Against *Rhipicephalus sanguineus* and *Dermacentor variabilis* on Cats

RESULTIX - ISOPROPYL MYRISTATE CONFERENCE CALL

Calendar Entry

Tue 12/14/2010 11:00 AM - 11:30 AM

Rooms: BPPD Conference Room S-8721/Potomac Yard One@EPA
BPPD Conference Room (S-8771)/Potomac Yard One@EPA
BPPD Library Pod (S-8981)/Pofomac Yard One@EPA

Description

Recommendation of Division Directors Reset Due Dates		
Decision #: 424226	**Registration #:** 86865-R	**Petition #:** N/A

Fee Category: B600	**PRIA Decision Time Frame:** 12 months	
Submitted by: Cheryl Greene	**Branch:** BPB	**Date:** December 21, 2010
Company: Piedmont Animal Health		
Original Due Date: December 29, 2010	**Proposed New Due Date:** August 25, 2011	
Previous Negotiated Due Dates: None		
Is the "Fix" in-house? No	**If not, date "Fix" expected:** January 10, 2011	

ISSUE: On December 3, 2009, EPA received the above-referenced application for registration of a new active ingredient (isopropyl myristate) in support of a proposed end-use product that kills ticks on dogs and cats via a non toxic mode of action (desiccation).

BPPD has reviewed the data/information submitted to support the application and identified deficiencies in the product performance and companion animal safety data submitted in support of the end-use product. These deficiencies must be successfully addressed before BPPD can proceed with its review and render a regulatory decision on the application.

There have been active communications with the Applicant's representative, and BPPD informed the applicant (Piedmont) of the significant deficiencies in a comprehensive letter dated December 9, 2010. Following transmission of the 75-day deficiency letter, BPPD and the Applicant engaged in a series of telephone and email discussions, including an extended conference call on December 11, 2011. During that call Piedmont advised BPPD that they have in hand all data/information needed to address the deficiencies detailed in the Agency's December 9, 2010, deficiency letter. Piedmont has also advised that they will be able to submit those data/information to the Agency on or before January 10, 2011. Piedmont has agreed to re-set the PRIA date for this action to 7 ½ month from the date of receipt of the required information, i.e., August 25, 2011.

Piedmont has been informed that a delay in receipt of the required data and information will result in establishment of a new due date.

Describe Interactions with Company (describe when contacted and company's response including response to previous negotiated due dates): BPPD has been in ongoing communications with the applicant's consultant by telephone, email, an interim draft deficiency letter, and an official deficiency letter. Based on these communications, the applicant is requesting to reset the current PRIA 2 due date to August 25, 2011.

"75 Day" Letter sent? _X_ **(Date sent) December 9, 2010** ____ **No and reason for none?**

Rationale for Proposed Due Date: A 7 ½ month resetting of the PRIA2 due date based on receipt of all required information by January 10, 2011, will allow BPPD sufficient time to conduct a review of the application and make a regulatory decision.

Registrant notified that this is the last negotiation? NO (this is first renegotiation)

Approve: ✓	**Disapprove:**
If disapproved, action to be taken:	
OD or DOD Signature:	**Date:** 12-22-10

RE: Need to set new PRIA 2 Due Date for RESULTIX
Matt Schneider to: Cheryl Greene 12/15/2010 05:04 PM
Cc: "Kathy Palma", "Susan Phillips", "Matt Schneider"

Re: Product: RESULTIX

EPA Registration # 86865-R

Dear Cheryl,

On behalf of our client, Piedmont Animal Health and in connection with the above referenced registration application, we agree to a 7 1/2 month extension of the current PRIA 2 due date to August 25, 2011. We acknowledge that this renegotiation date is contingent on Piedmont submitting by January 10, 2011 new and/or clarified information that addresses the deficiencies identified in the Agency's December 9, 2010 letter. We acknowledge that Piedmont understands that if the Agency does not receive a satisfactory resubmission package by January 10, 2011 the Agency may need to renegotiate the due date of August 25, 2011, to allow the Agency sufficient time to review any new information that would be subsequently submitted and render a regulatory decision.

We very much appreciate the helpful phone meeting yesterday that helped to clarify what is needed to complete a successful registration process.

Best regards,

Matt

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-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Wednesday, December 15, 2010 12:48 PM
To: Matt Schneider
Cc: Hollis.Linda@epamail.epa.gov
Subject: RE: Need to set new PRIA2 Due Date for RESULTIX
Importance: High

Thanks Matt.

I'll get the paperwork rolling now.  However, before I can send the
package  up for approval I need a statement (email is fine)  from you
specifically agreeing to a 7 1/2 month renegotiation of you current PRIA
2 due date to August 25, 2011. The statement should acknowledge that
this renegotiation date is contingent on Peidmont submitting by Jjanuary
10, 2011 new information that addresses the deficiencies identified in
the Agency's Oecember 9, 2010 letter.  The statement should also
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acknowledgint that Piedmont undeerstands that if the Agency does not receive a complete resubmission package by January 10, 2011 the Agency may need to renegotiate the due date of August 25, 2011, to allow the Agency sufficient time to review the submitted information and render a regulatory decision.

Once I get your statement agreeing to the renegotiation, I will send the package up for signature. Once the renegotiation request is approved, I will send yo an email confirming the approval. With any luck this will all happen by COB Friday. I'' keep you posted. In the meantime, let me know if you have questions or need additional information.

Regards,

From: "Matt Schneider" <MSchneider@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA

Cc: Angela Gonzales/DC/USEPA/US@EPA, Clara Fuentes/DC/USEPA/US@EPA, Linda Hollis/DC/USEPA/US@EPA, Andrew Bryceland/DC/USEPA/US@EPA, "Matt Schneider" <MSchneider@gsblaw.com>, "Susan Phillips" <SPhillips@gsblaw.com>

Oate: 12/15/2010 11:17 AM

Subject: RE: Need to set new PRIA2 Oue Date for RESULTIX

Cheryl,

We expect to be able to submit new information to the Agency to address the deficiencies by about January 10, 2011. Thanks again for all your help.

Regards,

Matt and Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [
mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Tuesday, December 14, 2010 3:12 PM
To: Susan Phillips; Matt Schneider
Cc: Gonzales.Angela@epamail.epa.gov; Fuentes.Clara@epamail.epa.gov; Hollis.Linda@epamail.epa.gov; Bryceland.Andrew@epamail.epa.gov
Subject: RE: Need to set new PRIA2 Due Date for RESULTIX

Hi Susan:

I need to get the paperwork for renegotiating the RESULTIX PRIA2 due date up to Sr. Management as soon as possible. We still need to make the December 17, 2010 renegotiation deadline. That said, will you be able to let me know by COB tomorrow how long you believe it will take Piedmont to submit new information to the Agency to address the deficiencies in our December 9, letter? Once I have this information I can determine the new PRIA 2 due date and get the paperwork rolling. As we discussed in the meeting, please keep in mind that the Agency will require seven and one-half (7 ½) months from the date of receipt of your response to this letter to review any newly submitted information and make a regulatory decision. This means that if Piedmont submits new information on January 15, 2011 we would renegotiate out from that date which would make the new PRIA2 2 due date August 30, 2011.

Please let me know if you have questions, need additional information or anything from me to help with estimating the amount of time you will need to resubmit.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA

Cc: "Matt Schneider" <MSchneider@gsblaw.com>, Linda Hollis/DC/USEPA/US@EPA

Date: 12/10/2010 07:02 AM

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Personal privacy information

Thanks for your prompt reply. A teleconference on Tuesday from 11-12 is the best for us. I will be at GSB on Tuesday for this telcon and therefore Matt's number can be used for this purpose (202 298 1787). We can add Dr. Palma to the call from our end. If you need to contact me before Tuesday, my home number is [redacted].

As for the agenda on Tuesday, the major issues are toxicology and the two safety and efficacy studies in cats and dogs (MRID 479253-17 and -18). Product chemistry and the draft label deficiencies are easily corrected and we see no reason to discuss these during the teleconference.

The safety and efficacy studies were submitted to fulfill both product performance and companion animal toxicity requirements. Based on the EPA deficiency letter, these two studies may not fulfill the companion animal toxicity requirements; however, product performance issues only concern label statement claims, which are easily correctible by revising the product label.

As for the toxicology deficiencies, the requested citation concerning dermal irritation will be submitted to the EPA in its entirety (approximately 84 pages) with an introduction indicating where the specific information is located in this review article. In addition, we are prepared to discuss additional rationales for requesting data

waivers for the developmental toxicity and the in vitro mammalian cell assay data requirements.

Consequently, the agenda for the teleconference only concern toxicity data requirements for dogs, cats and humans. Please feel free to contact me or Matt if you have further questions in advance of our call and we would appreciate confirmation once the conference call time is firmed up.

Thanks very much for fitting this in during a very busy time of the year.

Regards,
Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [
mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 5:10 PM
To: Susan Phillips
Cc: Matt Schneider; Hollis.Linda@epamail.epa.gov
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

Please see Linda Hollis's email below. Since Linda is not available next weed for a face-to face meeting, our next best option is a conference call. I'm working on pulling that together now. Please verify with your people that a conference call is acceptable. Also, please send me -- as soon as you possibly can -- a list containing the specific deficiencies/information Piedmont wishes to discuss or have clarified during the conference call. I need this list as soon as possible to ensure that I include the appropriate science folks on the call. At this point, I have identified two possible times for the call they are Monday, December 13, from 11:30 am to 12:30 PM or Tuesday December 14, 11:00 am to 12"00 noon. Please let me know which of these times best suite your people.

Also, the attachment below contains a pdf copy of the signed deficiency letter for RESULTIX. As I explained in my email earlier this month, this signed letter does not deviate in any significant way from the draft copy I forwarded to you on December 3, 2010. The original deficiency letter went out to you in the mail today.

Please let me know if you have questions or need more information .

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Susan: I just left a very detailed message with Matt . I would like your telephone number. At any rate, we can not accommodate a face to face meeting at anytime next week due to juggling schedules and previous commitments. However, my voice message to Matt was that we could entertain a conf call with all key players . I would like to do this preferably on Monday. I am available most of the morning and most of Tuesday. Wed - Friday are not options for me . I asked Matt that you forward a detailed list of topics for discussion . I am assuming that you really want to discuss product performance . Please let me know, we would be happy to provide further guidance as to how to move forward . Also, we recognize that the PRIA2 due date falls on a holiday (the 24th).
This essentially means that we will need to wrap this up with regard to a renegotiation days prior to that. Please work with Cheryl Greene and forward your telephone number.

Linda A. Hollis, MS

Chief, Biochemical Pesticides Branch
8iopesticides and Pollution Prevention Division Office of Pesticide Programs (7511P) U.S. Environmental Protection Agency One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202
hollis.linda@epa.gov
(703) 308-8733 (phone)
(703) 308-7026 (fax)
Visit http://www.epa.gov/pesticides

"The journey of 1000 miles begins with one step.....Take the step"

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA, "Matt Schneider" <MSchneider@gsblaw.com>

Cc: Linda Hollis/DC/USEPA/US@EPA

Date: 12/09/2010 03:55 PM

Subject: RE: Request for meeting with 8PPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 8686S-R

Thanks very much for your prompt response.

Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 3:19 PM
To: Susan Phillips; Matt Schneider
Cc: Hollis.Linda@epamail.epa.gov
Subject: Request for meeting with 8PPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 8686S-R
Importance: High

Hi Susan:

This email is to acknowledge receipt of Matt's email requesting for a meeting with BPPD to discuss the deficiency letter for RESULTIX . I hope to discuss this with my Branch Chief either later today or early tomorrow. As soon as I know her availability and the availability of the associated science folks, I will get back to you to let you know if Wednesday the 15th is possible and if so the time. In the meantime, let me know if you have questions or need more information .

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Re: Product: RESULTIX

EPA Registration # 86865-R

Your December 3, 2009 application for Section 3 Registration

PRIAII Code B600 EPA Decision # 424225

Good Morning Cheryl,

I am writing to you in response to your December 3 email to my colleague Susan Phillips containing a draft of a the deficiency letter pertaining to the above captioned matter. As you know, the draft letter states that if the PRIA 2 deadline is not renegotiated by December 17, 2010, EPA will issue a can not grant letter. While we have not yet received a final deficiency letter, we see that the timeframe available to take action before December 17 is very short and so we very much appreciate your forwarding the draft. On the assumption that the final deficiency

letter will be similar or identical to the draft, we need to move quickly. Accordingly, on behalf of our client, Piedmont Animal Health, we urgently and respectfully request a meeting to discuss the issues raised in the letter to clarify certain matters and hopefully reach agreement on a new PRIA 2 deadline in advance of December 17. In order for our client, Dr. Kathleen G. Palma, Vice President of Research and Development, Piedmont Animal Health, to be in attendance we were hoping that you would be able to schedule a meeting for Wednesday, December 15. I recognize this is short notice however, we only received the draft notice 14 days in advance of the deadline. We will make ourselves available any time on December 15 at your convenience. We very much appreciate whatever you can do to arrange the meeting at which Dr. Palma, Susan Phillips and I will be in attendance on behalf of Piedmont Animal Health.

Best regards,

Matt

MATTHEW R. 5CHNEIDER

Owner and Managing Director D.C. and NY Offices | 202.965.7880 x 17B7 Tel | 202.965.1729 Fax | mschneider@gsblaw.com

GARVEY SCHUBERT BARER | 5th Floor | 1000 Potomac Street NW | Washington, DC 20007 | GSBLaw.com

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intended recipient is prohibited.

RE: Need to set new PRIA 2 Due Date for RESULTIX
Matt Schneider to: Linda Hollis 12/15/2010 05:06 PM
Cc: Cheryl Greene, "Susan Phillips", "Kathy Palma", "Matt Schneider"

Linda, thanks for your comments. Perhaps a point of clarification would be helpful. Based on our very productive phone meeting with Cheryl and her team yesterday, we are expecting to submit supplementary and explanatory information and perhaps a revised study report for the efficacy studies, but not a new study. We are not expecting that the Agency will have a lot of new material to review and we are hopeful that this will expedite the process. We will do our best to submit a revised package that is persuasive, comprehensive and straightforward. Thanks for taking the time to comment. I hope you have a great Christmas. Best regards, Matt

-----Original Message-----
From: Hollis.Linda@epamail.epa.gov [mailto:Hollis.Linda@epamail.epa.gov]
Sent: Wednesday, December 15, 2010 3:46 PM
To: Greene.Cheryl@epamail.epa.gov
Cc: Matt Schneider
Subject: RE: Need to set new PRIA2 Due Date for RESULTIX

In addition, we would like to reiterate that this time is needed to review what may be, a new efficacy study and to review any response to deficiencies with regard to product chemistry and non targets , after which, should the information satisfy the data requirements , EPA will render its decision.

Linda A. Hollis, MS
Chief, Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs (7511P)
U.S. Environmental Protection Agency
One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202
hollis.linda@epa.gov
(703) 308-8733 (phone)
(703) 308-7026 (fax)
Visit http://www.epa.gov/pesticides

"The journey of 1000 miles begins with one step.....Take the step"

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| From:       |
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  |Cheryl
Greene/DC/USEPA/US
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| To:         |
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  |"Matt Schneider"
<MSchneider@gsblaw.com>
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  |Linda
Hollis/DC/USEPA/US@EPA
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|RE: Need to set new PRIA2 Due Date for
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Thanks Matt.

I'll get the paperwork rolling now. However, before I can send the package up for approval I need a statement (email is fine) from you specifically agreeing to a 7 1/2 month renegotiation of you current PRIA 2 due date to August 25, 2011. The statement should acknowledge that this renegotiation date is contingent on Peidmont submitting by Jjanuary 10, 2011 new information that addresses the deficiencies identified in the Agency's December 9, 2010 letter. The statement should also acknowledgint that Piedmont undeerstands that if the Agency does not receive a complete resubmission package by January 10, 2011 the Agency may need to renegotiate the due date of August 25, 2011, to allow the Agency sufficient time to review the submitted information and render a regulatory decision.

Once I get your statement agreeing to the renegotiation, I will send the package up for signature. Once the renegotiation request is approved, I will send yo an email confirming the approval. With any luck this will all happen by COB Friday. I'' keep you posted. In the meantime, let me know if you have questions or need additional information.

Regards,

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| From: |
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|"Matt Schneider"
<MSchneider@gsblaw.com>
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| To: |
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|Cheryl
Greene/DC/USEPA/US@EPA
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|Angela Gonzales/DC/USEPA/US@EPA, Clara Fuentes/DC/USEPA/US@EPA, Linda
Hollis/DC/USEPA/US@EPA, Andrew Bryceland/DC/USEPA/US@EPA, "Matt |
|Schneider" <MSchneider@gsblaw.com>, "Susan Phillips"
<SPhillips@gsblaw.com>
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|RE: Need to set new PRIA2 Due Date for
RESULTIX
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Cheryl,

We expect to be able to submit new information to the Agency to address the deficiencies by about January 10, 2011. Thanks again for all your help.

Regards,

Matt and Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [
mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Tuesday, December 14, 2010 3:12 PM
To: Susan Phillips; Matt Schneider
Cc: Gonzales.Angela@epamail.epa.gov; Fuentes.Clara@epamail.epa.gov; Hollis.Linda@epamail.epa.gov; Bryceland.Andrew@epamail.epa.gov
Subject: RE: Need to set new PRIA2 Due Date for RESULTIX

Hi Susan:

I need to get the paperwork for renegotiating the RESULTIX PRIA2 due date up to Sr. Management as soon as possible. We still need to make the December 17, 2010 renegotiation deadline. That said, will you be able to let me know by COB tomorrow how long you believe it will take Piedmont to submit new information to the Agency to address the deficiencies in our December 9, letter? Once I have this information I can determine the new PRIA 2 due date and get the paperwork rolling. As we discussed in the meeting, please keep in mind that the Agency will require seven and one-half (7 ½) months from the date of receipt of your response to this letter to review any newly submitted information and make a regulatory decision. This means that if Piedmont submits new information on January 15, 2011 we would renegotiate out from that date which would make the new PRIA2 2 due date August 30, 2011.

Please let me know if you have questions, need additional information or anything from me to help with estimating the amount of time you will need to resubmit.

Regards,

Cheryl F. Greene

Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA

Cc: "Matt Schneider" <MSchneider@gsblaw.com>, Linda Hollis/DC/USEPA/US@EPA

Date: 12/10/2010 07:02 AM

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks for your prompt reply. A teleconference on Tuesday from 11-12 is the best for us. I will be at GSB on Tuesday for this telcon and therefore Matt's number can be used for this purpose (202 298 1787). We can add Dr. Palma to the call from our end. If you need to contact me before Tuesday, my home number is [redacted].

As for the agenda on Tuesday, the major issues are toxicology and the two safety and efficacy studies in cats and dogs (MRID 479253-17 and -18). Product chemistry and the draft label deficiencies are easily corrected and we see no reason to discuss these during the teleconference.

The safety and efficacy studies were submitted to fulfill both product performance and companion animal toxicity requirements. Based on the EPA deficiency letter, these two studies may not fulfill the companion animal toxicity requirements; however, product performance issues only concern label statement claims, which are easily correctible by revising the product label.

Personal privacy information

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Consequently, the agenda for the teleconference only concern toxicity data requirements for dogs, cats and humans. Please feel free to contact me or Matt if you have further questions in advance of our call and we would appreciate confirmation once the conference call time is firmed up.

Thanks very much for fitting this in during a very busy time of the year.

Regards,
Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [
mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 5:10 PM
To: Susan Phillips
Cc: Matt Schneider; Hollis.Linda@epamail.epa.gov
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

Please see Linda Hollis's email below. Since Linda is not available next weed for a face-to face meeting, our next best option is a conference call. I'm working on pulling that together now. Please verify with your people that a conference call is acceptable. Also, please send me -- as soon as you possibly can -- a list containing the specific deficiencies/information Piedmont wishes to discuss or have clarified during the conference call. I need this list as soon as possible to ensure that I include the appropriate science folks on the call. At this point, I have identified two possible times for the call they are Monday, December 13, from 11:30 am to 12:30 PM or Tuesday December 14, 11:00 am to 12"00 noon. Please let me know which of these times best suite your people.

Also , the attachment below contains a pdf copy of the signed deficiency letter for RESULTIX. As I explained in my email earlier this month, this signed letter does not deviate in any significant way from the draft copy I forwarded to you on December 3, 2010. The original deficiency letter went out to you in the mail today .

Please let me know if you have questions or need more information .

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Susan: I just left a very detailed message with Matt . I would like your telephone number. At any rate, we can not accommodate a face to face meeting at anytime next week due to juggling schedules and previous commitments. However, my voice message to Matt was that we could entertain a conf call with all key players . I would like to do this preferably on Monday. I am available most of the morning and most of Tuesday. Wed - Friday are not options for me . I asked Matt that you forward a detailed list of topics for discussion . I am assuming that you really want to discuss product performance . Please let me know, we would be happy to provide further guidance as to how to move forward . Also, we recognize that the PRIA2 due date falls on a holiday (the 24th).
This essentially means that we will need to wrap this up with regard to

a renegotiation days prior to that. Please work with Cheryl Greene and forward your telephone number.

Linda A. Hollis, MS
Chief, Biochemical Pesticides Branch
8iopesticides and Pollution Prevention Division Office of Pesticide Programs (7S11P) U.S. Environmental Protection Agency One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202
hollis.linda@epa.gov
(703) 308-8733 (phone)
(703) 308-7026 (fax)
Visit http://www.epa.gov/pesticides

"The journey of 1000 miles begins with one step.....Take the step"

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA, "Matt Schneider" <MSchneider@gsblaw.com>

Cc: Linda Hollis/DC/USEPA/US@EPA

Date: 12/09/2010 03:S5 PM

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks very much for your prompt response.

Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 3:19 PM

To: Susan Phillips; Matt Schneider
Cc: Hollis.Linda@epamail.epa.gov
Subject: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

This email is to acknowledge receipt of Matt's email requesting for a meeting with BPPD to discuss the deficiency letter for RESULTIX . I hope to discuss this with my Branch Chief either later today or early tomorrow. As soon as I know her availability and the availability of the associated science folks, I will get back to you to let you know if Wednesday the 15th is possible and if so the time. In the meantime, let me know if you have questions or need more information .

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Re: Product: RESULTIX

EPA Registration # 86865-R

Your December 3, 2009 application for Section 3 Registration

PRIAII Code 8600 EPA Decision # 42422S

Good Morning Cheryl,

I am writing to you in response to your December 3 email to my colleague Susan Phillips containing a draft of a the deficiency letter pertaining

to the above captioned matter. As you know, the draft letter states that if the PRIA 2 deadline is not renegotiated by December 17, 2010, EPA will issue a can not grant letter. While we have not yet received a final deficiency letter, we see that the timeframe available to take action before December 17 is very short and so we very much appreciate your forwarding the draft. On the assumption that the final deficiency letter will be similar or identical to the draft, we need to move quickly. Accordingly, on behalf of our client, Piedmont Animal Health, we urgently and respectfully request a meeting to discuss the issues raised in the letter to clarify certain matters and hopefully reach agreement on a new PRIA 2 deadline in advance of December 17. In order for our client, Dr. Kathleen G. Palma, Vice President of Research and Development, Piedmont Animal Health, to be in attendance we were hoping that you would be able to schedule a meeting for Wednesday, December 15. I recognize this is short notice however, we only received the draft notice 14 days in advance of the deadline. We will make ourselves available any time on December 15 at your convenience. We very much appreciate whatever you can do to arrange the meeting at which Dr. Palma, Susan Phillips and I will be in attendance on behalf of Piedmont Animal Health.

Best regards,

Matt

MATTHEW R. SCHNEIDER

Owner and Managing Director D.C. and NY Offices | 202.965.7880 x 1787 Tel | 202.965.1729 Fax | mschneider@gsblaw.com

GARVEY SCHUBERT BARER | 5th Floor | 1000 Potomac Street NW | Washington, DC 20007 | GSBLaw.com

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RE: Need to set new PRIA2 Due Date for RESULTIX
Matt Schneider
to:
Cheryl Greene
12/15/2010 05:04 PM
Cc:
"Kathy Palma", "Susan Phillips", "Matt Schneider"
Show Details

Re: Product: RESULTIX

EPA Registration # 86865-R

Dear Cheryl,

On behalf of our client, Piedmont Animal Health and in connection with the above referenced registration application, we agree to a 7 1/2 month extension of the current PRIA 2 due date to August 25, 2011. We acknowledge that this renegotiation date is contingent on Piedmont submitting by January 10, 2011 new and/or clarified information that addresses the deficiencies identified in the Agency's December 9, 2010 letter. We acknowledge that Piedmont understands that if the Agency does not receive a satisfactory resubmission package by January 10, 2011 the Agency may need to renegotiate the due date of August 25, 2011, to allow the Agency sufficient time to review any new information that would be subsequently submitted and render a regulatory decision.

We very much appreciate the helpful phone meeting yesterday that helped to clarify what is needed to complete a successful registration process.

Best regards,

Matt

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Wednesday, December 15, 2010 12:48 PM
To: Matt Schneider
Cc: Hollis.Linda@epamail.epa.gov
Subject: RE: Need to set new PRIA2 Due Date for RESULTIX
Importance: High

Thanks Matt.

I'll get the paperwork rolling now. However, before I can send the package up for approval I need a statement (email is fine) from you specifically agreeing to a 7 1/2 month renegotiation of you current PRIA 2 due date to August 25, 2011. The statement should acknowledge that this renegotiation date is contingent on Peidmont submitting by Jjanuary 10, 2011 new information that addresses the deficiencies identified in the Agency's Oecember 9, 2010 letter. The statement should also acknowledgint that Piedmont undeerstands that if the Agency does not receive a complete resubmission package by 1anuary 10, 2011 the Agency may need to renegotiate the due date of August 2S, 2011, to allow the Agency sufficient time to review the submitted information and render a regulatory decision.

Once I get your statement agreeing to the renegotiation, I will send the package up for signature. Once the renegotiation request is approved, I will send yo an email confirming the approval. With any luck this will all happen by COB Friday. I'' keep you posted. In the meantime, let me know if you have questions or need additional information.

Regards,

From: "Matt Schneider" <MSchneider@gsblaw.com>

To: Cheryl Greene/OC/USEPA/US@EPA

Cc: Angela Gonzales/OC/USEPA/US@EPA, Clara Fuentes/DC/USEPA/US@EPA, Linda Hollis/DC/USEPA/US@EPA, Andrew Bryceland/OC/USEPA/US@EPA, "Matt Schneider" <MSchneider@gsblaw.com>, "Susan Phillips"

<SPhillips@gsblaw.com>

Date: 12/15/2010 11:17 AM

Subject: RE: Need to set new PRIA2 Due Date for RESULTIX

Cheryl,

We expect to be able to submit new information to the Agency to address the deficiencies by about January 10, 2011. Thanks again for all your help.

Regards,

Matt and Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [
mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Tuesday, December 14, 2010 3:12 PM
To: Susan Phillips; Matt Schneider
Cc: Gonzales.Angela@epamail.epa.gov; Fuentes.Clara@epamail.epa.gov;
Hollis.Linda@epamail.epa.gov; Bryceland.Andrew@epamail.epa.gov
Subject: RE: Need to set new PRIA2 Due Date for RESULTIX

Hi Susan:

I need to get the paperwork for renegotiating the RESULTIX PRIA2 due date up to Sr. Management as soon as possible. We still need to make the December 17, 2010 renegotiation deadline. That said, will you be able to let me know by COB tomorrow how long you believe it will take Piedmont to submit new information to the Agency to address the deficiencies in our December 9, letter? Once I have this information I can determine the new PRIA 2 due date and get the paperwork rolling. As we discussed in the meeting, please keep in mind that the Agency will require seven and one-half (7 ½) months from the date of receipt of your response to this letter to review any newly submitted information and make a regulatory decision. This means that if Piedmont submits new information on January 15, 2011 we would renegotiate out from that date which would make the new PRIA2 2 due date August 30, 1011.

Please let me know if you have questions, need additional information or anything from me to help with estimating the amount of time you will need to resubmit.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

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To: Cheryl Greene/DC/USEPA/US@EPA

Cc: "Matt Schneider" <MSchneider@gsblaw.com>, Linda Hollis/DC/USEPA/US@EPA

Date: 12/10/2010 07:02 AM

RE: Need to set new PRIA 2 Due Date for RESULTIX

Matt Schneider to: Cheryl Greene 12/15/2010 11:17 AM

Cc: Angela Gonzales, Clara Fuentes, Linda Hollis, Andrew Bryceland, "Matt Schneider", "Susan Phillips"

History: This message has been replied to.

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Personal privacy information

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Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

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Washington, DC 20004

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Linda A. Hollis, MS
Chief, Biochemical Pesticides Branch
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To: Cheryl Greene/DC/USEPA/US@EPA, "Matt Schneider" <MSchneider@gsblaw.com>

Cc: Linda Hollis/DC/USEPA/US@EPA

Date: 12/09/2010 03:55 PM

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks very much for your prompt response.

Susan

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Subject: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

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Regards,

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Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Re: Product: RESULTIX

EPA Registration # 86865-R

Your December 3, 2009 application for Section 3 Registration

PRIAII Code B600 EPA Decision # 424225

Good Morning Cheryl,

I am writing to you in response to your December 3 email to my colleague Susan Phillips containing a draft of a the deficiency letter pertaining to the above captioned matter. As you know, the draft letter states that if the PRIA 2 deadline is not renegotiated by December 17, 2010, EPA will issue a can not grant letter. While we have not yet received a final deficiency letter, we see that the timeframe available to take action before December 17 is very short and so we very much appreciate your forwarding the draft. On the assumption that the final deficiency letter will be similar or identical to the draft, we need to move quickly. Accordingly, on behalf of our client, Piedmont Animal Health,

we urgently and respectfully request a meeting to discuss the issues raised in the letter to clarify certain matters and hopefully reach agreement on a new PRIA 2 deadline in advance of December 17. In order for our client, Dr. Kathleen G. Palma, Vice President of Research and Development, Piedmont Animal Health, to be in attendance we were hoping that you would be able to schedule a meeting for Wednesday, December 15. I recognize this is short notice however, we only received the draft notice 14 days in advance of the deadline. We will make ourselves available any time on December 15 at your convenience. We very much appreciate whatever you can do to arrange the meeting at which Dr. Palma, Susan Phillips and I will be in attendance on behalf of Piedmont Animal Health.

Best regards,

Matt

MATTHEW R. SCHNEIDER

Owner and Managing Director D.C. and NY Offices | 202.965.7880 x 1787 Tel | 202.965.1729 Fax | mschneider@gsblaw.com

GARVEY SCHUBERT BARER | 5th Floor | 1000 Potomac Street NW | Washington, DC 20007 | ► GSBLaw.com

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RE: Need to set new PRIA2 Due Date for RESULTIX
Matt Schneider
to:
Cheryl Greene
12/14/2010 08:51 PM
Cc:
"Susan Phillips", "Kathy Palma"
Show Details

Hi Cheryl, Susan and I will get back to you shortly on the substance of your question, but in the meantime, as a matter of academic curiosity, I was surprised to learn in our conversation that a 7.5 month extension is required. Honestly, I can't find it in the law or the guidance that the Agency puts out. Below is an excerpt from the Agency summary of the law. In relevant part it states, "In estimating the amount of time that may be required to address the issues and then make a determination on the application, the Agency analyzes which steps in its process need to be completed and the amount of time required for each." I can't find any reference to a requirement that it be 7.5 months. Is there some other source of this requirement? Just curious and thanks again for putting our call together this morning. Best regards, Matt

Decision Review Periods (PRIA 2 Timeframes)Each PRIA 2 fee category has an associated period of time in which the Agency must make a determination, which has been called a decision review period or PRIA 2 timeframe. The Agency is committed to meeting the "PRIA 2 due dates." For applications that do not include a request for a waiver or exemption, the PRIA 2 timeframe begins 21 days after receipt of the application and fee. As previously described, for applications with a waiver or exemption request, the PRIA 2 timeframe begins when the request is granted, or in the case of a waiver request, if no additional fee is required, the earlier of (i) the date the Agency grants the waiver or (ii) the date that is 60 days after receipt of the application. If the Agency denies the request for a waiver or if it grants the waiver and additional fees are required, the decision review period begins when the Agency receives payment of the outstanding portion of the registration service fee.

At any time after the 21-day initial content screen and during the Agency's in-depth review of an application, the Agency may determine that an application is incomplete or that further information is needed in order to complete the Agency's review. A 75-day deficiency letter may be issued pursuant to 40 CFR 152.105 notifying the applicant that the applicant has 75 days in which to address the deficiencies or provide a schedule for addressing the deficiencies. If, after 75 days, the applicant has not responded, or fails to address the deficiencies within the time scheduled, the Agency will treat the application as if it has been withdrawn by the applicant. Once the Agency withdraws the application, a determination will be made on a refund as described in the section "Withdrawn Applications."

The Agency may also determine that there will be insufficient time for an applicant to submit the needed data/information and/or the Agency to review the data/information within the PRIA 2 timeframe. The Agency will then contact the applicant and discuss the situation. Some possible outcomes include:

withdrawal of the application (and a determination with respect to any refund);
negotiation of a new due date with the Agency;
a determination by the Agency on whether the application, in the absence of the data, can be granted; or
a denial of the application based on data (or lack thereof) before the Agency.
Top of page

Negotiated Due Oates or Due Date Extensions The PRIA 2 due date may be extended by a mutual agreement between the applicant and the Agency. The new due date is called a negotiated due date. Negotiated due dates occur predominately as a result of missing information or data or data deficiencies identified during an in-depth review of the application. The due date then is extended to allow the applicant the time to submit the data or information and for the Agency to review the data and make a determination.

In estimating the amount of time that may be required to address the issues and then make a determination on the application, the Agency analyzes which steps in its process need to be completed and the amount of time required for each. Steps in processing an application may include in-processing or intake of a submission, screening to determine its contents, data review, secondary or management review of documents, risk assessment, and regulatory decision-making. The amount of time that the applicant may take to submit the data or information is estimated and then the registering division estimates the amount of time it will take to reach a determination on the application.

Delays in submitting information may result in the applicant requesting additional extensions in the due date; however, additional delays in submitting the data or information may result in a determination that the Agency cannot grant the application or denial of the application. If substantial delays are expected in submitting the data or information or a new due date cannot be estimated by the applicant, the applicant is advised to withdraw the application and submit a new application with the data or information at a later date. The withdrawal procedures in the section "Withdrawn Applications" would apply.

The process for reaching a negotiated due date generally involves the applicant submitting its consent to an extension in writing (e-mail is sufficient) to the Agency representative, generally a Product Manager or Regulatory Action Leader. The registering division then finalizes the agreement by obtaining the approval of the Dffice Director or Deputy Office Director.

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From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Tuesday, December 14, 2010 3:12 PM
To: Susan Phillips; Matt Schneider

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Subject: RE: Need to set new PRIA2 Due Date for RESULTIX

Hi Susan:

I need to get the paperwork for renegotiating the RESULTIX PRIA2 due date up to Sr. Management as soon as possible. We still need to make the December 17, 2010 renegotiation deadline. That said, will you be able to let me know by COB tomorrow how long you believe it will take Piedmont to submit new information to the Agency to address the deficiencies in our December 9, letter? Once I have this information I can determine the new PRIA 2 due date and get the paperwork rolling. As we discussed in the meeting, please keep in mind that the Agency will require seven and one-half (7 ½) months from the date of receipt of your response to this letter to review any newly submitted information and make a regulatory decision. This means that if Piedmont submits new information on January 15, 2011 we would renegotiate out from that date which would make the new PRIA2 2 due date August 30, 2011.

Please let me know if you have questions, need additional information or anything from me to help with estimating the amount of time you will need to resubmit.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/8P8 (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA

Cc: "Matt Schneider" <MSchneider@gsblaw.com>, Linda Hollis/DC/USEPA/US@EPA

Date: 12/10/2010 07:02 AM

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks for your prompt reply. A teleconference on Tuesday from 11-12 is the best for us. I will be at GSB on Tuesday for this telcon and therefore Matt's number can be used for this purpose (202 298 1787). We can add Dr. Palma to the call from our end. If you need to contact me before Tuesday, my home number is [redacted].

As for the agenda on Tuesday, the major issues are toxicology and the two safety and efficacy studies in cats and dogs (MRID 479253-17 and -18). Product chemistry and the draft label deficiencies are easily corrected and we see no reason to discuss these during the teleconference.

The safety and efficacy studies were submitted to fulfill both product performance and companion animal toxicity requirements. Based on the EPA deficiency letter, these two studies may not fulfill the companion animal toxicity requirements; however, product performance issues only concern label statement claims, which are easily correctible by revising the product label.

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Consequently, the agenda for the teleconference only concern toxicity data requirements for dogs, cats and humans. Please feel free to contact me or Matt if you have further questions in advance of our call and we would appreciate confirmation once the conference call time is firmed up.

Thanks very much for fitting this in during a very busy time of the year.

Regards,
Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [
mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 5:10 PM
To: Susan Phillips
Cc: Matt Schneider; Hollis.Linda@epamail.epa.gov
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

Please see Linda Hollis's email below. Since Linda is not available next weed for a face-to face meeting, our next best option is a conference call. I'm working on pulling that together now. Please verify with your people that a conference call is acceptable. Also, please send me -- as soon as you possibly can -- a list containing the specific deficiencies/information Piedmont wishes to discuss or have clarified during the conference call. I need this list as soon as possible to ensure that I include the appropriate science folks on the call. At this point, I have identified two possible times for the call they are Monday, December 13, from 11:30 am to i2:30 PM or Tuesday December 14, 11:00 am to 12"00 noon. Please let me know which of these times best suite your people.

Also , the attachment below contains a pdf copy of the signed deficiency letter for RESULTIX. As I explained in my email earlier this month, this signed letter does not deviate in any significant way from the draft copy I forwarded to you on December 3, 2010. The original deficiency letter went out to you in the mail today.

Please let me know if you have questions or need more information.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/8P8 (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, OC 20004

Tel: 703 308-0352

Fax 703 308-7026
Email: greene.cheryl@epa.gov

Susan: I just left a very detailed message with Matt. I would like your telephone number. At any rate, we can not accommodate a face to face meeting at anytime next week due to juggling schedules and previous commitments. However, my voice message to Matt was that we could entertain a conf call with all key players. I would like to do this preferably on Monday. I am available most of the morning and most of Tuesday. Wed - Friday are not options for me. I asked Matt that you forward a detailed list of topics for discussion. I am assuming that you really want to discuss product performance. Please let me know, we would be happy to provide further guidance as to how to move forward. Also, we recognize that the PRIA2 due date falls on a holiday (the 24th).
This essentially means that we will need to wrap this up with regard to a renegotiation days prior to that. Please work with Cheryl Greene and forward your telephone number.

Linda A. Hollis, MS
Chief, Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division Office of Pesticide Programs (7511P) U.S. Environmental Protection Agency One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202
hollis.linda@epa.gov
(703) 308-8733 (phone)
(703) 308-7026 (fax)
Visit http://www.epa.gov/pesticides

"The journey of 1000 miles begins with one step.....Take the step"

From: "Susan Phillips" cSPhillips@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA, "Matt Schneider" <MSchneider@gsblaw.com>

Cc: Linda Hollis/DC/USEPA/US@EPA

Date: 12/09/2010 03:55 PM

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks very much for your prompt response.

Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 3:19 PM
To: Susan Phillips; Matt Schneider
Cc: Hollis.Linda@epamail.epa.gov
Subject: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

This email is to acknowledge receipt of Matt's email requesting for a meeting with BPPD to discuss the deficiency letter for RESULTIX. I hope to discuss this with my Branch Chief either later today or early tomorrow. As soon as I know her availability and the availability of the associated science folks, I will get back to you to let you know if Wednesday the 15th is possible and if so the time. In the meantime, let me know if you have questions or need more information.

Regards,

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Dffice of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Re: Product: RESULTIX

EPA Registration # 86865-R

Your December 3, 2009 application for Section 3 Registration

PRIAII Code B600 EPA Decision # 424225

Good Morning Cheryl,

I am writing to you in response to your December 3 email to my colleague Susan Phillips containing a draft of a the deficiency letter pertaining to the above captioned matter. As you know, the draft letter states that if the PRIA 2 deadline is not renegotiated by December 17, 2010, EPA will issue a can not grant letter. While we have not yet received a final deficiency letter, we see that the timeframe available to take action before December 17 is very short and so we very much appreciate your forwarding the draft. On the assumption that the final deficiency letter will be similar or identical to the draft, we need to move quickly. Accordingly, on behalf of our client, Piedmont Animal Health, we urgently and respectfully request a meeting to discuss the issues raised in the letter to clarify certain matters and hopefully reach agreement on a new PRIA 2 deadline in advance of December 17. In order for our client, Dr. Kathleen G. Palma, Vice President of Research and Development, Piedmont Animal Health, to be in attendance we were hoping that you would be able to schedule a meeting for Wednesday, December 15. I recognize this is short notice however, we only received the draft notice 14 days in advance of the deadline. We will make ourselves available any time on December 15 at your convenience. We very much appreciate whatever you can do to arrange the meeting at which Dr. Palma, Susan Phillips and I will be in attendance on behalf of Piedmont Animal Health.

Best regards,

Matt

MATTHEW R. SCHNEIDER

Owner and Managing Director D.C. and NY Offices | 202.965.7880 x 1787
Tel | 202.965.1729 Fax | mschneider@gsblaw.com

GARVEY SCHUBERT BARER | 5th Floor | 1000 Potomac Street NW |
Washington, DC 20007 | ► GSBLaw.com

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RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Cheryl Greene to: Susan Phillips 12/10/2010 12:06 PM
Cc: Linda Hollis, Angela Gonzales, Clara Fuentes, Jacob Moore

Hi Susan:

Thanks for your response. A meeting time of 11:00 am to 12:00 noon on Tuesday, December 14, 2010 works for us. If the three of you will be calling in from the same number the call-in number is 703 305-0123 repeat 703 305-0123. If you will be calling from separate numbers, please let me know as soon as you can so that I can get a multiple-line call in number for the meeting. Also, thanks for the agenda information. I will get it out to the folks here ASAP.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

"Susan Phillips" Thanks for your prompt reply. A teleconference... 12/10/2010 07:02:58 AM

From:	"Susan Phillips" <SPhillips@gsblaw.com>
To:	Cheryl Greene/DC/USEPA/US@EPA
Cc:	"Matt Schneider" <MSchneider@gsblaw.com>, Linda Hollis/DC/USEPA/US@EPA
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Importance: High

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Tel: 703 308-0352
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Re: Product: RESULTIX

EPA Registration # 86865-R

Your December 3, 2009 application for Section 3 Registration

PRIAII Code B600 EPA Decision # 424225

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Deficiency Letter re RESULTIX -- EPA Reg. No. 86865-R- Request for Meeting
Matt Schneider
to:
Cheryl Greene
12/09/2010 11:31 AM
Cc:
"Susan Phillips", "Kathy Palma", "Matt Schneider"
Show Details

Re: Product: RESULTIX
EPA Registration # 86865-R
Your December 3, 2009 application for Section 3 Registration
PRIAII Code B600 EPA Decision # 424225

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Matt

MATTHEW R. SCHNEIDER
Owner and Managing Director D.C. and NY Offices | 202.965.7880 x 1787 Tel | 202.965.1729 Fax | mschneider@gsblaw.com
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▶ GSBLaw.com

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UNITED S...TES ENVIRONMENTAL PROTECTI..J AGENCY

December 9, 2010

Susan Phillips, Science Advisor
Authorized Representative for Piedmont Animal Health LLC
Garvey Schubert Barer
Fifth Floor
Flour Mill Building
1000 Potomac Street, N.W.
Washington D.C. 2007-3501

Subject: Product: RESULTIX
EPA Registration # 86865-R
Your December 3, 2009 application for Section 3 Registration
PRIAII Code B600 EPA Decision # 424225

CONTAINS CONFIDENTIAL INFORMATION

Dear Ms. Phillips:

The Biopesticide and Pollution Prevention Division (BPPD) has received and reviewed the application referenced above which was, submitted in connection with an application for registration of a new product under section 3(c)(7)A of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, and the Pesticide Registration Improvement Act (PRIA II).

Piedmont Animal Health LLC (Piedmont) has submitted an application for registration of an end-use, spot-on product named Resultix, which contains 50% of a new active ingredient, isopropyl myristate, to kill ticks on dogs and cats. RESULTIX is formulated as a contact product that kills ticks on dogs and cats by dissolving the cuticle of the tick which causes death by desiccation.

Based on our review, the Agency has concluded that the referenced **application is deficient and not acceptable**, at this time. This conclusion is based on the deficiencies identified below. These deficiencies must be successfully addressed before the Agency can proceed with the review of your application and issue a registration decision for the proposed product.

Product Chemistry

The product chemistry data submission (MRIDs 479253-01 to 479253-08) is unacceptable as noted below and must be successfully addressed.

1. Piedmont submitted two Confidential Statements of Formula (CSF) in support of the referenced application. Both CSFs are dated 12/02/09.

URRENCES							
7511P							
Greene							
December 9, 2010							

OFFICIAL FILE COPY

a. The following deficiencies apply to the CSF submitted for the technical grade active ingredient (TGAI) [redacted] (Isopropyl Myristate):

   i. Column 10 - The CAS number for [redacted] must be corrected from [redacted].

   ii. Column 14 - The certified limits for isopropyl myristate and its related impurities are inconsistent with the certified limits presented in the preliminary analysis (MRID 479253-02) for the TGAI. Piedmont must correct the CSF for the TGAI to reflect the certified limits presented in the preliminary analysis.

   iii. Column 14(a) - The upper certified limit of isopropyl myristate cannot exceed 100%. Piedmont must revise the CSF such that the certified upper limit for isopropyl myristate is equal to or less than 100%. Alternately, Piedmont can submit an acceptable rationale for the percentage (102.9) noted on the CSF.

b. The following deficiencies apply to the CSF for the end-use product (RESULTIX).

   i. Column 13(b) - The nominal concentration of the active ingredient (isopropyl myristate) must match the label, which currently reads 50.0%. Piedmont must revise the nominal concentration of isopropyl myristate on the CSF to read 50.0%.

   ii. Column 10 - The source of the active ingredient is not noted on the CSF. Piedmont must list the source of [redacted] Isopropyl Myristate, [redacted] alongside the name of the active ingredient (isopropyl myristate).

2. The physical and chemical characteristics data/information submitted to support the proposed product is **acceptable. No additional data are required.**

Product Performance/Efficacy

The product performance/efficacy submission (MRID 47925317, MRID 479253-18) is unacceptable and must be successfully addressed as noted below before the Agency can proceed with its review of your application.

MRID 479253-17 - Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate Tick Spray against Rhipicephalus sanguineus and Dermacentor variabilis on Dogs.

1. The amount of product applied to each dog was not reported. Companion Animal Safety Guideline (OCSPP 870.7200) recommends that animals be treated with 1, 3 and 5 times the recommended dose. In the submitted study only one dose (2 sprays) was applied to each animal. Based on labeling instructions for RESULTIX and the proposed use pattern, the amount of product applied to each dog will vary depending on the number of ticks found on the dogs. As such, the study fails to investigate the effect

Product ingredient source information may be entitled to confidential treatment
Manufacturing process information may be entitled to confidential treatment

that increased doses of the proposed product will have on the health of dogs treated. Data/information demonstrating the effect of increased doses of the proposed product on dogs must be submitted before the Agency can proceed with its review.

2. The submitted label for the proposed product states that RESULTIX "starts killing ticks in seconds." Since the submitted data shows that death only occurs six 6 hours after treatment, the statement "starts killing ticks in seconds" is false and misleading because the user is not informed that it will take the treated ticks six (6) hours to actually die. Therefore, Piedmont must either submit new data that validates the claim that the product kills ticks in seconds or remove the statement from the product label or add language to the label that fully explains the time it will take a tick to die once it is treated.

3. The submitted label claims 100% efficacy. However, the submitted data records efficacy at less than 100%. The Agency therefore views the state 100% efficacy as false and misleading. Piedmont must either submit new data/information that validates the claim that RESULTIX is 100% efficacious or remove the statement from the product label.

4. The submitted data did not contain a discussion of food consumption and body weight of the test animals. As described in OCSPP Guideline 870.7200 (pages 6.and 7) data from Companion animal Safety studies should include the test animal(s) individual body weights (measured at specific intervals throughout the study) and the measures of individual food consumption of test animals on a daily basis. These data are critical markers of the health of the test animals and of the effect of the product on the animal(s). This information must be submitted before the Agency can proceed with its review.

5. The Agency's review has determined that the submitted data/information is missing certain individual data parameters for hematology and clinical chemistry analysis. Specifically, the following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC). This information must be submitted before the Agency can proceed with its review.

6. The Agency's review has determined that some clinical pathology values [CK (U/L; GGT (U/L); Cholesterol (mg/dL); Total CO2 (MeQ/l); Chloride (mEq/L), and Potassium (mEq/L)] were outside of the reference range prior to treatment. Based on these values, the Agency questions whether the dogs in the study were healthy prior to and during the study (Refer to MRID 479253-17 page 16, Table 2, Summary Clinical Chemistry Data). Piedmont must submit data/information that successfully demonstrates the health of the studied animial(s) before the Agency can proceed with its review.

<u>MRID 479253-18</u> - Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate Tick Spray against Rhipicephalus sanuineus and Dermacentor variabilis on Cats.

1. The amount of product applied to each cat was not reported. Companion Animal Safety Guideline OCSPP 870.7200 recommends that animals be treated with 1, 3 and 5 times the recommended dose. In

the submitted study only one dose (2 sprays) was applied to each animal. Based on labeling instructions and the proposed use pattern, the amount of product applied to each cat will vary depending on the number of ticks found on the cats. As such, the study fails to investigate the effect that increased doses of the proposed product will have on the health of cats treated. Data/information demonstrating the effect of increased doses of the proposed product on cats must be submitted before the Agency can proceed with its review.

2. The submitted data did not contain a discussion of food consumption and body weight of the test animals. As described in OCSPP Guideline 870.7200 (pages 6.and 7) data from Companion animal Safety studies should include the test animal(s) individual body weights (measured at specific intervals throughout the study) and the measures of individual food consumption of test animals on a daily basis. These data are critical markers of the health of the test animals and of the effect of the product on the animal(s). This information must be submitted before the Agency can proceed with its review.

3. The submitted label for the proposed product states that RESULTIX "starts killing ticks in seconds." Since the submitted data shows that death only occurs six 6 hours after treatment, the statement "starts killing ticks in seconds" is false and misleading because the user is not informed that it will take the treated ticks six (6) hours to actually die. Therefore, Piedmont must either submit new data that validates the claim that the product kills ticks in seconds or remove the statement from the product label or add language to the label that fully explains the time it will take a tick to die once it is treated.

4. The submitted label claims 100% efficacy. However, the submitted data records efficacy at less than 100%. The Agency therefore views the statement 100% efficacy as false and misleading. Piedmont must either submit new data/information validating the claim that RESULTIX is 100% efficacious or remove the statement from the product label.

5. The Agency's review has determined that individual data parameters for hematology and clinical chemistry analysis is missing fro the submitted data package. Specifically, the following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC).

7. Some of the clinical pathology values [Alk Phos (U/L); CK(U/L); GGT (U/L); UN (mg/dL), and phosphorous (mg/dL)] were outside of the reference range prior to treatment, which leads to the question of whether the cats in the study were healthy prior to and during the study (Refer to page 15, Table 2, Summary Clinical Chemistry Data; Pre and Post Treatment in MRID 479253-18). Piedmont must submit data/information that successfully demonstrates the health of the studied animial(s) before the Agency can proceed with its review.

Toxicology

Data submitted to address toxicology is deficient and unacceptable. The deficiencies identified below must be successfully addressed before the Agency can proceed with its review of the referenced application. The deficiencies are:

URRENCES								
	7511P							
	Greene							
	December 9, 2010							

Inert ingredient information may be entitled to confidential treatment

The following deficiencies apply to the active ingredient (isopropyl myristate)

a. Regarding the dermal irritation data requirement (OCSPP 870.2500) – The referenced 1997 study from RTECS that indicates that the active ingredient is mildly irritating was not included in your application (Refer to MRID 47925309). The Agency cannot make a determination on the data submitted for dermal irritation until a review of the RTECS study has been reviewed. Piedmont must submit this study before the Agency can proceed.

b. Regarding the developmental (OCSPP 870.3700) and *in vitro* mammalian cell assay (OCSPP 870.5300 and 870.5375) data requirements – The data/rationale submitted to fulfill these data requirements is insufficient. Piedmont states that significant occupational exposure is not expected because application is often seasonal. However, this rationale fails to consider that applications may occur more often in warmer climates where ticks may be prevalent year-round. Moreover, based on the available information, significant exposure to isopropyl myristate may occur in an occupational setting (e.g.: veterinary office, grooming salon) through use of the proposed product. The data/information submitted to satisfy occupational exposure also does not address either of these exposure scenarios. Piedmont must submit data/information that addresses both of these exposure scenarios before the Agency can proceed with its review..

The following deficiency applies to the end-use product(RESULTIX)

c. The test substance utilized in the submitted studies is interchangeably referenced by different names, including "Resultix Tick Spray", "Pediculocide 100", "Piedmont Pediculocide 1" and "Piedmont Pediculocide 2". Piedmont must submit data/information verifying that the test substance(s) referred to in the studies is identical to the proposed product, "RESULTIX".

Ecotoxicology

The Agency has evaluated the potential for toxicity of the compound isopropyl myristate to aquatic and terrestrial ecosystems and concludes that the potential for exposure to the environment is insignificant or unlikely. RESULTIX™ is applied to dogs and cats as a spot treatment to kill ticks and is not expected to impact nontarget species because of limited exposure (indoor settings). Isopropyl myristate is used in cosmetic and topical medicinal preparations where good absorption through the skin is desired. [redacted] However, the Agency concludes that under the proposed use pattern, RESULTIX should not enter the environment in a quantity or concentration that constitutes a danger to ecosystems. Rationales submitted by Piedmont have provided sufficient information to support waivers for Aquatic Invertebrate Acute Toxicity, Freshwater Fish Acute Toxicity, Avian Acute Oral Toxicity, Avian Dietary Toxicity, Seedling Emergence Tier I, Vegetative Vigor Tier I, and Nontarget Insect Testing for RESULTIX and the draft product label contains adequate environmental hazard language to mitigate potential toxicity to aquatic

organisms and to prevent accidental release to aquatic environments and water bodies. **No additional data are required at this time.**

Product Label Deficiencies

The Agency considers the above deficiencies to be gross and therefore has deferred review of the submitted proposed product label until the deficiencies described in this document have been successfully addressed. Once all deficiencies have been resolved, the Agency will proceed with a thorough review of the proposed label.

As stated above the Agency cannot advance this application until Piedmont acceptably addresses the deficiencies described in this letter. Your application as submitted under the Pesticide Registration Improvement Act (PRIA II) guaranteed you a regulatory decision for the action category B600 of twelve (12) months; and a decision due date of December 24, 2010. By regulation, the Agency is obligated to give Piedmont 75 days (40 CFR § 152.105) in which to address the deficiencies identified above. However, the PRIA decision date (December 24, 2010) precedes the 75 day date (February 16, 2010).

If Piedmont chooses to address the deficiencies and proceed with its application, the Agency must renegotiate the PRIA 2 due date to allow time for Piedmont to submit new data/information and for the Agency to review any new submission and render a regulatory decision. Based on the deficiencies outlined in this letter, the Agency will require seven and one-half (7 ½) months from the date of receipt of your response to this letter to review any newly submitted information and make a regulatory decision. If Piedmont chooses to renegotiate the PRIA 2 due date for this action a renegotiation agreement between Piedmont and the Agency must be confirmed by December 17, 2010. If renegotiation of the PRIA 2 due date for this action does not occur by December 17, 2010 the Agency will issue a can not grant letter under PRIA 2. If the Agency does issue a letter stating it cannot grant your application under PRIA 2 and Piedmont submits the required information within 75 days from the date of this letter, the Agency will continue to work on the referenced application but it will not be subject to the PRIA time frame. Alternatively, Piedmont may withdraw the application and resubmit it after all deficiencies have been satisfactorily addressed

If you have questions or need additional information, you may contact Regulatory Action Leader Cheryl Greene, at (703) 308-0353 or by email at greene.cheryl@epa.gov

Sincerely,

Linda Hollis, Chief
Biochemical Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)

CURRENCES							
7511P							
Greene							
December 9, 2010							

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

DEC 09 2010

Susan Phillips, Science Advisor
Authorized Representative for Piedmont Animal Health LLC
Garvey Schubert Barer
Fifth Floor
Flour Mill Building
1000 Potomac Street, N.W.
Washington D.C. 2007-3501

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: Product: RESULTIX
EPA Registration # 86865-R
Your December 3, 2009 application for Section 3 Registration
PRIAII Code B600 EPA Decision # 424225
PRIA II Due Date: December 24, 2010

CONTAINS CONFIDENTIAL INFORMATION

Dear Ms. Phillips:

The Biopesticide and Pollution Prevention Division (BPPD) has received and reviewed the application referenced above which was, submitted in connection with an application for registration of a new product under section 3(c)(7)A of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, and the Pesticide Registration Improvement Act (PRIA II).

Piedmont Animal Health LLC (Piedmont) has submitted an application for registration of an end-use, spot-on product named Resultix, which contains 50% of a new active ingredient, isopropyl myristate, to kill ticks on dogs and cats. RESULTIX is formulated as a contact product that kills ticks on dogs and cats by dissolving the cuticle of the tick which causes death by desiccation.

Based on our review, the Agency has concluded that the referenced **application is deficient and not acceptable**, at this time. This conclusion is based on the deficiencies identified below. These deficiencies must be successfully addressed before the Agency can proceed with the review of your application and issue a registration decision for the proposed product.

Product Chemistry

The product chemistry data submission (MRIDs 479253-01 to 479253-08) is unacceptable as noted below and must be successfully addressed.

1. Piedmont submitted two Confidential Statements of Formula (CSF) in support of the referenced application. Both CSFs are dated 12/02/09.

a. The following deficiencies apply to the CSF submitted for the technical grade active ingredient (TGAI) [redacted] (Isopropyl Myristate):

   i. Column 10 - The CAS number for [redacted] must be corrected from [redacted]

   ii. Column 14 - The certified limits for isopropyl myristate and its related impurities are inconsistent with the certified limits presented in the preliminary analysis (MRID 479253-02) for the TGAI. Piedmont must correct the CSF for the TGAI to reflect the certified limits presented in the preliminary analysis.

   iii. Column 14(a) - The upper certified limit of isopropyl myristate cannot exceed 100%. Piedmont must revise the CSF such that the certified upper limit for isopropyl myristate is equal to or less than 100%. Alternately, Piedmont can submit an acceptable rationale for the percentage (102.9) noted on the CSF.

b. The following deficiencies apply to the CSF for the end-use product (RESULTIX).

   i. Column 13(b) - The nominal concentration of the active ingredient (isopropyl myristate) must match the label, which currently reads 50.0%. Piedmont must revise the nominal concentration of isopropyl myristate on the CSF to read 50.0%.

   ii. Column 10 - The source of the active ingredient is not noted on the CSF. Piedmont must list the source of [redacted] Isopropyl Myristate, [redacted] alongside the name of the active ingredient (isopropyl myristate).

2. The physical and chemical characteristics data/information submitted to support the proposed product **is acceptable. No additional data are required.**

<u>Product Performance/Efficacy</u>

The product performance/efficacy submission (MRID 47925317, MRID 479253-18) is unacceptable and must be successfully addressed as noted below before the Agency can proceed with its review of your application.

<u>MRID 479253-17</u> **- Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate Tick Spray against Rhipicephalus sanguineus and Dermacentor variabilis on Dogs.**

1. The amount of product applied to each dog was not reported. Companion Animal Safety Guideline (OCSPP 870.7200) recommends that animals be treated with 1, 3 and 5 times the recommended dose. In the submitted study only one dose (2 sprays) was applied to

Product ingredient source information may be entitled to confidential treatment
Manufacturing process information may be entitled to confidential treatment

each animal. Based on labeling instructions for RESULTIX and the proposed use pattern, the amount of product applied to each dog will vary depending on the number of ticks found on the dogs. As such, the study fails to investigate the effect that increased doses of the proposed product will have on the health of dogs treated. Data/information demonstrating the effect of increased doses of the proposed product on dogs must be submitted before the Agency can proceed with its review.

2. The submitted label for the proposed product states that RESULTIX "starts killing ticks in seconds." Since the submitted data shows that death only occurs six 6 hours after treatment, the statement "starts killing ticks in seconds" is false and misleading because the user is not informed that it will take the treated ticks six (6) hours to actually die. Therefore, Piedmont must either submit new data that validates the claim that the product kills ticks in seconds or remove the statement from the product label or add language to the label that fully explains the time it will take a tick to die once it is treated.

3. The submitted label claims 100% efficacy. However, the submitted data records efficacy at less than 100%. The Agency therefore views the state 100% efficacy as false and misleading. Piedmont must either submit new data/information that validates the claim that RESULTIX is 100% efficacious or remove the statement from the product label.

4. The submitted data did not contain a discussion of food consumption and body weight of the test animals. As described in OCSPP Guideline 870.7200 (pages 6.and 7) data from Companion animal Safety studies should include the test animal(s) individual body weights (measured at specific intervals throughout the study) and the measures of individual food consumption of test animals on a daily basis. These data are critical markers of the health of the test animals and of the effect of the product on the animal(s). This information must be submitted before the Agency can proceed with its review.

5. The Agency's review has determined that the submitted data/information is missing certain individual data parameters for hematology and clinical chemistry analysis. Specifically, the following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC). This information must be submitted before the Agency can proceed with its review.

6. The Agency's review has determined that some clinical pathology values [CK (U/L; GGT (U/L); Cholesterol (mg/dL); Total CO2 (MeQ/l); Chloride (mEq/L), and Potassium (mEq/L)] were outside of the reference range prior to treatment. Based on these values, the Agency questions whether the dogs in the study were healthy prior to and during the study (Refer to MRID 479253-17 page 16, Table 2, Summary Clinical Chemistry Data). Piedmont must submit data/information that successfully demonstrates the health of the studied animial(s) before the Agency can proceed with its review.

MRID 479253-18 - Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate Tick Spray against Rhipicephalus sanuineus and Dermacentor variabilis on Cats.

1. The amount of product applied to each cat was not reported. Companion Animal Safety Guideline OCSPP 870.7200 recommends that animals be treated with 1, 3 and 5 times the recommended dose. In the submitted study only one dose (2 sprays) was applied to each animal. Based on labeling instructions and the proposed use pattern, the amount of product applied to each cat will vary depending on the number of ticks found on the cats. As such, the study fails to investigate the effect that increased doses of the proposed product will have on the health of cats treated. Data/information demonstrating the effect of increased doses of the proposed product on cats must be submitted before the Agency can proceed with its review.

2. The submitted data did not contain a discussion of food consumption and body weight of the test animals. As described in OCSPP Guideline 870.7200 (pages 6.and 7) data from Companion animal Safety studies should include the test animal(s) individual body weights (measured at specific intervals throughout the study) and the measures of individual food consumption of test animals on a daily basis. These data are critical markers of the health of the test animals and of the effect of the product on the animal(s). This information must be submitted before the Agency can proceed with its review.

3. The submitted label for the proposed product states that RESULTIX "starts killing ticks in seconds." Since the submitted data shows that death only occurs six 6 hours after treatment, the statement "starts killing ticks in seconds" is false and misleading because the user is not informed that it will take the treated ticks six (6) hours to actually die. Therefore, Piedmont must either submit new data that validates the claim that the product kills ticks in seconds or remove the statement from the product label or add language to the label that fully explains the time it will take a tick to die once it is treated.

4. The submitted label claims 100% efficacy. However, the submitted data records efficacy at less than 100%. The Agency therefore views the statement 100% efficacy as false and misleading. Piedmont must either submit new data/information validating the claim that RESULTIX is 100% efficacious or remove the statement from the product label.

5. The Agency's review has determined that individual data parameters for hematology and clinical chemistry analysis is missing fro the submitted data package. Specifically, the following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC).

7. Some of the clinical pathology values [Alk Phos (U/L); CK(U/L); GGT (U/L); UN (mg/dL), and phosphorous (mg/dL)] were outside of the reference range prior to treatment, which leads to the question of whether the cats in the study were healthy prior to and during the study (Refer to page 15, Table 2, Summary Clinical Chemistry Data; Pre and Post Treatment in MRID 479253-18). Piedmont must submit data/information

that successfully demonstrates the health of the studied animial(s) before the Agency can proceed with its review.

Toxicology

Certain data submitted to address toxicology are deficient and unacceptable. The deficiencies identified below must be successfully addressed before the Agency can proceed with its review of the referenced application. The deficiencies are:

The following deficiencies apply to the active ingredient (isopropyl myristate)

a. Regarding the dermal irritation data requirement (OCSPP 870.2500) – The referenced 1997 study from RTECS that indicates that the active ingredient is mildly irritating was not included in your application (Refer to MRID 47925309). The Agency cannot make a determination on the data submitted for dermal irritation until a review of the RTECS study has been reviewed. Piedmont must submit this study before the Agency can proceed.

b. Regarding the developmental (OCSPP 870.3700) and *in vitro* mammalian cell assay (OCSPP 870.5300 and 870.5375) data requirements – The data/rationale submitted to fulfill these data requirements is insufficient. Piedmont states that significant occupational exposure is not expected because application is often seasonal. However, this rationale fails to consider that applications may occur more often in warmer climates where ticks may be prevalent year-round. Moreover, based on the available information, significant exposure to isopropyl myristate may occur in an occupational setting (e.g.: veterinary office, grooming salon) through use of the proposed product. The data/information submitted to satisfy occupational exposure also does not address either of these exposure scenarios. Piedmont must submit data/information that addresses both of these exposure scenarios before the Agency can proceed with its review.

***The following deficiency applies to the* end-use product(RESULTIX)**

c. The test substance utilized in the submitted studies is interchangeably referenced by different names, including "Resultix Tick Spray", "Pediculocide 100", "Piedmont Pediculocide 1" and "Piedmont Pediculocide 2". Piedmont must submit data/information verifying that the test substance(s) referred to in the studies is identical to the proposed product, "RESULTIX".

Ecotoxicology

The Agency has evaluated the potential for toxicity of the compound isopropyl myristate to aquatic and terrestrial ecosystems and concludes that the potential for exposure to the environment is insignificant or unlikely. RESULTIX™ is applied to dogs and cats as a spot treatment to kill ticks and is not expected to impact nontarget species because of limited

exposure (indoor settings). Isopropyl myristate is used in cosmetic and topical medicinal preparations where good absorption through the skin is desired. [redacted]. However, the Agency concludes that under the proposed use pattern, RESULTIX should not enter the environment in a quantity or concentration that constitutes a danger to ecosystems. Rationales submitted by Piedmont have provided sufficient information to support waivers for Aquatic Invertebrate Acute Toxicity, Freshwater Fish Acute Toxicity, Avian Acute Oral Toxicity, Avian Dietary Toxicity, Seedling Emergence Tier I, Vegetative Vigor Tier I, and Nontarget Insect Testing for RESULTIX and the draft product label contains adequate environmental hazard language to mitigate potential toxicity to aquatic organisms and to prevent accidental release to aquatic environments and water bodies. **No additional data are required at this time.**

Product Label Deficiencies

The Agency considers the above deficiencies to be gross and therefore has deferred review of the submitted proposed product label until the deficiencies described in this document have been successfully addressed. Once all deficiencies have been resolved, the Agency will proceed with a thorough review of the proposed label.

As stated above the Agency cannot advance this application until Piedmont acceptably addresses the deficiencies described in this letter. Your application as submitted under the Pesticide Registration Improvement Act (PRIA II) guaranteed you a regulatory decision for the action category B600 of twelve (12) months; and a decision due date of December 24, 2010. By regulation, the Agency is obligated to give Piedmont 75 days (40 CFR § 152.105) in which to address the deficiencies identified above. However, the PRIA decision date (December 24, 2010) precedes the 75 day date (February 16, 2010).

If Piedmont chooses to address the deficiencies and proceed with its application, the Agency must renegotiate the PRIA 2 due date to allow time for Piedmont to submit new data/information and for the Agency to review any new submission and render a regulatory decision. Based on the deficiencies outlined in this letter, the Agency will require seven and one-half (7 ½) months from the date of receipt of your response to this letter to review any newly submitted information and make a regulatory decision. If Piedmont chooses to renegotiate the PRIA 2 due date for this action a renegotiation agreement between Piedmont and the Agency must be confirmed by December 17, 2010. If renegotiation of the PRIA 2 due date for this action does not occur by December 17, 2010 the Agency will issue a can not grant letter under PRIA 2. If the Agency does issue a letter stating it cannot grant your application under PRIA 2 and Piedmont submits the required information within 75 days from the date of this letter, the Agency will continue to work on the referenced application but it will not be subject to the PRIA time frame. Alternatively, Piedmont may withdraw the application and resubmit it after all deficiencies have been satisfactorily addressed

Inert ingredient information may be entitled to confidential treatment

If you have questions or need additional information, you may contact Regulatory Action Leader Cheryl Greene, at (703) 308-0353 or by email at greene.cheryl@epa.gov

Sincerely,

Linda Hollis, Chief
Biochemical Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)

RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Susan Phillips to: Cheryl Greene 12/10/2010 07:02 AM
Cc: "Matt Schneider", Linda Hollis

History: This message has been replied to and forwarded.

Personal privacy information

Thanks for your prompt reply. A teleconference on Tuesday from 11-12 is the best for us. I will be at GSB on Tuesday for this telcon and therefore Matt's number can be used for this purpose (202 298 1787). We can add Dr. Palma to the call from our end. If you need to contact me before Tuesday, my home number is [redacted].

As for the agenda on Tuesday, the major issues are toxicology and the two safety and efficacy studies in cats and dogs (MRID 479253-17 and -18). Product chemistry and the draft label deficiencies are easily corrected and we see no reason to discuss these during the teleconference.

The safety and efficacy studies were submitted to fulfill both product performance and companion animal toxicity requirements. Based on the EPA deficiency letter, these two studies may not fulfill the companion animal toxicity requirements; however, product performance issues only concern label statement claims, which are easily correctible by revising the product label.

As for the toxicology deficiencies, the requested citation concerning dermal irritation will be submitted to the EPA in its entirety (approximately 84 pages) with an introduction indicating where the specific information is located in this review article. In addtion, we are prepared to discuss additional rationales for requesting data waivers for the developmental toxicity and the in vitro mammalian cell assay data requirements.

Consequently, the agenda for the teleconference only concern toxicity data requirements for dogs, cats and humans. Please feel free to contact me or Matt if you have further questions in advance of our call and we would appreciate confirmation once the conference call time is firmed up.

Thanks very much for fitting this in during a very busy time of the year.

Regards,
Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 5:10 PM
To: Susan Phillips
Cc: Matt Schneider; Hollis.Linda@epamail.epa.gov
Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

Please see Linda Hollis's email below. Since Linda is not available next weed for a face-to face meeting, our next best option is a conference call. I'm working on pulling that together now. Please

verify with your people that a conference call is acceptable. Also, please send me -- as soon as you possibly can -- a list containing the specific deficiencies/information Piedmont wishes to discuss or have clarified during the conference call. I need this list as soon as possible to ensure that I include the appropriate science folks on the call. At this point, I have identified two possible times for the call they are Monday, December 13, from 11:30 am to 12:30 PM or Tuesday December 14, 11:00 am to 12"00 noon. Please let me know which of these times best suite your people.

Also , the attachment below contains a pdf copy of the signed deficiency letter for RESULTIX. As I explained in my email earlier this month, this signed letter does not deviate in any significant way from the draft copy I forwarded to you on December 3, 2010. The original deficiency letter went out to you in the mail today.

Please let me know if you have questions or need more information.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Susan: I just left a very detailed message with Matt. I would like your telephone number. At any rate, we can not accommodate a face to face meeting at anytime next week due to juggling schedules and previous committments. However, my voice message to Matt was that we could entertain a conf call with all key players. I would like to do this preferably on Monday. I am available most of the morning and most of Tuesday. Wed - Friday are not options for me. I asked Matt that you forward a detailed list of topics for discussion. I am assuming that you really want to discuss product performance. Please let me know, we would be happy to provide further guidance as to how to move forward.
Also, we recognize that the pria due date falls on a holiday (the 24th). This essentially means that we will need to wrap this up with regard to a renegotiation days prior to that. Please work with Cheryl Greene and forward

your telephone number.

Linda A. Hollis, MS
Chief, Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division Office of Pesticide Programs
(7511P) U.S. Environmental Protection Agency One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202
hollis.linda@epa.gov
(703) 308-8733 (phone)
(703) 308-7026 (fax)
Visit http://www.epa.gov/pesticides

"The journey of 1000 miles begins with one step.....Take the step"

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Cheryl Greene/DC/USEPA/US@EPA, "Matt Schneider" <MSchneider@gsblaw.com>

Cc: Linda Hollis/DC/USEPA/US@EPA

Date: 12/09/2010 03:55 PM

Subject: RE: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R

Thanks very much for your prompt response.

Susan

-----Original Message-----
From: Greene.Cheryl@epamail.epa.gov [mailto:Greene.Cheryl@epamail.epa.gov]
Sent: Thursday, December 09, 2010 3:19 PM
To: Susan Phillips; Matt Schneider
Cc: Hollis.Linda@epamail.epa.gov
Subject: Request for meeting with BPPD to discuss deficiency letter for RESULTIX -- EPA Reg. No. 86865-R
Importance: High

Hi Susan:

This email is to acknowledge receipt of Matt's email requesting for a meeting with BPPD to discuss the deficiency letter for RESULTIX. I hope to discuss this with my Branch Chief either later today or early tomorrow. As soon as I know her availability and the availability of the associated science folks, I will get back to you to let you know if Wednesday the 15th is possible and if so the time. In the

meantime, let me know if you have questions or need more information.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances Office of Pesticide Programs, BPPD/BPB (7511P) U.S. Environmental Protection Agency 1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Re: Product: RESULTIX

EPA Registration # 86865-R

Your December 3, 2009 application for Section 3 Registration

PRIAII Code B600 EPA Decision # 424225

Good Morning Cheryl,

I am writing to you in response to your December 3 email to my colleague Susan Phillips containing a draft of a the deficiency letter pertaining to the above captioned matter. As you know, the draft letter states that if the PRIA 2 deadline is not renegotiated by December 17, 2010, EPA will issue a can not grant letter. While we have not yet received a final deficiency letter, we see that the timeframe available to take action before December 17 is very short and so we very much appreciate your forwarding the draft. On the assumption that the final deficiency letter will be similar or identical to the draft, we need to move quickly. Accordingly, on behalf of our client, Piedmont Animal Health, we urgently and respectfully request a meeting to discuss the issues raised in the letter to clarify certain matters and hopefully reach agreement on a new PRIA 2 deadline in advance of December 17. In order for our client, Dr. Kathleen G. Palma, Vice President of Research and Development, Piedmont Animal Health, to be in attendance we were hoping that you would be able to schedule a meeting for Wednesday, December 15. I recognize this is short notice however, we only received the draft notice 14 days in advance of the deadline. We will make ourselves available any time on December 15 at your convenience. We very much appreciate whatever you can do to arrange the meeting at which Dr.
Palma, Susan Phillips and I will be in attendance on behalf of Piedmont Animal Health.

Best regards,

Matt

MATTHEW R. SCHNEIDER

Owner and Managing Director D.C. and NY Offices | 202.965.7880 x 1787 Tel | 202.965.1729 Fax | mschneider@gsblaw.com

GARVEY SCHUBERT BARER | 5th Floor | 1000 Potomac Street NW | Washington, DC 20007 | ► GSBLaw.com

Unless expressly stated otherwise, any federal tax advice contained in this communication (including attachments) is not intended to be used, and cannot be used, for the purpose of avoiding federal tax penalties.

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Resultix Submission
Kathy Palma
to:
Leonard Cole
10/12/2010 04:48 PM
Cc:
Cheryl Greene
Show Details

Mr. Cole,

I received a phone call from Ms. Greene. Subsequently through Piedmont Animal Health's consultant received a thorough update on the status of our submission. Ms. Greene was very professional and informative with her update. Piedmont Animal Health greatly appreciates your support and Ms. Greene's efforts in managing this submission. Piedmont Animal Health looks forward to working with you both toward a successful registration.

Gratefully,
Kathy Palma

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

DEC 09 2010

Susan Phillips, Science Advisor
Authorized Representative for Piedmont Animal Health LLC
Garvey Schubert Barer
Fifth Floor
Flour Mill Building
1000 Potomac Street, N.W.
Washington D.C. 2007-3501

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Subject: Product: RESULTIX
EPA Registration # 86865-R
Your December 3, 2009 application for Section 3 Registration
PRIAII Code B600 EPA Decision # 424225
PRIA II Due Date: December 24, 2010

CONTAINS CONFIDENTIAL INFORMATION

Dear Ms. Phillips:

The Biopesticide and Pollution Prevention Division (BPPD) has received and reviewed the application referenced above which was, submitted in connection with an application for registration of a new product under section 3(c)(7)A of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, and the Pesticide Registration Improvement Act (PRIA II).

Piedmont Animal Health LLC (Piedmont) has submitted an application for registration of an end-use, spot-on product named Resultix, which contains 50% of a new active ingredient, isopropyl myristate, to kill ticks on dogs and cats. RESULTIX is formulated as a contact product that kills ticks on dogs and cats by dissolving the cuticle of the tick which causes death by desiccation.

Based on our review, the Agency has concluded that the referenced **application is deficient and not acceptable**, at this time. This conclusion is based on the deficiencies identified below. These deficiencies must be successfully addressed before the Agency can proceed with the review of your application and issue a registration decision for the proposed product.

Product Chemistry

The product chemistry data submission (MRIDs 479253-01 to 479253-08) is unacceptable as noted below and must be successfully addressed.

1. Piedmont submitted two Confidential Statements of Formula (CSF) in support of the referenced application. Both CSFs are dated 12/02/09.

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Based on our review, the Agency has concluded that the referenced **application is deficient and not acceptable**, at this time. This conclusion is based on the deficiencies identified below. These deficiencies must be successfully addressed before the Agency can proceed with the review of your application and issue a registration decision for the proposed product.

Product Chemistry

The product chemistry data submission (MRIDs 479253-01 to 479253-08) is unacceptable as noted below and must be successfully addressed.

1. Piedmont submitted two Confidential Statements of Formula (CSF) in support of the referenced application. Both CSFs are dated 12/02/09.

a. The following deficiencies apply to the CSF submitted for the technical grade active ingredient (TGAI) [redacted] (Isopropyl Myristate):

   i. Column 10 - The CAS number for [redacted] must be corrected from [redacted]

   ii. Column 14 - The certified limits for isopropyl myristate and its related impurities are inconsistent with the certified limits presented in the preliminary analysis (MRID 479253-02) for the TGAI. Piedmont must correct the CSF for the TGAI to reflect the certified limits presented in the preliminary analysis.

   iii. Column 14(a) - The upper certified limit of isopropyl myristate cannot exceed 100%. Piedmont must revise the CSF such that the certified upper limit for isopropyl myristate is equal to or less than 100%. Alternately, Piedmont can submit an acceptable rationale for the percentage (102.9) noted on the CSF.

b. The following deficiencies apply to the CSF for the end-use product (RESULTIX).

   i. Column 13(b) - The nominal concentration of the active ingredient (isopropyl myristate) must match the label, which currently reads 50.0%. Piedmont must revise the nominal concentration of isopropyl myristate on the CSF to read 50.0%.

   ii. Column 10 - The source of the active ingredient is not noted on the CSF. Piedmont must list the source of [redacted] Isopropyl Myristate. [redacted] alongside the name of the active ingredient (isopropyl myristate).

2. The physical and chemical characteristics data/information submitted to support the proposed product **is acceptable. No additional data are required.**

Product Performance/Efficacy

The product performance/efficacy submission (MRID 47925317, MRID 479253-18) is unacceptable and must be successfully addressed as noted below before the Agency can proceed with its review of your application.

MRID 479253-17 - Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate Tick Spray against Rhipicephalus sanguineus and Dermacentor variabilis on Dogs.

1. The amount of product applied to each dog was not reported. Companion Animal Safety Guideline (OCSPP 870.7200) recommends that animals be treated with 1, 3 and 5 times the recommended dose. In the submitted study only one dose (2 sprays) was applied to

Product ingredient source information may be entitled to confidential treatment
Manufacturing process information may be entitled to confidential treatment

each animal. Based on labeling instructions for RESULTIX and the proposed use pattern, the amount of product applied to each dog will vary depending on the number of ticks found on the dogs. As such, the study fails to investigate the effect that increased doses of the proposed product will have on the health of dogs treated. Data/information demonstrating the effect of increased doses of the proposed product on dogs must be submitted before the Agency can proceed with its review.

2. The submitted label for the proposed product states that RESULTIX "starts killing ticks in seconds." Since the submitted data shows that death only occurs six 6 hours after treatment, the statement "starts killing ticks in seconds" is false and misleading because the user is not informed that it will take the treated ticks six (6) hours to actually die. Therefore, Piedmont must either submit new data that validates the claim that the product kills ticks in seconds or remove the statement from the product label or add language to the label that fully explains the time it will take a tick to die once it is treated.

3. The submitted label claims 100% efficacy. However, the submitted data records efficacy at less than 100%. The Agency therefore views the state 100% efficacy as false and misleading. Piedmont must either submit new data/information that validates the claim that RESULTIX is 100% efficacious or remove the statement from the product label.

4. The submitted data did not contain a discussion of food consumption and body weight of the test animals. As described in OCSPP Guideline 870.7200 (pages 6.and 7) data from Companion animal Safety studies should include the test animal(s) individual body weights (measured at specific intervals throughout the study) and the measures of individual food consumption of test animals on a daily basis. These data are critical markers of the health of the test animals and of the effect of the product on the animal(s). This information must be submitted before the Agency can proceed with its review.

5. The Agency's review has determined that the submitted data/information is missing certain individual data parameters for hematology and clinical chemistry analysis. Specifically, the following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC). This information must be submitted before the Agency can proceed with its review.

6. The Agency's review has determined that some clinical pathology values [CK (U/L; GGT (U/L); Cholesterol (mg/dL); Total CO2 (MeQ/l); Chloride (mEq/L), and Potassium (mEq/L)] were outside of the reference range prior to treatment. Based on these values, the Agency questions whether the dogs in the study were healthy prior to and during the study (Refer to MRID 479253-17 page 16, Table 2, Summary Clinical Chemistry Data). Piedmont must submit data/information that successfully demonstrates the health of the studied animial(s) before the Agency can proceed with its review.

MRID 479253-18 - Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate Tick Spray against Rhipicephalus sanuineus and Dermacentor variabilis on Cats.

1. The amount of product applied to each cat was not reported. Companion Animal Safety Guideline OCSPP 870.7200 recommends that animals be treated with 1, 3 and 5 times the recommended dose. In the submitted study only one dose (2 sprays) was applied to each animal. Based on labeling instructions and the proposed use pattern, the amount of product applied to each cat will vary depending on the number of ticks found on the cats. As such, the study fails to investigate the effect that increased doses of the proposed product will have on the health of cats treated. Data/information demonstrating the effect of increased doses of the proposed product on cats must be submitted before the Agency can proceed with its review.

2. The submitted data did not contain a discussion of food consumption and body weight of the test animals. As described in OCSPP Guideline 870.7200 (pages 6.and 7) data from Companion animal Safety studies should include the test animal(s) individual body weights (measured at specific intervals throughout the study) and the measures of individual food consumption of test animals on a daily basis. These data are critical markers of the health of the test animals and of the effect of the product on the animal(s). This information must be submitted before the Agency can proceed with its review.

3. The submitted label for the proposed product states that RESULTIX "starts killing ticks in seconds." Since the submitted data shows that death only occurs six 6 hours after treatment, the statement "starts killing ticks in seconds" is false and misleading because the user is not informed that it will take the treated ticks six (6) hours to actually die. Therefore, Piedmont must either submit new data that validates the claim that the product kills ticks in seconds or remove the statement from the product label or add language to the label that fully explains the time it will take a tick to die once it is treated.

4. The submitted label claims 100% efficacy. However, the submitted data records efficacy at less than 100%. The Agency therefore views the statement 100% efficacy as false and misleading. Piedmont must either submit new data/information validating the claim that RESULTIX is 100% efficacious or remove the statement from the product label.

5. The Agency's review has determined that individual data parameters for hematology and clinical chemistry analysis is missing fro the submitted data package. Specifically, the following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC).

7. Some of the clinical pathology values [Alk Phos (U/L); CK(U/L); GGT (U/L); UN (mg/dL), and phosphorous (mg/dL)] were outside of the reference range prior to treatment, which leads to the question of whether the cats in the study were healthy prior to and during the study (Refer to page 15, Table 2, Summary Clinical Chemistry Data; Pre and Post Treatment in MRID 479253-18). Piedmont must submit data/information

that successfully demonstrates the health of the studied animial(s) before the Agency can proceed with its review.

Toxicology

Certain data submitted to address toxicology are deficient and unacceptable. The deficiencies identified below must be successfully addressed before the Agency can proceed with its review of the referenced application. The deficiencies are:

The following deficiencies apply to the active ingredient (isopropyl myristate)

a. Regarding the dermal irritation data requirement (OCSPP 870.2500) – The referenced 1997 study from RTECS that indicates that the active ingredient is mildly irritating was not included in your application (Refer to MRID 47925309). The Agency cannot make a determination on the data submitted for dermal irritation until a review of the RTECS study has been reviewed. Piedmont must submit this study before the Agency can proceed.

b. Regarding the developmental (OCSPP 870.3700) and *in vitro* mammalian cell assay (OCSPP 870.5300 and 870.5375) data requirements – The data/rationale submitted to fulfill these data requirements is insufficient. Piedmont states that significant occupational exposure is not expected because application is often seasonal. However, this rationale fails to consider that applications may occur more often in warmer climates where ticks may be prevalent year-round. Moreover, based on the available information, significant exposure to isopropyl myristate may occur in an occupational setting (e.g.: veterinary office, grooming salon) through use of the proposed product. The data/information submitted to satisfy occupational exposure also does not address either of these exposure scenarios. Piedmont must submit data/information that addresses both of these exposure scenarios before the Agency can proceed with its review.

***The following deficiency applies to the* end-use product(RESULTIX)**

c. The test substance utilized in the submitted studies is interchangeably referenced by different names, including "Resultix Tick Spray", "Pediculocide 100", "Piedmont Pediculocide 1" and "Piedmont Pediculocide 2". Piedmont must submit data/information verifying that the test substance(s) referred to in the studies is identical to the proposed product, "RESULTIX".

Ecotoxicology

The Agency has evaluated the potential for toxicity of the compound isopropyl myristate to aquatic and terrestrial ecosystems and concludes that the potential for exposure to the environment is insignificant or unlikely. RESULTIX™ is applied to dogs and cats as a spot treatment to kill ticks and is not expected to impact nontarget species because of limited

exposure (indoor settings). Isopropyl myristate is used in cosmetic and topical medicinal preparations where good absorption through the skin is desired. [redacted]. However, the Agency concludes that under the proposed use pattern, RESULTIX should not enter the environment in a quantity or concentration that constitutes a danger to ecosystems. Rationales submitted by Piedmont have provided sufficient information to support waivers for Aquatic Invertebrate Acute Toxicity, Freshwater Fish Acute Toxicity, Avian Acute Oral Toxicity, Avian Dietary Toxicity, Seedling Emergence Tier I, Vegetative Vigor Tier I, and Nontarget Insect Testing for RESULTIX and the draft product label contains adequate environmental hazard language to mitigate potential toxicity to aquatic organisms and to prevent accidental release to aquatic environments and water bodies. **No additional data are required at this time.**

Product Label Deficiencies

The Agency considers the above deficiencies to be gross and therefore has deferred review of the submitted proposed product label until the deficiencies described in this document have been successfully addressed. Once all deficiencies have been resolved, the Agency will proceed with a thorough review of the proposed label.

As stated above the Agency cannot advance this application until Piedmont acceptably addresses the deficiencies described in this letter. Your application as submitted under the Pesticide Registration Improvement Act (PRIA II) guaranteed you a regulatory decision for the action category B600 of twelve (12) months; and a decision due date of December 24, 2010. By regulation, the Agency is obligated to give Piedmont 75 days (40 CFR § 152.105) in which to address the deficiencies identified above. However, the PRIA decision date (December 24, 2010) precedes the 75 day date (February 16, 2010).

If Piedmont chooses to address the deficiencies and proceed with its application, the Agency must renegotiate the PRIA 2 due date to allow time for Piedmont to submit new data/information and for the Agency to review any new submission and render a regulatory decision. Based on the deficiencies outlined in this letter, the Agency will require seven and one-half (7 ½) months from the date of receipt of your response to this letter to review any newly submitted information and make a regulatory decision. If Piedmont chooses to renegotiate the PRIA 2 due date for this action a renegotiation agreement between Piedmont and the Agency must be confirmed by December 17, 2010. If renegotiation of the PRIA 2 due date for this action does not occur by December 17, 2010 the Agency will issue a can not grant letter under PRIA 2. If the Agency does issue a letter stating it cannot grant your application under PRIA 2 and Piedmont submits the required information within 75 days from the date of this letter, the Agency will continue to work on the referenced application but it will not be subject to the PRIA time frame. Alternatively, Piedmont may withdraw the application and resubmit it after all deficiencies have been satisfactorily addressed

Inert ingredient information may be entitled to confidential treatment

If you have questions or need additional information, you may contact Regulatory Action Leader Cheryl Greene, at (703) 308-0353 or by email at greene.cheryl@epa.gov

Sincerely,

Linda Hollis, Chief
Biochemical Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)

Isopropyl myristate
PC Code: 000207
Product Chemistry

DP Number: 383262
EPA Reg. No.: 86865-R

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

OFFICE OF CHEMICAL SAFETY AND PESTICIDE PRODUCTS

MEMORANDUM

DATE: November 18, 2010

SUBJECT: Science Review in Support of the Registration of Resultix, Containing [redacted] Isopropyl Myristate As Its Active Ingredient.

Decision Number:	**424225**
DP Number:	**383262**
EPA File Symbol Number:	**86865-R**
Chemical Class:	**Biochemical**
PC Code:	**000207**
CAS Number:	**110-27-0**
Active Ingredient Tolerance Exemptions:	**Non-food use**
MRID Numbers:	**479253-01 to-08**

FROM: Jacob S. Moore, Chemist
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

TO: Cheryl Greene, Regulatory Action Leader
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

THE FOLLOWING CONTAINS CONFIDENTIAL BUSINESS INFORMATION

ACTION REQUESTED

Piedmont Animal Health LLC requests registration of Resultix, which is intended for use as an insecticide on dogs and cats against ticks. In support of this registration, the registrant has submitted a label, Confidential Statements of Formula dated 12/02/2009, and biochemical pesticide product chemistry data in MRIDs 479253-01 to -08.

Product ingredient source information may be entitled to confidential treatment

RECOMMENDATIONS AND CONCLUSIONS

1. CSFs dated 12/02/09 are **UNACCEPTABLE, but upgradable upon resolution of the following:**
   a. The following applies for the CSF of [redacted] (TGAI)
      i. The CAS number for [redacted] must be corrected from [redacted]
      ii. The certified limits for isopropyl myristate and its related impurities must be corrected to reflect the information presented in the preliminary analysis. Currently the certified limits reflect the Agency standard but are not representative of what is presented in MRID 479253-02.
      iii. The upper certified limit of isopropyl myristate cannot exceed 100%.
   b. The following applies for the CSF of Resultix (EP).
      i. The nominal concentration of the active ingredient must match the label, which currently reads 50.0%.
      ii. The source of the active ingredient, [redacted] must be noted alongside the name of the active.

2. Physical and chemical characteristics are **ACCEPTABLE. No additional data are required.** See Table 1 below.

<u>Note to RAL:</u>

1. This review does not include any study summaries outside of Table 1 presented below.

Product ingredient source information may be entitled to confidential treatment
Manufacturing process information may be entitled to confidential treatment

TABLE 1. Physical and Chemical Properties for RESULTIX™ and isopropyl myristate TGAI[a]

Guideline Reference No./Property	Description of Result	Methods
830.6302 Color	TGAI: colorless EP: colorless	Visual inspection
830.6303 Physical State	TGAI: liquid EP: liquid	Visual inspection
830.6304 Odor	TGAI: odorless EP: odorless	Olfactory inspection
830.6313 Stability	TGAI: stable EP: stable	Storage stability studies[b,c]
830.6315 Flammability	TGAI: flash point 164.4°C closed cup EP: flash point 85.0°C closed cup; 95.0°C open cup	FDA, 16 CFR 1500.3 (c)(6) and 43 (a)[e]
830.6317 Storage Stability	TGAI: No loss of isopropyl myristate and no container leachate components identified. EP: No loss of isopropyl myristate and no container leachate components identified.	TGAI: Stored in 100 mL carbon steel containers at 25° and 40°C / 60% relative humidity for 48 months.[b] EP: Stored in 1 oz. and 2 oz. HDPE bottles at 25° and 40°C / 60% relative humidity for 48 months.[c]
830.6319 Miscibility	TGAI: not required EP: Not applicable, the product is not intended for dilution with petroleum solvents.	
830.6320 Corrosion Characteristics	TGAI: Not required EP: Not expected to be corrosive.	Storage stability studies[b,c]
830.7000 pH	TGAI: not applicable EP: not applicable	Both the TGAI and EP are not soluble or dispersible in water.
830.7100 Viscosity	TGAI: not required EP: 3.5 – 3.7 cP	Storage stability studies[c]
830.7200 Melting Range	TGAI: Not applicable, the product is a liquid. EP: not required	
830.7220 Boiling Range	TGAI: 192.6°C EP: not required	CIR (1982)[f]
830.7300 Density/Relative Density/Bulk Density	TGAI: 0.85 to 0.86 g/mL EP: 0.85 to 0.86 g/mL	CIR (1982)[f]
830.7370 Dissociation Constant in Water	TGAI: Not applicable, the product is not pure active ingredient and is insoluble in water. EP: not required	CIR (1982)[f]
830.7550 Partition	TGAI: 7.17 – 7.43	CIR (1982)[f]

Coefficient	EP: not required	
830.7840 Water Solubility	TGAI: insoluble in water EP: not required	CIR (1982)[f]
830.7950 Vapor Pressure	TGAI: <1 Torr EP: not required	CIR (1982)[g]

[a]Data from MRID 47925301

[b]Data from MRID 47925304

[c]Data from MRID 47925306, 47925307, 48132301

[d]Data from MRID 47925303

[e]Data from MRID 47925306

[f]Cosmetic Ingredient Review (CIR), Final Report on the Safety Assessment of Myristyl Myristate and Isopropyl Myristate, Journal of the American College of Toxicology, Vol. 1, No. 4, 1982. Appended to MRID 47925301.

cc: J. Moore, C. Greene, BPPD Science Review File, IHAD/ARS
J. Moore, FT, PY-S: 11/18/2010

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

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: November 16, 2010

SUBJECT: Science Review in Support of Resultix™, Containing 50% Isopropyl Myristate As Its Active Ingredient.

Decision Number: 424225
DP Number: 383262
EPA File Symbol Number: 86865-R
Chemical Class: Biochemical
PC Code: 000207
CAS Number: 110-27-0
Active Ingredient Tolerance Exemptions: Nonfood-use
MRID Numbers: 47925309- 47925316, 47925319

FROM: Angela L. Gonzales, Biologist 11/16/10
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

TO: Cheryl Greene, Regulatory Action Leader
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

ACTION REQUESTED

Piedmont Animal Health LLC requests registration of Resultix™ containing isopropyl myristate, which is intended for use kill ticks on dogs and cats. The chemical is a new biochemical active ingredient. In support of the toxicology data requirements the registrant has submitted data and information in MRIDs 47925309-47925316 and 47925319. The following is the description of the deficiencies associated with this submission.

RECOMMENDATIONS AND CONCLUSIONS

1. The toxicology submission is UNACCEPTABLE, but upgradeable pending resolution of the deficiencies listed below.

Regarding Isopropyl Myristate:

a. Regarding the dermal irritation data requirement (OCSPP 870.2500), the registrant must provide the referenced 1997 study from RTECS that indicates that the active ingredient is mildly irritating. Refer to MRID 47925309.

b. Regarding the developmental (OCSPP 870.3700) and *in vitro* mammalian cell assay (OCSPP 870.5300 and 870.5375) data requirements, the registrant must provide more information regarding occupational exposure. Based on the available information, significant exposure to IPM may occur in an occupational setting (e.g.: veterinary office, grooming salon) through use of the proposed product. Additionally, although the registrant states that significant exposure is not expected because application is often seasonal, application may occur more often in warmer climates where ticks may be prevalent year-round. Because toxicity data were not submitted and the rationale provided to support these data requirements is inadequate because it is based primarily on the lack of exposure, more information regarding occupational exposure and/or toxicity is required to support these data requirements.

Regarding Resultix™:

a. The test substance utilized in some of the toxicity studies is referenced by different names, including "Resultix Tick Spray", "Pediculocide 100", "Piedmont Pediculocide 1" and "Piedmont Pediculocide 2". The registrant must verify that the test substance in these studies is identical to the proposed product, "Resultix™".

b. Regarding the companion animal safety (OCSPP 870.7200) data requirement deficiencies, refer to the memorandum from C. Fuentes to C. Greene dated November 4, 2010.

cc: Angela L. Gonzales, Cheryl Greene, BPPD Science Review File, IHAD/ARS
A. L. Gonzales, FT, PY-S: 11/16/10

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

OFFICE PREVENTION,
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM **November 10, 2010**

SUBJECT: Registration of new active ingredient, Isopropyl myristtate, for the controlof ticks.

EPA Reg. #:	86865-R
CAS #:	110-27-0
PC Code	800207
DP #:	383262
Decision #:	424225
MRID #	47925320

FROM: Miachel Rexrode, Ph.D., Senior Biologist /s/ 11/10/2010
Biochemical Pesticides Branch
Biopesticide & Pollution Prevention Division (7511P)

TO: Cheryl Greene, Regulatory Action Leader /s/ 11/10/2010
Biochemical Pesticides Branch
Biopesticide & Pollution Prevention Division (7511P)

ACTION REQUESTED

The applicant, Piedmont Animal Health LLC, has submitted a Section 3 Registration for RESULTIX End-Use Product (EPA Reg. # 86865-R). The product is composed of isopropyl myristate as the active ingredient with [redacted] as the inert solvent which the EPA has granted non food use applications. This compound kills ticks on cat and dogs by dissolving the surface of the arthropod cuticle which results in death of the tick through desiccation. The applicant is requesting waivers for ecotoxicity studies that include the following: Aquatic Invertebrate Acute Toxicity (850.1010), Freshwater Fish Acute Toxicity (850.1075), Avian Acute Oral Toxicity (850.2100), Avian Dietary Toxicity (850.2200), Seedling Emergence, Tier I (850.4100), Vegetative Vigor, Tier I (850.4150), and Nontarget Insect Testing (850.4350).

Inert ingredient information may be entitled to confidential treatment

RECOMMENDATIONS AND CONCLUSIONS

Registrant's Justification for Waiver Request

Acute Toxicity Aquatic Invertebrates (Daphnids) – TGAI & EP
A search of available environmental fate and toxicity databases indicate no acute toxicity data for daphnids were available for isopropyl myristate (IPM). The environmental fate data available indicate that IPM would be readily metabolized by aquatic organisms, although it is highly lipophilic and may potentially bioaccumulate. IPM is also semivolatile and would not persist in aquatic environments.

The applicant states that a daphnid toxicity study would be required for the RESULTIX™ because the inert ingredient, [redacted]. Consequently, in lieu of conducting this study utilizing either the active ingredient or the EP, the Environmental Hazards statement on the draft label for both the TGAI and the EP will have the following statement and the registrant requests a waiver from further aquatic invertebrate toxicity testing:

"This pesticide is toxic to invertebrates and fish. Do not discharge this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage authority. For guidance, contact your State Water Board or Regional Office of the EPA."

Freshwater Fish Acute Toxicity - TGAI & EP
A search of available environmental fate and toxicity databases indicate one acute 96-hour LC_{50} (100 mg/L; slightly toxicity) in fish was reported for IPM. The environmental fate data available indicate that IPM would be readily metabolized by aquatic organisms, although it is highly lipophilic and may potentially bioaccumulate. IPM is also semivolatile and would not persist in aquatic environments.

The applicant states that an acute fish toxicity study would be required for the EP because the inert ingredient, [redacted] has the potential for aquatic toxicity; although it is highly volatile. Data available for [redacted] suggest the potential for toxicity. [redacted] is expected to be toxic to fish. Consequently, in lieu of conducting this study utilizing either the active ingredient or the EP, the Environmental Hazards statement on the draft label for both the TGAI and the EP will have the following statement and the registrant requests a waiver from fish toxicity testing:

"This pesticide is toxic to invertebrates and fish. Do not discharge this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in

Inert ingredient information may be entitled to confidential treatment

writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage authority. For guidance, contact your State Water Board or Regional Office of the EPA."

Avian Acute Oral and Dietary Toxicity Avian - TGAI & EP
The applicant has requested a waiver of avian acute toxicity testing based on the following information:

- The potential routes of exposure to birds from the commercial use of RESULTIX™ is inhalation, dermal, and oral. The route of exposure for these two studies is oral (gavage and dietary); the other routes are not applicable. Because the EP is a colorless and practically odorless liquid product, it is unlikely that the EP would be gastronomically attractive for birds to ingest. Usually toxicity to birds is from ingestion of pesticide products that resemble seeds (e.g., granular formulation) or from ingestion of pesticide-residues on plant and other food items (insects).

- The EP container is small (20 mL) and spillage of the colorless fluid would result in minimal amounts present on soil or plant surfaces. Birds are also unlikely to mistake accidental spillage of RESULTIX™ as water, particularly because of the small volume and rapid volatilization of IPM and [redacted].

Terrestrial Plant Toxicity Seedling Emergence and Vegetative Vigor - TGAI & EP
The target species for RESULTIX™ ticks are ectoparasite on domestic dogs and cats. Direct or indirect application of the EP to terrestrial plants is not expected to occur if label instructions are followed.

Nontarget Insect Testing - TGAI & EP
Because RESULTIX™ is used to kill ticks by desiccation (solubilizing the cuticle), it is likely to have this affect on all insects and other arthropods. However, the use pattern and limited application (20 ml) precludes contact with nontarget insects, particularly honeybees.

Reviewer's Comments

The Agency has evaluated the potential for toxicity of this compound to aquatic and terrestrial ecosystems and concludes that the potential for exposure to the environment is insignificant or unlikely. RESULTIX™ is applied to dog and cats as a spot treatment to combat tick and is not expected to impact nontarget species because of limited exposure. Isopropyl myristate is used in cosmetic and topical medicinal preparations where good absorption through the skin is desired. [redacted]. The EPA, however, concludes that the EP under the prescribe use pattern, should not enter the environment in a quantity or concentration that constitutes a danger to ecosystems. Relative to label information, there is sufficient information to support the requested waivers for Aquatic Invertebrate Acute Toxicity, Freshwater Fish Acute Toxicity, Avian Acute Oral Toxicity, Avian Dietary Toxicity, Seedling Emergence Tier I, Vegetative Vigor Tier I, and Nontarget Insect Testing for RESULTIX™ at this

Inert ingredient information may be entitled to confidential treatment

time. The draft product label contains environmental hazard information regarding potential toxicity to aquatic organisms and to prevent accidental release to aquatic environments and water bodies.

[redacted]

Inert ingredient information may be entitled to confidential treatment

Pages 250-253 are a duplicate of pages 246-249

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

NOV 04 2010

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: November 4, 2010.

SUBJECT: Science Review in Support of the Registration of Resultix, containing 50 % Isopropyl Myristate as Active Ingredient.

Decision Number: 424225
DP Number: 383262
EPA File Symbol Number: 86865-R
Chemical Class: Biochemical
PC Code: 000207
CAS Number: 110-27-0
Active Ingredient Tolerance Exemptions: N/A non-food
MRID Numbers: 479253-17 and 479253-18.

FROM: Clara Fuentes, Entomologist
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

TO: Cheryl Greene, Regulatory Action Leader
Biochemical Pesticides Branch
Biopesticides & Pollution Prevention Division (7511P)

ACTION REQUESTED

Piedmont Animal Health LLC (Piedmont) is requesting registration of an end-use, spot-on product, Resultix, containing 50% of a new active ingredient, Isopropyl Myristate, to control ticks on dogs and cats. The product kills ticks on their hosts on contact by dissolving the cuticle of the tick and causing death by desiccation.

RECOMMENDATIONS AND CONCLUSIONS

MRID 47925317 is unacceptable. The identified study deficiencies are listed below:

1. The amount of product applied to each dog was not reported. The 870.7200 Guideline recommends that animals be treated with 1, 3 and 5 times the recommended dose. In this study only one dose (2 sprays) was applied to each animal. The amount of product applied to each dog will vary depending on the number of ticks found on the dogs. The study fails to investigate the effect of increased doses on dogs' health.

2. The product label states that the product starts killing ticks in seconds. The product label also claims 100% efficacy, but that level was achieved only after 6 hours post treatment in the case of *Dermaceptor variabilis.*

3. Food consumption and body weight were not reported.

4. Individual data parameters for hematology and clinical chemistry analysis were under reported. The following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC).

5. Some of the clinical pathology values were outside of the reference range prior to treatment, which leads to the question of whether the dogs in the study were healthy.

MRID 479253-18 is unacceptable. The identified study deficiencies are listed below:

1. The amount of product applied to cats was not reported. In this study only one dose (2 sprays) was applied to each animal. The amount of product applied to each cat will vary depending on the number of ticks found on the host. The study fails to investigate the effect of increased doses on cats' health.

2. Food consumption and body weight were not reported.

3. The product level claims 100% efficacy but that level was not attained in the study.

4. Individual data parameters for hematology and clinical chemistry analysis were under reported. The following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC).

STUDY SUMMARIES

MRID 47925317:

The study objective was to evaluate the safety and efficacy of Resultix formulation, containing 50% w/w active ingredient, isopropyl myrstrate, when sprayed on dogs for the control of ticks.

1. The amount of product applied to each dog was not reported. The 870.7200 Guideline recommends that animals be treated with 1, 3 and 5 times the recommended dose. In this study only one dose (2 sprays) was applied to each animal. The amount of product applied to each dog will vary depending on the number of ticks found on the dogs. The study fails to investigate the effect of increased doses on dogs' health.

2. The product label states that the product starts killing ticks in seconds. The product label also claims 100% efficacy, but that level was achieved only after 6 hours post treatment in the case of *Dermaceptor variabilis.*

3. Food consumption and body weight were not reported.

4. Individual data parameters for hematology and clinical chemistry analysis were under reported. The following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC).

5. Some of the clinical pathology values [CK (U/L; GGT (U/L); Choesterol (mg/dL); Total CO2 (MeQ/l); Chloride (mEq/L), and Potassium (mEq/L)] were outside of the reference range prior to treatment, which leads to the question of whether the dogs in the study were healthy (Refer to page 16, Table 2, Summary Clinical Chemistry Data in MRID 479253-17).

MRID 479253-18 is unacceptable. The identified study deficiencies are listed below:

1. The amount of product applied to cats was not reported. In this study only one dose (2 sprays) was applied to each animal. The amount of product applied to each cat will vary depending on the number of ticks found on the host. The study fails to investigate the effect of increased doses on cats' health.

2. Food consumption and body weight were not reported.

3. The product level claims 100% efficacy but that level was not attained in the study.

4. Individual data parameters for hematology and clinical chemistry analysis were under reported. The following hematological parameters were not reported: platelet count, blood clotting measurements (thromboplastin time, fibrinogen, and prothrombin time), reticulocyte count, mean corpuscular HGB (MCH), and MCH concentration (MCHC).

5. Some of the clinical pathology values [Alk Phos (U/L); CK(U/L); GGT (U/L); UN (mg/dL), and phosphorous (mg/dL)] were outside of the reference range prior to treatment, which leads to the question of whether the cats in the study were healthy (Refer to page 15, Table 2, Summary Clinical Chemistry Data; Pre and Post Treatment in MRID 479253-18).

STUDY SUMMARIES

MRID 47925317:

The study objective was to evaluate the safety and efficacy of Resultix formulation, containing 50% w/w active ingredient, isopropyl myrstrate, when sprayed on dogs for the control of ticks. Twelve Beagle dogs, 6 males and 6 females were selected for the study based on general health conditions and their ability to sustain tick infestations. All dogs in the study were able to maintain a good tick burden prior to treatment (mean tick counts/dog = 28.9, ranging from 7 to 46 ticks /dog). Dogs were observed daily for general health. Body weight was recorded on day 7 and not reported. Food consumption was not recorded. Hematology and clinical parameters were measured pre- and post treatment. Only some parameters were reported. All dogs survived the study. Dogs were infested with 50 unfed *R. sanguineus* ticks during pre-test period to determine tick host suitability. The dogs were combed for tick counts 24 hours later. Dogs were infested with 50 *R. sanguineus* ticks at the beginning of the test, and with 50 *Dermaceptor variabilis* ticks on day 6. The same procedure was followed after day 6. Six Beagle dogs, 3 males and 3 females, were randomly assigned to either control treatment or treated with 50% isopropyl myristate formulation. Water was used as control. Each dog pair constituted a treatment replication so that each treatment was replicated three times. Three groups per treatment of 1 male and 1 female dog were treated with either 50% isopropyl myristate formulation or water, and tick mortality was recorded after 3, 6 and 24 hours post-treatment. The amount of control and test material applied to ticks on dogs was approximately, 0.1 mL/spray. Ticks were directly sprayed until fully covered whether they were attached to the host or not. Tick mortality was recorded at 3, 6 and 24 hours post-treatment. Technicians conducting the counts were blinded to the treatment groups. Percent mortality at 24 hours was calculated by dividing the cumulative number of dead ticks by the total number of ticks that were treated. Geometric means of live tick counts at 3, 6 and 24 hours were calculated for control and treated dogs. To compare the means, the difference between geometric means of live ticks from treated and control dogs was divided by the geometric mean of live ticks on control dogs. (X – Y / X) 100 [X= geometric mean of live ticks on controls; Y = geometric mean of live ticks on treated dogs]. The percent mortality of *D. variabilis* after 3, 6 and 24 hours post-treatment was 98.2 %, 100 % and 97.1 %, respectively. Overall, percent *D. variabilis* tick mortality for treated dogs was 106.1 % compared to 14.4 % for controls. The percent mortality of *R. sanguineus* after 3, 6 and 24 hours post-treatment was 92.4 %, 91.4 % and 90.9 %, respectively. Overall, percent *R. sanguineus* tick mortality for treated dogs was 95.6% compared to 11.1% for controls. The percent mortality for *R. sanguineous* ticks was 95.6%, and 106.1% for *D. variabilis* ticks. Percent control of both species was >90% at all times post-treatment.
The mortality rate in excess of 100% for *D. variabilis* and slight drop in calculated control of live ticks observed after 24 hours are explained by difficulty in assuring that all ticks are treated and counted.

MRID 479253-18:

The study objective was to evaluate the safety and efficacy of Resultix formulation, containing 50% w/w active ingredient, isopropyl myrstrate, when sprayed on cats for the control of ticks. Twelve domestic long and short hair cats, 6 males and 6 females, were selected for the study based on general health conditions and their ability to sustain tick infestations. Cats were infested with 50 unfed *R. sanguineus* ticks during pre-test period to determine tick host suitability. The cats were combed for tick counts 24 hours later. Mean tick counts on cats were 10.9 ticks/cat, ranging from 2 to 23 ticks/cat. Cats were fitted with Elizabethan collars and infested with 50 *R. sanguineus* ticks at the beginning of the test, and with 50 *Dermaceptor variabilis* ticks on day 6. The same procedure was followed after day 6. Six cats, 3 males and 3 females, were randomly assigned to either control treatment or treated with 50% isopropyl myristate formulation. Water was used as control. Each cat pair constituted a treatment replication so that each treatment was replicated three times. Three groups per treatment of 1 male and 1 female cat were treated with either 50% isopropyl myristate formulation or water, and tick mortality was recorded after 3 (±15 minutes) hours post-treatment. The amount of control and test material applied to ticks on cats was approximately, 0.1 mL/spray. Ticks were directly sprayed twice whether they were attached to the host or not. Tick mortality was recorded at 3 (±15 minutes) hours post-treatment. Technicians conducting the counts were blinded to the treatment groups. Percent mortality at 3 (±15 minutes) hours was calculated by dividing the cumulative number of dead ticks by the total number of ticks that were treated. Geometric means of live tick counts at 3 (±15 minutes) hours were calculated for control and treated cats. To compare the means, the difference between geometric means of live ticks from treated and control cats was divided by the geometric mean of live ticks on control cats (X – Y / X) 100 [X= geometric mean of live ticks on controls; Y = geometric mean of live ticks on treated cats]. The percent mortality of *D. variabilis* and *R. sanguineus* after 3 hours post-treatment was 95.2 % and 98.8 %, respectively. Percent control of both species was >90%.

cc: *Clara Fuentes*, Cheryl Greene, BPPD Chron File, IHAD/ARS
, FT, PY-S: *Nov. 4, 2010.*

Bean 3

DATA PACKAGE BEAN SHEET

Date: 19-Oct-2010

Decision #: 424225
DP #: (383262)
PRIA
Parent DP #:
Submission #:

* * * Registration Information * * *

Registration: 86865-R - RESULTIX TM

Company: 86865 - PIEDMDNT ANIMAL HEALTH

Risk Manager: RM 91 - Linda Hollis - (703) 308-8733 Room# PY1 S-8761

Risk Manager Reviewer: Cheryl Greene CGREENE1

Sent Date: 10/19/2010 Calculated Due Date: 12/24/2010 Edited Due Date: —

Type of Registration: Product Registration - Section 3

Action Desc: B600

Ingredients: 000207, Isopropyl myristate([redacted])

* * * Data Package Information * * *

Expedite: (X) Yes ● No Date Sent: 19-Oct-2010 Due Back: ~~12/~~ 3/5/2011

DP Ingredient: 000207, Isopropyl myristate

DP Title: REgistration Package

CSF Included: ● Yes ○ No Label Included: ● Yes ○ No Parent DP #:

Assigned To		Date In	Date Out		
Organization:	BPPD / BPB			Last Possible Science Due Date:	~~03-Jan-2010~~ March 5, 2011
Team Name:	OPP RM BPB NEW AI TEAM			Science Due Date:	
Reviewer Name:				Sub Data Package Due Date:	
Contractor Name:					

* * * Studies Sent for Review * * *

Printed on Page 2

* * * Additional Data Package for this Decision * * *

Can be printed on its own page

* * * Data Package Instructions * * *

Dear Science manager:

Attached is a data package submitted in support of registration of a new active ingredient for the control of ticks. this package has been through primary review and is being forwarded to you for BPPD internal secondary review. Please review the package and let me know if the data supports the new active ingredient and the roposed two new products. if you have questions or need more intormtion, let me kow. C. Greene 703 308-0352

Product ingredient source information may be entitled to confidential treatment

MRID	MRID Status	Citation/Reference	Guideline
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.1100/Acute Oral Toxicity
47925318		Young, D. (2009) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanuineus and Dermacentor variabilis on Cats. Project Number: PAH/09/0065. Unpublished study prepared by Young Veterinary Research Services. 18 p.	870.7200/Companion animal safety
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.2400/Acute eye irritation
47925312		Kuhn, J. (2002) Piedmont Pediculicide 1: Final Report: Acute Eye Irritation Study in Rabbits. Project Number: 7089/02. Unpublished study prepared by Stillmeadow, Inc. 16 p.	870.2400/Acute eye irritation
47825304		Carr, G. (2009) Storage Stability of Isopropyl Myristate Manufacturing-Use Product at 25 degrees Celsius and 40 degrees Celsius in Carbon Steel Containers for up to 48 Months: Resultix. Project Number: PED/SP/019/0706/R1. Unpublished study prepared by Patheon. 41 p.	830.6320/Corrosion characteristics
47925315		Goldenthal, E. (2003) 28-Day Oral Toxicity Study in Rats with a 14-Day Recovery: Resultix. Project Number: 1016/001. Unpublished study prepared by MPI Research, Inc. 603 p.	870.3050/Repeated dose 28-day oral toxicity in rodents
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6303/Physical state
47925303		Omoruan, P. (2005) The Forced Degradation Study for Isopropyl Myristate Drug Substance and Isopropyl Myristate Solution (50% w/w) by GC: (Resultix). Project Number: PED/AR/014/0105/R0. Unpublished Study Prepared by Patheon, Inc. 79 p.	830.6320/Corrosion characteristics
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7520/Particle size, fiber length, and diamater distribution
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7100/Viscosity
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.1300/Acute inhalation toxicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6319/Miscibility
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6302/Color
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.5100/Bacterial reverse mutation test
47925304		Carr, G. (2009) Storage Stability of Isopropyl Myristate Manufacturing-Use Product at 25 degrees Celsius and 40 degrees Celsius in Carbon Steel Containers for up to 48 Months: Resultix. Project Number: PED/SP/019/0706/R1. Unpublished study prepared by Patheon. 41 p.	830.6317/Storage stability
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3200/21/28-day dermal toxicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.1800/Enforcement analytical method
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.2100/Avian acute oral toxicity test
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3050/Repeated dose 28-day oral toxicity in rodents
47925305		Kaminsky, M. (2007) IPM Solution: Flammability/Flash Point: (Resultix). Project Number: 10633/07. Unpublished study prepared by Stillmeadow, Inc. 9 p.	830.6315/Flammability
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.2200/Avian dietary toxicity test
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.4200/Carcinogenicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	880.1400/Discussion of formation of impurities
47925308		Carr, G. (2007) An Investigation of the UV/Visible Absorbance Properties of Isopropyl Myristate 50% Solution, Isopropyl Myristate and [redacted] (Resultix). Project Number: PED/MIS/024/0307/R0. Unpublished Study Prepared by Patheon, Inc. 14 p.	830.7050/UV/Visible absorption
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7840/Water solubility: Column elution method, shake flask method

Inert ingredient information may be entitled to confidential treatment

DP#: (372778) *** Studies Sent for Review *** Decision#: (424225)

MRID	MRID Status	Citation Reference	Guideline
47925317		Young, D. (2009) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanguineus and Dermacentor variabilis on Dogs. Project Number: PAH/09/0036. Unpublished study prepared by Young Veterinary Research Services. 19 p.	810.3300/Treatments to control pests of humans and pets
47925318		Young, D. (2009) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanuineus and Dermacentor variabilis on Cats. Project Number: PAH/09/0065. Unpublished study prepared by Young Veterinary Research Services. 18 p.	810.3300/Treatments to control pests of humans and pels
47925302		Ballard, T. (2009) Determination of the Percent Active Ingredient and Impurities in Five Batches of Isopropyl Myristate Technical Grade Active Material: (Resultix). Project Number: 09/0033, PAH/09/0057. Unpublished study prepared by En-Cas Analytical Laboratories. 107 p.	830.1700/Preliminary analysis
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	880.1200/Description of starting materials, production and formulation process
47925302		Ballard, T. (2009) Determination of the Percent Active Ingredient and Impurities in Five Batches of Isopropyl Myristate Technical Grade Active Material: (Resultix). Project Number: 09/0033, PAH/09/0057. Unpublished study prepared by En-Cas Analytical Laboratories. 107 p.	830.1750/Certified limits
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7000/pH
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.4100/Terrestrial plant toxicity, Tier 1 (seeding emergence)
47925302		Ballard, T. (2009) Determination of the Percent Active Ingredient and Impurities in Five Batches of Isopropyl Myristate Technical Grade Active Material: (Resultix). Project Number: 09/0033, PAH/09/0057. Unpublished study prepared by En-Cas Analytical Laboratories. 107 p.	830.1800/Enforcement analytical method
47925314		Kuhn, J. (2009) Resultix Tick Spray: Final Report: Skin Sensitization Study in Guinea Pigs. Project Number: 13304/09. Unpublished study prepared by Stillmeadow, Inc. 16 p.	870.2600/Skin sensitization
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.5300/In vitro mammalian cell gene mutation test
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.1700/Preliminary analysis
47925319		Garg, D. (2005) Pharmacokinetic, Safety and Tolerance Study of RESULTZ Pediculicide Rinse in Pediatric Subjects with Pediculosis Capitis. Project Number: 04/12394 t/ t08. Unpublished study prepared by Hill Top Research, Inc. 103 p.	870.7485/Metabolism and pharmacokinetics
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.4150/Terrestrial plant toxicity, Tier 1 (vegetative vigor)
47925317		Young, D. (2009) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanguineus and Dermacentor variabilis on Dogs. Project Number: PAH/09/0036. Unpublished study prepared by Young Veterinary Research Services. 19 p.	870.7200/Companion animal safety
47925303		Omoruan, P. (2005) The Forced Degradation Study for Isopropyl Myristate Drug Substance and Isopropyl Myristate Solution (50% w/w) by GC: (Resultix). Project Number: PED/AR/014/0105/R0. Unpublished Study Prepared by Patheon, Inc. 79 p.	830.6313/Stability to normal and elevated temperatures, metals, and metal ions
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.1750/Certified limits
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7220/Boiling point/boiling range
47925306		Serrano, S. (2007) Analysis of Extractables and Leachables in HDPE Bottles and PP Caps Used to Package the Isopropyl Myristate [redacted] Formulation (Feasibility Study): (Resultix). Project Number: R061229B. Unpublished study prepared by Guidelines, Inc. 47 p.	830.6320/Corrosion characteristics
47925313		Kuhn, J. (2002) Piedmont Pediculocide 1: Final Report: Acute Dermal Irritation Study in Rabbits. Project Number: 7090/02. Unpublished study prepared by Stillmeadow, Inc. 11 p.	870.2500/Acute dermal irritation
47925306		Serrano, S. (2007) Analysis of Extractables and Leachables in HDPE Bottles and PP Caps Used to Package the Isopropyl Myristate [redacted] Formulation (Feasibility Study): (Resultix). Project Number: R061229B. Unpublished study prepared by Guidelines, Inc. 47 p.	830.6317/Storage stability
47925307		Serrano, S. (2007) Photostability Protocol, Testing Schedule and Results for Isopropyl Myristate Solution (50% w/w), ANDA: (Resultix). Project Number: PED/SP/022/0107/R0. Unpublished Study Prepared by Patheon, Inc. 10 p.	830.6317/Storage stability

Inert ingredient information may be entitled to confidential treatment

[redacted]	MRID Status	Citation Reference	Guideline
47925316		Goldenthal, E. (2003) 28-Day Dermal Toxicity Study in Pigs with a 14-Day Recovery: Resultix. Project Number: 1016/002. Unpublished study prepared by MPI Research, Inc. 442 p.	870.3200/21/28-day dermal toxicity
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.2600/Skin sensitization
47925304		Carr, G. (2009) Storage Stability of Isopropyl Myristate Manufacturing-Usa Product at 25 degrees Celsius and 40 degrees Celsius in Carbon Steel Containers for up to 48 Months: Resultix. Project Number: PED/SP/019/0706/R1. Unpublished study prepared by Patheon. 41 p.	830.8313/Stability to normal and elevated temperatures, metals, and metal ions
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.1010/Aquatic invertebrate acute toxicity, test, freshwater daphnids
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3465/90-day inhalation toxicity
47925303		Omoruan, P. (2005) The Forced Degradation Study for Isopropyl Myristate Drug Substance and Isopropyl Myristate Solution (50% w/w) by GC: (Resultix). Project Number: PED/AR/014/0105/R0. Unpublished Study Prepared by Patheon, Inc. 79 p.	830.6317/Storage stability
47925307		Serrano, S. (2007) Photostability Protocol, Testing Schedule and Results for Isopropyl Myristate Solution (50% w/w), ANDA: (Resultix). Project Number: PED/SP/022/0107/R0. Unpublished Study Prepared by Patheon, Inc. 10 p.	830.7050/UV/Visible absorption
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.5375/In vitro mammalian chromosome aberration test
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6304/Odor
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7300/Density/relative density
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.1075/Fish acute toxicity test, freshwater and marine
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3100/90-Day oral toxicity in rodents
47925308		Carr, G. (2007) An Investigation of the UV/Visible Absorbance Properties of Isopropyl Myristate 50% Solution, Isopropyl Myristate and [redacted]: (Resultix). Project Number: PED/MIS/024/0307/R0. Unpublished Study Prepared by Patheon, Inc. 14 p.	830.6317/Storage stability
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7200/Melting point/melting range
47925310		Kuhn, J. (2002) Piedmont Pediculicide 2: Final Report: Acute Dermal Toxicity Study in Rabbits. Project Number: 7205/02. Unpublished study prepared by Stillmeadow, Inc. 31 p.	870.1200/Acute dermal toxicity
47925311		Kuhn, J. (2002) Piedmont Pediculocide 2: Final Report: Acute Dermal Toxicity Study in Rats: Final Report. Project Number: 7204/02. Unpublished study prepared by Stillmeadow, Inc. 33 p.	870.1200/Acute dermal toxicity
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.7485/Metabolism and pharmacokinetics
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6317/Storage stability
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7950/Vapor pressure
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3700/Prenatal developmental toxicity study
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.1200/Acute dermal toxicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6315/Flammability
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7550/Partition coefficient (n-octanol/water), shake flask method
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3250/90-day dermal toxicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	880.1100/Product identity and composition

Inert ingredient information may be entitled to confidential treatment

OAK RIDGE NATIONAL LABORATORY

MANAGED BY UT-BATTELLE FOR THE DEPARTMENT OF ENERGY

October 14, 2010

CUSTODY RECEIPT FOR FIFRA CONFIDENTIAL BUSINESS INFORMATION

TO:	FROM:
Pamela Landis Biopesticides and Pollution Prevention Division Office of Pesticide Programs U.S. Environmental Protection Agency One Potomac Yard 2777 South Crystal Drive Arlington, VA 22202	R. H. Ross, Group Leader Toxicology and Hazard Assessment Group 1060 Commerce Park Oak Ridge, Tennessee 37830 (865) 574-7797 FAX (865) 574-5353 email rossrh@ornl.gov

INSTRUCTIONS:

1. Original of this receipt to be signed by recipient and returned to sender.
2. Duplicate of this receipt to be retained by recipient.

TASK No.	MRIDs	Chemical/Agent	WAM	Material Sent	Status	Hours	
						Est. Hours	Actual Hours
10-026	47925310-19 47925301, 48132301, 47925309	Isopropyl Myristate	Landis	13 DERs 21 Study reports 1 Custody sheet 1 CD	Draft	96	198

I have personally received from the sender material, enclosures, and attachments as identified above. I assume full responsibility for the safe handling, storage, and transmittal of this material in accordance with existing FIFRA Confidential Business Information regulation

DATE RECEIVED: _____ SIGNATURE: _____

DATA PACKAGE BEAN SHEET

Date: 13-Sep-2010

Decision #: 424225
DP #: (372778)
PRIA
Parent DP #:
Submission #: 863571

* * * Registration Information * * *

Registration: 86865-R - RESULTIX TM

Company: 86865 - PIEDMONT ANIMAL HEALTH

Risk Manager: RM 91 - Linda Hollis - (703) 308-8733 Room# PY1 S-8761

Risk Manager Reviewer: Andrew Bryceland ABRYCELA

Sent Date: Calculated Due Date: 29-Dec-2010 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: (B600) NEW AI;NON-FOOD USE;MICROBIAL/BIOCHEMICAL;

Ingredients: 000207, Isopropyl myristate [redacted]%)

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 07-Jan-2010 Due Back:

DP Ingredient: 000207, Isopropyl myristate

DP Title:

CSF Included: ○ Yes ● No Label Included: ○ Yes ● No Parent DP #:

	Assigned To	Date In	Date Out		
Organization:	BPPD / BPB	07-Jan-2010		Last Possible Science Due Date:	03-Jan-2010
Team Name:	RM 91	07-Jan-2010		Science Due Date:	
Reviewer Name:	Greene, Cheryl	07-Jan-2010		Sub Data Package Due Date:	
Contractor Name:					

* * * Studies Sent for Review * * *

Printed on Page 2

* * * Additional Data Package for this Decision * * *

No Additional Data Packages

* * * Data Package Instructions * * *

Contractor,

Please provide DERs for the attached data volumes.

Cheryl Greene
703-308-0352

Product ingredient source information may be entitled to confidential treatment

MRID	MRID Status	Citation Reference	Guideline
47925317		Young, D. (2009) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanguineus and Dermacentor variabilis on Dogs. Project Number: PAH/09/0036. Unpublished study prepared by Young Veterinary Research Services. 19 p.	810.3300/Treatments to control pests of humans and pets
47925318		Young, D. (2009) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanuineus and Dermacentor variabilis on Cats. Project Number: PAH/09/0065. Unpublished study prepared by Young Veterinary Research Services. 18 p.	810.3300/Treatments to control pests of humans and pets
47925302		Ballard, T. (2009) Determination of the Percent Active Ingredient and Impurities in Five Batches of Isopropyl Myristate Technical Grade Active Material: (Resultix). Project Number: 09/0033, PAH/09/0057. Unpublished study prepared by En-Cas Analytical Laboratories. 107 p.	830.1700/Preliminary analysis
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	880.1200/Description of starting materials, production and formulation process
47925302		Ballard, T. (2009) Determination of the Percent Active Ingredient and Impurities in Five Batches of Isopropyl Myristate Technical Grade Active Material: (Resultix). Project Number: 09/0033, PAH/09/0057. Unpublished study prepared by En-Cas Analytical Laboratories. 107 p.	830.1750/Certified limits
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7000/pH
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.4100/Terrestrial plant toxicity, Tier 1 (seeding emergence)
47925302		Ballard, T. (2009) Determination of the Percent Active Ingredient and Impurities in Five Batches of Isopropyl Myristate Technical Grade Active Material: (Resultix). Project Number: 09/0033, PAH/09/0057. Unpublished study prepared by En-Cas Analytical Laboratories. 107 p.	830.1800/Enforcement analytical method
47925314		Kuhn, J. (2009) Resultix Tick Spray: Final Report: Skin Sensitization Study in Guinea Pigs. Project Number: 13304/09. Unpublished study prepared by Stillmeadow, Inc. 16 p.	870.2600/Skin sensitization
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.5300/In vitro mammalian cell gene mutation test
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.1700/Preliminary analysis
47925319		Garg, D. (2005) Pharmacokinetic, Safety and Tolerance Study of RESULTZ Pediculicide Rinse in Pediatric Subjects with Pediculosis Capitis. Project Number: 04/12394 1/108. Unpublished study prepared by Hill Top Research, Inc. 103 p.	870.7485/Metabolism and pharmacokinetics
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.4150/Terrestrial plant toxicity, Tier 1 (vegetative vigor)
47925317		Young, D. (2009) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanguineus and Dermacentor variabilis on Dogs. Project Number: PAH/09/0036. Unpublished study prepared by Young Veterinary Research Services. 19 p.	870.7200/Companion animal safety
47925303		Omoruan, P. (2005) The Forced Degradation Study for Isopropyl Myristate Drug Substance and Isopropyl Myristate Solution (50% w/w) by GC: (Resultix). Project Number: PED/AR/0 14/0 105/R0. Unpublished Study Prepared by Patheon, Inc. 79 p.	830.6313/Stability to normal and elevated temperatures, metals, and metal ions
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.1750/Certified limits
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7220/Boiling point/boiling range
47925306		Serrano, S. (2007) Analysis of Extractables and Leachables in HDPE Bottles and PP Caps Used to Package the Isopropyl Myristate [redacted] Formulation (Feasibility Study): (Resultix). Project Number: R061229B. Unpublished study prepared by Guidelines, Inc. 47 p.	830.6320/Corrosion characteristics
47925313		Kuhn, J. (2002) Piedmont Pediculocide 1: Final Report: Acute Dermal Irritation Study in Rabbits. Project Number: 7090/02. Unpublished study prepared by Stillmeadow, Inc. 11 p.	870.2500/Acute dermal irritation
47925306		Serrano, S. (2007) Analysis of Extractables and Leachables in HDPE Bottles and PP Caps Used to Package the Isopropyl Myristate [redacted] Formulation (Feasibility Study): (Resultix). Project Number: R061229B. Unpublished study prepared by Guidelines, Inc. 47 p.	830.6317/Storage stability
47925307		Serrano, S. (2007) Photostability Protocol, Testing Schedule and Results for Isopropyl Myristate Solution (50% w/w), ANDA: (Resultix). Project Number: PED/SP/022/0107/R0. Unpublished Study Prepared by Patheon, Inc. 10 p.	830.6317/Storage stability

Inert ingredient information may be entitled to confidential treatment

DP#: (372778) * * * Studies Sent for Review * * * Decision#: (424225)

MRID	MRID Status	Citation Reference	Guideline
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.1100/Acute Oral Toxicity
47925318		Young, D. (2009) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanuineus and Dermacentor variabilis on Cats. Project Number: PAH/09/0065. Unpublished study prepared by Young Veterinary Research Services. t8 p.	870.7200/Companion animal safety
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.2400/Acute eye irritation
47925312		Kuhn, J. (2002) Piedmont Pediculicide t: Final Report: Acute Eye Irritation Study in Rabbits. Project Number: 7089/02. Unpublished study prepared by Stillmeadow, Inc. 16 p.	870.2400/Acute eye irritation
47925304		Carr, G. (2009) Storage Stability of Isopropyl Myristate Manufacturing-Use Product at 25 degrees Celsius and 40 degrees Celsius in Carbon Steel Containers for up to 48 Months: Resultix. Project Number: PED/SP/019/0706/R1. Unpublished study prepared by Patheon. 41 p.	830.6320/Corrosion characteristics
47925315		Goldenthal, E. (2003) 28-Day Oral Toxicity Study in Rats with a 14-Day Recovery: Resultix. Project Number: 1016/001. Unpublished study prepared by MPI Research, Inc. 603 p.	870.3050/Repeated dose 28-day oral toxicity in rodents
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6303/Physical state
47925303		Omoruan, P. (2005) The Forced Degradation Study for Isopropyl Myristate Drug Substance and Isopropyl Myristate Solution (50% w/w) by GC: (Resultix). Project Number: PED/AR/014/0105/R0. Unpublished Study Prepared by Patheon, Inc. 79 p.	830.6320/Corrosion characteristics
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7520/Particle size, fiber length, and diameter distribution
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7100/Viscosity
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.1300/Acute inhalation toxicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6319/Miscibility
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6302/Color
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.5100/Bacterial reverse mutation test
47925304		Carr, G. (2009) Storage Stability of Isopropyl Myristate Manufacturing-Use Product at 25 degrees Celsius and 40 degrees Celsius in Carbon Steel Containers for up to 48 Months: Resultix. Project Number: PED/SP/019/0706/R1. Unpublished study prepared by Patheon. 41 p.	830.6317/Storage stability
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3200/21/28-day dermal toxicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.1800/Enforcement analytical method
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.2100/Avian acute oral toxicity test
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3050/Repeated dose 28-day oral toxicity in rodents
47925305		Kaminsky, M. (2007) IPM Solution: Flammability/Flash Point: (Resultix). Project Number: 10633/07. Unpublished study prepared by Stillmeadow, Inc. 9 p.	830.6315/Flammability
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.2200/Avian dietary toxicity test
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.4200/Carcinogenicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	880.1400/Discussion of formation of impurities
47925308		Carr, G. (2007) An Investigation of the UV/Visible Absorbance Properties of Isopropyl Myristate 50% Solution, Isopropyl Myristate and [redacted] (Resultix). Project Number: PED/MIS/024/0307/R0. Unpublished Study Prepared by Patheon, Inc. 14 p.	830.7050/UV/Visible absorption
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7840/Water solubility: Column elution method, shake flask method

Inert ingredient information may be entitled to confidential treatment

MRID	MRID Status	Citation Reference	Guideline
47925316		Goldenthal, E. (2003) 28-Day Dermal Toxicity Study in Pigs with a 14-Day Recovery: Resultix. Project Number: 1016/002. Unpublished study prepared by MPI Research, Inc. 442 p.	870.3200/21/28-day dermal toxicity
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.2600/Skin sensitization
47925304		Carr, G. (2009) Storage Stability of Isopropyl Myristate Manufacturing-Use Product at 25 degrees Celsius and 40 degrees Celsius in Carbon Steel Containers for up to 48 Months: Resultix. Project Number: PED/SP/019/0706/R1. Unpublished study prepared by Patheon. 41 p.	830.6313/Stability to normal and elevated temperatures, metals, and metal ions
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.1010/Aquatic invertebrate acute toxicity, test, freshwater daphnids
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3465/90-day inhalation toxicity
47925303		Omoruan, P. (2005) The Forced Degradation Study for Isopropyl Myristate Drug Substance and Isopropyl Myristate Solution (50% w/w) by GC: (Resultix). Project Number: PED/AR/014/0105/R0. Unpublished Study Prepared by Patheon, Inc. 79 p.	830.6317/Storage stability
47925307		Serrano, S. (2007) Photostability Protocol, Testing Schedule and Results for Isopropyl Myristate Solution (50% w/w), ANDA: (Resultix). Project Number: PED/SP/022/0107/R0. Unpublished Study Prepared by Patheon, Inc. 10 p.	830.7050/UV/Visible absorption
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.5375/In vitro mammalian chromosome aberration test
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6304/Odor
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7300/Density/relative density
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.1075/Fish acute toxicity test, freshwater and marine
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3100/90-Day oral toxicity in rodents
47925308		Carr, G. (2007) An Investigation of the UV/Visible Absorbance Properties of Isopropyl Myristate 50% Solution, Isopropyl Myristate and [redacted] (Resultix). Project Number: PED/MIS/024/0307/R0. Unpublished Study Prepared by Patheon, Inc. 14 p.	830.6317/Storage stability
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7200/Melting point/melting range
47925310		Kuhn, J. (2002) Piedmont Pediculicide 2: Final Report: Acute Dermal Toxicity Study in Rabbits. Project Number: 7205/02. Unpublished study prepared by Stillmeadow, Inc. 31 p.	870.1200/Acute dermal toxicity
47925311		Kuhn, J. (2002) Piedmont Pediculocide 2: Final Report: Acute Dermal Toxicity Study in Rats: Final Report. Project Number: 7204/02. Unpublished study prepared by Stillmeadow, Inc. 33 p.	870.1200/Acute dermal toxicity
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.7485/Metabolism and pharmacokinetics
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6317/Storage stability
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7950/Vapor pressure
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3700/Prenatal developmental toxicity study
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.1200/Acute dermal toxicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6315/Flammability
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7550/Partition coefficient (n-octanol/water), shake flask method
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3250/90-day dermal toxicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	880.1100/Product identity and composition

Inert ingredient information may be entitled to confidential treatment

Bean 2

Decision #: 424225
DP #: (372778)
PRIA
Parent DP #:
Submission #: 863571

DATA PACKAGE BEAN SHEET

Date: 12-Aug-2010

* * * Registration Information * * *

Registration: 86865-R - RESULTIX TM

Company: 86865 - PIEDMONT ANIMAL HEALTH

Risk Manager: RM 91 - Linda Hollis - (703) 308-8733 Room# PY1 S-8761

Risk Manager Reviewer: Cheryl Greene

Sent Date: Calculated Due Date: 29-Dec-2010 Edited Due Date:

Type of Registration: Product Registration - Section 3

Action Desc: (B600) NEW AI;NON-FOOD USE;MICROBIAL/BIOCHEMICAL;

Ingredients: 000207, isopropyl myristate([redacted]

* * * Data Package Information * * *

Expedite: ○ Yes ● No Date Sent: 07-Jan-2010 Due Back:

DP Ingredient:

DP Title:

CSF Included: ○ Yes ● No Label Included: ○ Yes ● No Parent DP #:

	Assigned To	Date In	Date Out	
Organization:	BPPD / BPB	07-Jan-2010		Last Possible Science Due Date: 03-Jan-2010
Team Name:	RM 91	07-Jan-2010		Science Due Date:
Reviewer Name:	Greene, Cheryl	07-Jan-2010		Sub Data Package Due Date:
Contractor Name:				

* * * Studies Sent for Review * * *

Printed on Page 2

* * * Additional Data Package for this Decision * * *

No Additional Data Packages

* * * Data Package Instructions * * *

Dear Contractor:
Please review the following data to determine its acceptability for the registration of the product noted.

Please provide the following:

- DERs for all MRIDS;
- - REVIEW THE CSF for accuracy and completeness;
- assign PC codes on the CSF for active and inert ingredients;
- summarize any /all data waiver requests and provide a toxicity category for the product.

If you have questions or need additional information, please contact me at 703 308-0352 or by email at Greene.cheryl@eEPA.GOV

Product ingredient source information may be entitled to confidential treatment

MRID	MRID Status	Citation Reference	Guideline
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.1100/Acute Oral Toxicity
[illegible]5318		Young, O. (2009) Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against Rhipicephalus sanuineus and Dermacentor variabilis on Cats. Project Number: PAH/09/0065. Unpublished study prepared by Young Veterinary Research Services. 18 p.	870.7200/Companion animal safety
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.2400/Acute eye irritation
47925312		Kuhn, J. (2002) Piedmont Pediculicide 1: Final Report: Acute Eya Irritation Study in Rabbits. Project Number: 7089/02. Unpublished study prepared by Stillmeadow, Inc. 16 p.	870.2400/Acute eye irritation
47925304		Carr, G. (2009) Storage Stability of Isopropyl Myristate Manufacturing-Use Product at 25 degrees Celsius and 40 degrees Celsius in Carbon Steel Containers for up to 48 Months: Resultix. Project Number: PED/SP/019/0706/R1. Unpublished study prepared by Patheon. 41 p.	830.6320/Corrosion characteristics
47925315		Goldanthal, E. (2003) 28-Day Oral Toxicity Study in Rats with a 14-Day Recovery: Resultix. Project Number: 1016/001. Unpublished study prepared by MPI Research, Inc. 603 p.	870.3050/Repeated dose 28-day oral toxicity in rodents
47825301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6303/Physical state
47925303		Omoruen, P. (2005) The Forced Degradation Study for Isopropyl Myristate Drug Substance and Isopropyl Myristate Solution (50% w/w) by GC: (Resultix). Project Number: PEO/AR/014/0105/R0. Unpublished Study Prepared by Patheon, Inc. 79 p.	830.6320/Corrosion characteristics
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7520/Particle size, fiber length, and diameter distribution
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7100/Viscosity
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.1300/Acute inhalation toxicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6319/Miscibility
301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6302/Color
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.5100/Bacterial reverse mutation test
47925304		Carr, G. (2009) Storage Stability of Isopropyl Myristate Manufacturing-Use Product at 25 degrees Celsius and 40 degrees Celsius in Carbon Steel Containers for up to 48 Months: Resultix. Project Number: PED/SP/019/0706/R1. Unpublished study prepared by Patheon. 41 p.	830.6317/Storage stability
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3200/21/28-day dermal toxicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.1800/Enforcement analytical method
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.2100/Avian acute oral toxicity test
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3050/Repeated dose 28-day oral toxicity in rodents
47925305		Kaminsky, M. (2007) IPM Solution: Flammability/Flash Point: (Resultix). Project Number: 10833/07. Unpublished study prepared by Stillmeadow, Inc. 9 p.	830.6315/Flammability
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.2200/Avian dietary toxicity test
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.4200/Carcinogenicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	880.1400/Discussion of formation of impurities
47925308		Carr, G. (2007) An Investigation of the UV/Visible Absorbance Properties of Isopropyl Myristate 50% Solution, Isopropyl Myristate and [redacted]: (Resultix). Project Number: PED/MIS/024/0307/R0. Unpublished Study Prepared by Patheon, Inc. 14 p.	830.7050/UV/Visible absorption
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7840/Water solubility: Column elution method, shake flask method

Inert ingredient information may be entitled to confidential treatment

DP#: (372778) *** Studies Sent for Review *** Decision#: (424225)

MRID	MRID Status	Citation Reference	Guideline
47925316		Goldenthal, E. (2003) 28-Day Dermal Toxicity Study in Pigs with a 14-Day Recovery: Resultix. Project Number: 1016/002. Unpublished study prepared by MPI Research, Inc. 442 p.	870.3200/21/28-day dermal toxicity
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.2600/Skin sensitization
47925304		Carr, G. (2009) Storage Stability of Isopropyl Myristate Manufacturing-Use Product at 25 degrees Celsius and 40 degrees Celsius in Carbon Steel Containers for up to 48 Months: Resultix. Project Number: PED/SP/019/0706/R1. Unpublished study prepared by Patheon. 41 p.	830.6313/Stability to normal and elevated temperatures, metals, and metal ions
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.1010/Aquatic invertebrate acute toxicity, test, freshwater daphnids
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3465/90-day inhalation toxicity
47925303		Omoruan, P. (2005) The Forced Degradation Study for Isopropyl Myristate Drug Substance and Isopropyl Myristate Solution (50% w/w) by GC: (Resultix). Project Number: PED/AR/014/0105/R0. Unpublished Study Prepared by Patheon, Inc. 79 p.	830.6317/Storage stability
47925307		Serrano, S. (2007) Photostability Protocol, Testing Schedule and Results for Isopropyl Myristate Solution (50% w/w), ANDA: (Resultix). Project Number: PED/SP/022/0107/R0. Unpublished Study Prepared by Patheon, Inc. 10 p.	830.7050/UV/Visible absorption
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.5375/In vitro mammalian chromosome aberration test
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6304/Odor
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7300/Density/relative density
47925320		Phillips, S. (2009) Environmental Fate Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 76 p.	850.1075/Fish acute toxicity test, freshwater and marine
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3100/90-Day oral toxicity in rodents
47925308		Carr, G. (2007) An Investigation of the UV/Visible Absorbance Properties of Isopropyl Myristate 50% Solution, Isopropyl Myristate and [redacted]: (Resultix). Project Number: PED/MIS/024/0307/R0. Unpublished Study Prepared by Patheon, Inc. 14 p.	830.6317/Storage stability
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7200/Melting point/melting range
47925310		Kuhn, J. (2002) Piedmont Pediculicide 2: Final Report: Acute Dermal Toxicity Study in Rabbits. Project Number: 7205/02. Unpublished study prepared by Stillmeadow, Inc. 31 p.	870.1200/Acute dermal toxicity
47925311		Kuhn, J. (2002) Piedmont Pediculicide 2: Final Report: Acute Dermal Toxicity Study in Rats: Final Report. Project Number: 7204/02. Unpublished study prepared by Stillmeadow, Inc. 33 p.	870.1200/Acute dermal toxicity
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.7485/Metabolism and pharmacokinetics
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6317/Storage stability
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7950/Vapor pressure
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3700/Prenatal developmental toxicity study
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.1200/Acute dermal toxicity
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.6315/Flammability
47925301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	830.7550/Partition coefficient (n-octanol/water), shake flask method
47925309		Phillips, S. (2009) Miscellaneous Toxicology Information: (Resultix). Unpublished study prepared by Piedmont Animal Health. 315 p.	870.3250/90-day dermal toxicity
[illegible]301		Phillips, S. (2009) Miscellaneous Chemistry Information: Resultix. Unpublished study prepared by Piedmont Animal Health. 77 p.	880.1100/Product identity and composition

Inert ingredient information may be entitled to confidential treatment

ENVIRONMENTAL PROTECTION AGENCY

[EPA-HQ-OPP-2010-0096; FRL-8811-6]

Pesticide Products; Registration Applications

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: EPA has received applications to register pesticide products containing active ingredients not included in any previously registered pesticide products. Pursuant to the provisions of section 3(c)(4) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), EPA is hereby providing notice of receipt and opportunity to comment on these applications.

DATES: Comments must be received on or before April 9, 2010.

ADDRESSES: Submit your comments, identified by docket identification (ID) number and the File Symbol(s) of interest as shown in the body of this document, by one of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the on-line instructions for submitting comments.
- *Mail:* Office of Pesticide Programs (OPP) Regulatory Public Docket (7502P), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001.
- *Delivery:* OPP Regulatory Public Docket (7502P), Environmental Protection Agency, Rm. S–4400, One Potomac Yard (South Bldg.), 2777 S. Crystal Dr., Arlington, VA. Deliveries are only accepted during the Docket Facility's normal hours of operation (8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays). Special arrangements should be made for deliveries of boxed information. The Docket Facility telephone number is (703) 305–5805.

Instructions: Direct your comments to the docket Identification (ID) number and the File Symbol(s) for the application(s) of interest as shown in the body of this document. EPA's policy is that all comments received will be included in the docket without change and may be made available on-line at *http://www.regulations.gov,* including any personal information provided, unless the comment includes information claimed to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Do not submit information that you consider to be CBI or otherwise protected through regulations.gov or e-mail. The regulations.gov website is an "anonymous access" system, which means EPA will not know your identity or contact information unless you provide it in the body of your comment. If you send an e-mail comment directly to EPA without going through regulations.gov, your e-mail address will be automatically captured and included as part of the comment that is placed in the docket and made available on the Internet. If you submit an electronic comment, EPA recommends that you include your name and other contact information in the body of your comment and with any disk or CD-ROM you submit. If EPA cannot read your comment due to technical difficulties and cannot contact you for clarification, EPA may not be able to consider your comment. Electronic files should avoid the use of special characters, any form of encryption, and be free of any defects or viruses.

Docket: All documents in the docket are listed in the docket index available at *http://www.regulations.gov.* Although listed in the index, some information is not publicly available, e.g., CBI or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, is not placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available either in the electronic docket at *http://www.regulations.gov,* or, if only available in hard copy, at the OPP Regulatory Public Docket in Rm. S–4400, One Potomac Yard (South Bldg.), 2777 S. Crystal Dr., Arlington, VA. The hours of operation of this Docket Facility are from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The Docket Facility telephone number is (703) 305–5805.

FOR FURTHER INFORMATION CONTACT: The Regulatory Action Leader, Biopesticides and Pollution Prevention Division (7511P), listed in the following table:

Regulatory Action Leader	Telephone Number and E-mail Address	Mailing Address	File Symbol(s)
Driss Benmhend	(703) 308–9525 *benmhend.driss@epa.gov*	Biopesticides and Pollution Prevention Division (7511P) Office of Pesticide Programs Environmental Protection Agency 1200 Pennsylvania Ave., NW. Washington, DC 20460–0001	5481–LAI 5481–LAO 5481–LTN 5481–LTR
Susanne Cerrelli	(703) 308–8077 *cerrelli.susanne@epa.gov*	Do.	86174–E 86174–G 86174–R 86174–U
Cheryl Greene	(703) 308–0352 *greene.cheryl@epa.gov*	Do.	86865–R
Denise Greenway	(703) 308–8263 *greenway.denise@epa.gov*	Do.	70051–RNL 84888–E 84888–R
Anna Gross	(703) 305–5614 *gross.anna@epa.gov*	Do.	67986–A

Regulatory Action Leader	Telephone Number and E-mail Address	Mailing Address	File Symbol(s)
Jeannine Kausch	(703) 347–8920 *kausch.jeannine@epa.gov*	Do.	68539–I 68539–O 68539–RN 81179–E 84059–O 84059–RN
Kathleen Martin	(703) 308–2857 *martin.kathleen@epa.gov*	Do.	239–ETNE 239–ETNG 239–ETNU 73314–A 73314–T
Chris Pfeifer	(703) 308–0031 *pfeifer.chris@epa.gov*	Do.	83028–RN
Ann Sibold	(703) 305–6502 *sibold.ann@epa.gov*	Do.	84059–RR
Menyon Adams	(703) 347-8496 *adams.menyon@epa.gov*	Do.	80286-RA 80286-RT

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. Potentially affected entities may include, but are not limited to:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed in this unit could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether this action might apply to certain entities. If you have any questions regarding the applicability of this action to a particular entity, consult the person associated with the File Symbol of interest and listed under **FOR FURTHER INFORMATION CONTACT.**

B. What Should I Consider as I Prepare My Comments for EPA?

1. *Submitting CBI.* Do not submit this information to EPA through regulations.gov or e-mail. Clearly mark the part or all of the information that you claim to be CBI. For CBI information in a disk or CD-ROM that you mail to EPA, mark the outside of the disk or CD-ROM as CBI and then identify electronically within the disk or CD-ROM the specific information that is claimed as CBI. In addition to one complete version of the comment that includes information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public docket. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2.

2. *Tips for preparing your comments.* When submitting comments, remember to:

i. Identify the document by docket ID number and other identifying information (subject heading, Federal Register date, and page number). If you are commenting on a docket that addresses multiple products, please indicate to which File Symbol(s) your comment applies.

ii. Follow directions. The Agency may ask you to respond to specific questions or organize comments by referencing a Code of Federal Regulations (CFR) part or section number.

iii. Explain why you agree or disagree; suggest alternatives and substitute language for your requested changes.

iv. Describe any assumptions and provide any technical information and/or data that you used.

v. If you estimate potential costs or burdens, explain how you arrived at your estimate in sufficient detail to allow for it to be reproduced.

vi. Provide specific examples to illustrate your concerns and suggest alternatives.

vii. Explain your views as clearly as possible, avoiding the use of profanity or personal threats.

viii. Make sure to submit your comments by the comment period deadline identified.

II. Registration Applications

EPA received applications to register pesticide products containing active ingredients not included in any previously registered products. Pursuant to the provision of section 3(c)(4) of FIFRA, EPA is hereby providing notice of receipt and opportunity to comment on these applications. Notice of receipts of these applications does not imply a decision by the Agency on the applications.

1. *File Symbol:* 239–ETNE. *Docket Number:* EPA–HQ–OPP–2010–0094. *Applicant:* OMC Consulting, 828 Tanglewood Lane, East Lansing, MI 48823 (on behalf of The Scotts Company LLC, d/b/a The Ortho Group, P.O. Box 190, Marysville, OH 43040). *Product Name:* Phoma Tech. *Active Ingredient:* *Phoma macrostoma* strain 94–44B at 92%. *Proposed Classification/Use:* Manufacturing-use product. (K. Martin).

2. *File Symbol:* 239–ETNG. *Docket Number:* EPA–HQ–OPP–2010–0094. *Applicant:* OMC Consulting, 828 Tanglewood Lane, East Lansing, MI 48823 (on behalf of The Scotts Company LLC, d/b/a The Ortho Group, P.O. Box 190, Marysville, OH 43040). *Product Name:* Phoma H. *Active Ingredient:* *Phoma macrostoma* strain 94–44B at 92%. *Proposed Classification/Use:* Terrestrial (nonfood, residential outdoor). (K. Martin).

3. *File Symbol:* 239–ETNU. *Docket Number:* EPA–HQ–OPP–2010–0094. *Applicant:* OMC Consulting, 828 Tanglewood Lane, East Lansing, MI 48823 (on behalf of The Scotts Company LLC, d/b/a The Ortho Group, P.O. Box

190, Marysville, OH 43040). *Product Name*: Phoma P. *Active Ingredient*: *Phoma macrostomo* strain 94-44B at 92%. *Proposed Classificotion/Use*: Terrestrial (nonfood, residential outdoor, nurseries, greenhouses). (K. Martin).

4. *File Symbol*: 5481–LAI. *Docket Number*: EPA–HQ–OPP–2010–0064. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of AMVAC Chemical Corporation, 4695 Macarthur Court, Suite 1250, Newport Beach, CA 92660–1706). *Product Name*: AMV-1018 Technical. *Active Ingredient*: 3-decen-2-one at 98%. *Proposed Classification/Use*: Manufacturing-use product. (D. Benmhend).

5. *File Symbal*: 5481–LAO. *Docket Number*: EPA–HQ–OPP–2010–0064. *Applicont*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of AMVAC Chemical Corporation, 4695 Macarthur Court, Suite 1250, Newport Beach, CA 92660–1706). *Product Name*: AMV-1018 67.5 EC. *Active Ingredient*: 3-decen-2-one at 67.5%. *Proposed Classification/Use*: Potato sprout inhibitor for indoor use only. (D. Benmhend).

6. *File Symbol*: 5481–LTN. *Docket Number*: EPA–HQ–OPP–2010–0064. *Applicont*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of AMVAC Chemical Corporation, 4695 Macarthur Court, Suite 1250, Newport Beach, CA 92660–1706). *Product Name*: AMV-1018 90 EC. *Active Ingredient*: 3-decen-2-one at 90%. *Proposed Classification/Use*: Potato sprout inhibitor for indoor use only. (D. Benmhend).

7. *File Symbol*: 5481–LTR. *Docket Number*: EPA–HQ–OPP–2010–0064. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of AMVAC Chemical Corporation, 4695 Macarthur Court, Suite 1250, Newport Beach, CA 92660–1706). *Product Nome*: AMV-1018 EP. *Active Ingredient*: 3-decen-2-one at 98%. *Proposed Classification/Use*: Potato sprout inhibitor for indoor use only. (D. Benmhend).

8. *File Symbal*: 67986–A. *Docket Number*: EPA–HQ–OPP–2009–0539. *Applicant*: Interregional Research Project Number 4 (IR-4), Rutgers University, 500 College Road East, Suite 201W, Princeton, NJ 08540 (on behalf of OmniLytics, 5450 W. Wiley Post Way, Salt Lake City, UT 84116). *Product Name*: AgriPhage CMM. *Active Ingredient*: Bacteriophage of *Clavibacter michiganensis* subsp. *michigonensis* at 0.05%. *Proposed Classificatian/Use*: Bactericide far use against canker on tomato. (A. Gross).

9. *File Symbol*: 68539–I. *Docket Number*: EPA–HQ–OPP–2010–0057. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of BioWorks Incorporated, 100 Rawson Road, Suite 205, Victor, NY 14564). *Product Name*: G-41 Technical. *Active Ingredient*: *Trichoderma virens* strain G-41 at 12.1%. *Proposed Classification/Use*: Manufacturing-use product. (J. Kausch).

10. *File Symbol*: 68539–O. *Docket Number*: EPA–HQ–OPP–2010–0057. *Applicont*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of BioWorks Incorporated, 100 Rawson Road, Suite 205, Victor, NY 14564). *Product Name*: BW240 WP. *Active Ingredient*: *Trichodermo virens* strain G-41 at 0.61%. *Proposed Classification/Use*: Preventative fungicide for control of disease organisms such as *Pythium*, *Phytaphthora*, *Rhizoctonio*, and *Fusarium* on various crops. (J. Kausch)

11. *File Symbol*: 68539–RN. *Docket Number*: EPA–HQ–OPP–2010–0057. *Applicont*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of BioWorks Incorporated, 100 Rawson Road, Suite 205, Victor, NY 14564). *Praduct Name*: BW240 G. *Active Ingredient*: *Trichoderma virens* strain G-41 at 0.61%. *Proposed Classification/Use*: Preventative fungicide for control of disease organisms such as *Pythium*, *Phytophthora*, *Rhizoctonia*, and *Fusarium* on various crops. (J. Kausch).

12. *File Symbol*: 70051–RNL. *Docket Number*: EPA–HQ–OPP–2010–0103. *Applicont*: Certis USA LLC, 9145 Guilford Road, Suite 175, Columbia, MD 21046. *Praduct Name*: CX-9090. *Active Ingredient*: *Bocillus subtilis* strain CX-9060 at 25.0%. *Praposed Classification/Use*: For the control or suppression of fungal and bacterial diseases of horticultural crops. (D. Greenway).

13. *File Symbal*: 73314–A. *Docket Number*: EPA–HQ–OPP–2010–0093. *Applicont*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of Natural Industries Incorporated, 6223 Theall Road, Houston, TX 77066). *Product Name*: NoFly(tm). *Active Ingredient*: *Poecilomyces fumosoroseus* strain FE 9901 at 18%. *Proposed Classification/Use*: Greenhouse (only) for control of whiteflies, aphids, thrips, psyllids, mealybugs, leaf hoppers, plant bugs, weevils, grasshoppers, mormon crickets, locust, and beetles on all greenhouse and nursery crops including ornamentals, vegetables, and herbs. (K. Martin).

14. *File Symbol*: 73314–T. *Docket Number*: EPA–HQ–OPP–2010–0093. *Applicont*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of Natural Industries Incorporated, 6223 Theall Road, Houston, TX 77066). *Product Name*: NoFly(tm) Technical. *Active Ingredient*: *Paecilomyces fumosoroseus* strain FE 9901 at 69%. *Praposed Classificotian/Use*: Manufacturing-use product. (K. Martin).

15. *File Symbol*: 81179–E. *Docket Number*: EPA–HQ–OPP–2010–0056. *Applicant*: Interregional Research Project Number 4 (IR-4), Rutgers University, 500 College Road East, Suite 201W, Princeton, NJ 08540 (on behalf of BioProdex Incorporated, 8520 NW 2 Place, Gainesville, FL 32607–1423). *Product Name*: SolviNix. *Active Ingredient*: *Tobocco Mild Green Mosaic Tobamavirus* at 3%. *Proposed Classification/Use*: Post-emergent herbicide for control of tropical soda apple (*Solanum viarum*) in citrus, forestry, grass pastures, rangeland, sod-production fields, roadsides, sugarcane, temperate fruits and nuts, tropical fruits and nuts, turf, Conservation Reserve Program and other natural areas, and rights-of-way. (J. Kausch).

16. *File Symbol*: 83028–RN. *Docket Number*: EPA–HQ–OPP–2010–0080. *Applicant*: NCA Biotech Incorporated, 3406 Pomona Boulevard, Pomona, CA 91768. *Product Name*: Technical Salicylic Acid. *Active Ingredient*: Salicylic Acid at 98.7%. *Propased Classification/Use*: Manufacturing-use product for formulation into plant growth regulator end-use products. (J. Pfeifer).

17. *File Symbol*: 84059–O. *Docket Number*: EPA–HQ–OPP–2010–0058. *Applicont*: Marrone Bio Innovations Incorporated, 2121 Second Street, Suite B-107, Davis, CA 95618. *Product Name*: MBI-203 TGAI. *Active Ingredient*: *Chromobocterium subtsugae* strain PRAA4-1^T at 100.00%. *Praposed Classification/Use*: Manufacturing-use product. (J. Kausch).

18. *File Symbol*: 84059–RN. *Docket Number*: EPA–HQ–OPP–2010–0058. *Applicant*: Marrone Bio Innovatians Incorporated, 2121 Second Street, Suite B-107, Davis, CA 95618. *Product Name*: MBI-203 EP. *Active Ingredient*: *Chromobacterium subtsugoe* strain PRAA4-1^T at 94.50%. *Proposed Classification/Use*: Insecticide for use in the control or suppression of many

foliar-feeding pests such as caterpillars, foliage-feeding coleopteran, aphids, whiteflies, and plant-sucking mites on ornamental plants, turf, and various edible crops. (J. Kausch).

19. *File Symbol*: 84059–RR. *Docket Number*: EPA–HQ–OPP–2010–0079. *Applicant*: Marrone Bio Innovations Incorporated, 2121 Second Street, Suite B-107, Davis, CA 95618. *Product Name*: MBI-005. *Active Ingredient*: *Streptomyces acidiscabies* strain RL-110^T at 100%. *Proposed Classification/Use*: Manufacturing-use product. (A. Sibold).

20. *File Symbol*: 84888–E. *Docket Number*: EPA–HQ–OPP–2010–0090. *Applicant*: Technology Sciences Group Incorporated, 712 Fifth Street, Suite A, Davis, CA 95616 (on behalf of Agrium Advanced Technologies RP Incorporated, 10 Craig Street, Brantford, Ontario Canada N3R 7J1). *Product Name*: Nivalis. *Active Ingredient*: *Typhula phacorrhiza* strain 94671 at 4.00%. *Proposed Classification/Use*: Biofungicide for turf. (D. Greenway).

21. *File Symbol*: 84888–R. *Docket Number*: EPA–HQ–OPP–2010–0090. *Applicant*: Technology Sciences Group Incorporated, 712 Fifth Street, Suite A, Davis, CA 95616 (on behalf of Agrium Advanced Technologies RP Incorporated, 10 Craig Street, Brantford, Ontario Canada N3R 7J1). *Product Name*: Nivalis Technical. *Active Ingredient*: *Typhula phacorrhiza* strain 94671 at 4.00%. *Proposed Classification/Use*: Manufacturing-use product. (D. Greenway).

22. *File Symbol*: 86174–E. *Docket Number*: EPA–HQ–OPP–2010–0100. *Applicant*: SciReg Incorporated, 12733 Director's Loop, Woodbridge, VA 22192 (on behalf of Bio-Ferm GmbH, Konrad Lorenz Strasse 20, A-3430, Tulln, Austria). *Product Name*: *Aureobasidium pullulans* strain DSM 14940 Technical. *Active Ingredient*: *Aureobasidium pullulans* strain DSM 14940 at 80%. *Proposed Classification/Use*: Manufacturing-use product. (S. Cerrelli).

23. *File Symbol*: 86174–G. *Docket Numbers*: EPA–HQ–OPP–2010–0100 and EPA–HQ–OPP–2010–0106. *Applicant*: SciReg Incorporated, 12733 Director's Loop, Woodbridge, VA 22192 (on behalf of Bio-Ferm GmbH, Konrad Lorenz Strasse 20, A-3430, Tulln, Austria). *Product Name*: Botector. *Active Ingredients*: *Aureobasidium pullulans* strain DSM 14940 at 50% and *Aureobasidium pullulans* strain DSM 14941 at 50%. *Proposed Classification/Use*: Fungicide for agricultural, commercial, and residential use on citrus, grapes, pome fruits, stone fruits, and strawberries. (S. Cerrelli).

24. *File Symbol*: 86174–R. *Docket Number*: EPA–HQ–OPP–2010–0106. *Applicant*: SciReg Incorporated, 12733 Director's Loop, Woodbridge, VA 22192 (on behalf of Bio-Ferm GmbH, Konrad Lorenz Strasse 20, A-3430, Tulln, Austria). *Product Name*: *Aureobasidium pullulans* strain DSM 14941 Technical. *Active Ingredient*: *Aureobasidium pullulans* strain DSM 14941 at 80%. *Proposed Classification/Use*: Manufacturing-use product. (S. Cerrelli).

25. *File Symbol*: 86174–U. *Docket Numbers*: EPA–HQ–OPP–2010–0100 and EPA–HQ–OPP–2010–0106. *Applicant*: SciReg Incorporated, 12733 Director's Loop, Woodbridge, VA 22192 (on behalf of Bio-Ferm GmbH, Konrad Lorenz Strasse 20, A-3430, Tulln, Austria). *Product Name*: Blossom Protect. *Active Ingredients*: *Aureobasidium pullulans* strain DSM 14940 at 32.25% and *Aureobasidium pullulans* strain DSM 14941 at 32.25%. *Proposed Classification/Use*: Fungicide for agricultural, commercial, and residential use to prevent fire blight on pome fruits. (S. Cerrelli).

26. *File Symbol*: 86865–R. *Docket Number*: EPA–HQ–OPP–2010–0082. *Applicant*: Piedmont Animal Health, 204 Muirs Chapel Road, Suite 200, Greensboro, NC 27410. *Product Name*: Resultix(tm). *Active Ingredient*: Isopropyl Myristate at 50%. *Proposed Classification/Use*: Insecticide for use against ticks on cats and dogs. (C. Greene).

27. *File Symbol*: 80286-RT. *Docket Number*: EPA-HQ-OPP-2010-0040. *Applicant*: ISCA Technologies Incorporated, 1230 Spring Street, Riverside, CA 92507. *Product Name*: ISCA TuTa MP. *Active Ingredient*: (E,Z,Z)-3,8,11-Tetradecatrienyl Acetate at 96.31%. *Proposed Classification/Use*: Manufacturing-use product. (M. Adams).

28. *File Symbol*: 80286-RA. *Docket Number*: EPA-HQ-OPP-2010-0040. *Applicant*: ISCA Technologies Incorporated, 1230 Spring Street, Riverside, CA 92507. *Product Name*: SPLAT TuTa(tm). *Active Ingredient*: (E,Z,Z)-3,8,11-Tetradecatrienyl Acetate at 0.3%. *Proposed Classification/Use*: Straight-carbon-chain Lepidoptera pheromone (SCLP) for use against tomato leafminer on all crops and in non-crop areas. (M. Adams).

List of Subjects

Environmental protection, Pesticides and pests.

Dated: March 1, 2010.

Keith A. Matthews,

Acting Director, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs.

[FR Doc. 2010–4835 Filed 3–9–10; 8:45 am]

BILLING CODE 6560–50–S

FEDERAL DEPOSIT INSURANCE CORPORATION

Agency Information Collection Activities: Submission for OMB Review; Comment Request

AGENCY: Federal Deposit Insurance Corporation (FDIC).

ACTION: Notice of information collections to be submitted to OMB for review and approval under the Paperwork Reduction Act of 1995.

SUMMARY: In accordance with the requirements of the Paperwork Reduction Act of 199 (44 U.S.C. chapter 35), the FDIC hereby gives notice that it plans to submit to the Office of Management and Budget (OMB) a request for OMB review and renewal of its "Foreign Banks" information collection (OMB No. 3064–0114).

DATES: Comments must be submitted on or before April 9, 2010.

ADDRESSES: Interested parties are invited to submit written comments. All comments should refer to the name of the collection. Comments may be submitted by any of the following methods:

- *http://www.FDIC.gov/regulations/laws/federal/propose.html.*
- *E-mail: comments@fdic.gov.*
- *Mail:* Leneta G. Gregorie (202.898.3719), Counsel, Federal Deposit Insurance Corporation, PA1730–3000, 550 17th Street, NW., Washington, DC 20429.
- *Hand Delivery:* Comments may be hand-delivered to the guard station at the rear of the 550 17th Street Building (located on F Street), on business days between 7 a.m. and 5 p.m.

All comments should refer to the relevant OMB control number. A copy of the comments may also be submitted to the FDIC Desk Officer, Office of Information and Regulatory Affairs, Office of Management and Budget, New Executive Office Building, Room 10235, Washington, DC 20503.

FOR FURTHER INFORMATION CONTACT: For further information about the information collection discussed in this notice, please contact Leneta G. Gregorie, by telephone at (202) 898–3719 or by mail at the address identified above.

To: Patti TenBrook/R9/USEPA/US,
Cc:
Bcc:
Subject: Re: Isopropyl myristate
From: Cheryl Greene/DC/USEPA/US - Thursday 03/11/2010 05:03 PM

Dear Doctor TenBrook:

Thank you for your email. It is pretty early in the review process for this action so, I don't have any substantative informatio that I can pass on to you yet. However, I can tell you that we will do thorough environmental fate, and ecological effects reviews. I am passing your information on to the science review team for Isopropyl myristate. I will followup with them over the next week for feedback and keep you posted. In the meantime, if the inquiry you received came from someone from the general public, would you ask that person to submit his/her comments, questions or concerns via the docket for Isopropyl myristate or through our public participation process. That way the concern is in the public record and we will be able to address it in our decision document.

As soon as I get feedback from my science reviewers I will hopefully have more specific informatio to pass on to you. In the meantime, if you have questions or additional concerns/comments, please let me know.

Regards,

Cheryl F. Greene
Office of Prevention, Pesticides and Toxic Substances
Office of Pesticide Programs, BPPD/BPB (7511P)
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20004

Tel: 703 308-0352
Fax 703 308-7026
Email: greene.cheryl@epa.gov

Patti TenBrook Cheryl, I saw that you are the Regulatory Action... 03/11/2010 10:10:03 AM

From: Patti TenBrook/R9/USEPA/US
To: Cheryl Greene/DC/USEPA/US@EPA
Date: 03/11/2010 10:10 AM
Subject: Isopropyl myristate

Cheryl,

I saw that you are the Regulatory Action Leader for the isopropyl myristate product, Resultix, that has been submitted for registration. I've had an inquiry as to whether EPA would include a down-the-drain

analysis since this product is for use on pets and has a potential pathway to sanitary sewers. Pesticides in the sanitary sewers can present problems for wastewater treatment plants, by, for example, upsetting secondary treatment processes, or causing NPDES permit compliance challenges.

Resultix is for use on pets, and as such, has the potential to be washed down drains if people wash their pets indoors. This seems like a small thing, and this use of isopropyl myristate might pale in comparison to its use in cosmetic products, or as an inert ingredient in other pesticide products, but as we move toward (hopefully) less toxic alternatives to pyrethroids in pet products, it is important to ensure that problems with new chemicals won't just replace problems we are currently having with pyrethroids.

Are you able to share any details of what kind of environmental fate assessment will be done for this chemical?

Regards,
Patti

Patti L. TenBrook, Ph.D.
Life Scientist
U.S. EPA Region 9, CED-5
75 Hawthorne St.
San Francisco, CA 94105
415-947-4223

Isopropyl myristate
Patti TenBrook to: Cheryl Greene 03/11/2010 10:10 AM

Cheryl,

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Patti

Patti L. TenBrook, Ph.D.
Life Scientist
U.S. EPA Region 9, CED-5
75 Hawthorne St.
San Francisco, CA 94105
415-947-4223

Please read instructions on reverse before com ng form. Form Approv OMB No. 2070-0060, Approval expires 2-28-95

EPA

United States
Environmental Protection Agency
Washington, DC 20460

✓ **Registration**
Amendment
Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number 86865-R	2. EPA Product Manager L. Hollis	3. Proposed Classification ☐ None ☐ Restricted
4. Company/Product (Name) ResultixTM	PM# 91	
5. Name and Address of Applicant *(Include ZIP Code)* Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410 ☐ *Check if this is a new address*	6. **Expedited Reveiw.** In accordance with FIFRA Section 3(c)(3)(b)(i), my product is similar or identical in composition and labeling to: EPA Reg. No. 86865-R Product Name	

Section - II

☐ Amendment - Explain below.
☐ Resubmission in response to Agency letter dated _____
☐ Notification - Explain below.
☐ Final printed labels in rapsonse to Agency letter dated Aug
☐ "Me Too" Application.
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)
A 75% waiver of registration service fees under PRIA2 is requested, based on <500 employees and <$10 million in pesticide annual revenue; required documentation is included in Volume 1. The PRIA2 fee schedule is B600.

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes ☐ No ** Certification must be submitted*	☐ Yes ✓ No If "Yes" Unit Packaging wgt. / No. per container	☐ Yes ✓ No If "Yes" Package wgt / No. per container	☐ Metal ✓ Plastic ☐ Glass ☐ Paper ☐ Other (Specify) _____

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
✓ Label ☐ Container	20 mL (0.65 fl oz)	☐ Container

6. Manner in Which Label is Affixed to Product: ✓ Lithograph, Paper glued, Stenciled ☐ Other _____

Section - IV

1. Contact Point *(Complete items directly below for identification of individual to be contacted, if necessary, to process this application.)*

Name	Title	Telephone No. (Include Area Code)
Kathleen G. Palma, Ph.D.	VP Research & Development	336-544-0320 x 202

Certification

I certify that the statements I have made on this form and all attachments thereto are true, accurate and complete. I acknowledge that any knowlingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature Kathleen G. Palma, Ph.D.	3. Title VP Research & Development
4. Typed Name Kathleen G. Palma, Ph.D.	5. Date 02 DEC 2009

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

WASHINGTON, D.C. OFFICE
fifth floor
flour mill building
1000 potomac street nw
washington, d.c. 20007-3501
TEL 202 965 7880 FAX 202 965 1729

OTHER OFFICES
beijing, china
new york, new york
portland, oregon
seattle, washington
GSBLAW.COM

GARVEY SCHUBERT BARER

Inert ingredient information may be entitled to confidential treatment

December 3, 2009

Linda A. Hollis
Biochemical Pesticides Branch
Biopesticides and Pollution Prevention Division
U.S. EPA – OPPTS **(Mail Code 7515P)**
Ariel Rios Building
1200 Pennsylvania Avenue NW
Washington, DC 20460

Re: Pesticide Registration Submission for RESULTIX™ End-Use Product (EPA Registration No. 86865-R)

Dear Ms. Hollis:

On behalf Piedmont Animal Health LLC (Piedmont), we are submitting a pesticide registration application for RESULTIX™ End-Use Product (EPA Registration No. 86865-R). This product is composed of isopropyl myristate as the active ingredient and [redacted] as the inert ingredient solvent at a ratio by weight of 1:1. It kills ticks on cats and dogs by dissolving the cuticle on the surface of the arthropod, which results in the death of the tick by desiccation. This nonfood use is classified as a B600 category under PRIA 2, with a registration fee of $15,700; Piedmont is requesting a waiver of 75% of this registration service fee.

During a presubmission meeting between Piedmont and members of the Biochemical Pesticides Branch of the EPA, the EPA agreed to accept a "reduced safety data set" for registration and that all Tier I requirements are to be addressed individually. These Tier I requirements are listed in the Data Matrix in Volume 1 and information pertaining to each set of requirements are described further in the appropriate volumes indicated below.

Included in this submission package are the following items:

- Volume 1 Administrative Materials, including EPA registration forms, draft labels for the active ingredient (active) and for the end-use product (EP), and PRIA2 documentation;

- Volumes 2 through 9, physical and chemical properties of the active and of the EP;
- Volumes 10 through 17, toxicology of the active and of the EP;
- Volumes 18 and 19, efficacy and safety of the EP on cats and dogs;
- Volume 20, pharmacokinetics of the EP; and
- Volume 21, environmental effects of the active and inert ingredients.

If you have any questions or need additional information, please do not hesitate to contact me. My telephone number is 202-298-1785 and my email address is sphillips@gsblaw.com.

Regards,

Susan Phillips

Susan D. Phillips, M.S.
Science Advisor

Attachment

WASHINGTON, D.C. OFFICE
fifth floor
flour mill building
1000 potomac street nw
washington, d.c. 20007-3501
TEL 202 965 7880 FAX 202 965 1729

OTHER OFFICES
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Washington, DC 20460

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Regards,

Susan D. Phillips, M.S.
Science Advisor

Attachment

TRANSMITTAL DOCUMENT

1. Name and Address of Submitter

Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

Agent

Kathleen G. Palma, Ph.D.
Vice President of Research & Development
Email: kpalma@piedmontpharma.com
Telephone: 336-544-0320 x 202

2. Regulatory Action for which this Package is Submitted

Pesticide Registration Submission
RESULTIX™
EPA File Symbol No. 86865-R
Registration for the End-Use Product

3. Transmittal Date

December 3, 2009

4. List of Submitted Documents

Volume 1 Administrative Materials

- Transmittal Document
- EPA Form 8570-1 (Application for Pesticide Registration)
- EPA Form 8570-4 (Confidential Statement of Formula) – one for the active, one for the EP
- Draft labels, 2 sets (5 copies each; one set for the active, one set for the EP)
- EPA Form 8570-35 (Data Matrix) (with Notes)
- EPA Form 8570-36 (Summary of the Physical/Chemical Properties)
- EPA Form 8570-37 (Self-Certification Statement for the Physical/Chemical Properties)
- EPA Form 3540-8 (Application for Registration of Pesticide-Producing and Device-Producing Establishment) (2 pages)
- Justification for Substitutions and not Conducting Various Tests
- EPA Meeting Minutes for April 30, 2009 and EPA Response Letter

- PRIA2 Fee Waiver Documentation, including EPA Small Business Certification Form and verification of online payment of 25% of registration fee

Volume 2	Miscellaneous Chemistry Information
Volume 3	Determination of the Percent Active Ingredient and Impurities in Five Batches of Isopropyl Myristate Technical Grade Material (EN-CAS Project #09-0033)
Volume 4	Report for the Forced Degradation Study on Isopropyl Myristate Drug Substance and Isopropyl Myristate Solution (50% w/w) by GC (Document Control No. PED-AR-014-0105-R0)
Volume 5	Storage Stability of Isopropyl Myristate Manufacturing-Use Product at 25 and 40° C in Carbon Steel Containers for up to 48 Months (Document Control No. PED-SP-019-0706-R1)
Volume 6	Flammability / Flashpoint (Study No. 10633-07)
Volume 7	Analysis of Extractables and Leachables in HDPE Bottles and PP Caps Used to Package the Isopropyl Myristate [redacted] Formulation (Feasibility Study) (Report No. R061229B)
Volume 8	Photostability Protocol, Testing Schedule and Results for Isopropyl Myristate Solution (50% w/w), ANDA (Document Control No. PED-SP-022-0107-R0)
Volume 9	An Investigation of the UV/Visible Absorbance Properties of Isopropyl Myristate 50% Solution, Isopropyl Myristate and [redacted] (Document Control No.: PED-MIS-024-0307-R0)
Volume 10	Miscellaneous Toxicology Information.
Volume 11	Acute Dermal Toxicity Study in Rabbits (Study No. 7205-02)
Volume 12	Acute Dermal Toxicity Study in Rats (Study No. 7204-02)
Volume 13	Acute Eye Irritation Study in Rabbits (Study No. 7089-02)
Volume 14	Acute Dermal Irritation Study in Rabbits (Study No. 7090-02)
Volume 15	Skin Sensitization Study in Guinea Pigs (Study No. 13304-09)
Volume 16	28-Day Oral Toxicity Study in Rats with a 14-Day Recovery (Study No. 1016-001)
Volume 17	28-Day Dermal Toxicity Study in Pigs with a 14-Day Recovery (Study No.1016-002)
Volume 18	Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against *Rhipicephalus sanguineus* and *Dermacentor variabilis* on Dogs (Study No. PAH-09-0036)

Inert ingredient information may be entitled to confidential treatment

Volume 19	Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against *Rhipicephalus sanguineus* and *Dermacentor variabilis* on Cats (Study No. PAH-09-0065)
Volume 20	Pharmacokinetic, Safety and Tolerance Study of Resultz Pediculicide Rinse in Pediatric Subjects with *Pediculosis Capitis* (HTR Study No. 04-123941-108)
Volume 21	Environmental Fate Information

5. Company Contacts

MATTHEW R. SCHNEIDER

mschneider@gsblaw.com

GARVEY SCHUBERT BARER
fifth floor
1000 potomac street nw
washington, dc 20007-3501

TEL 202 965 7880 x1787

SUSAN PHILLIPS
sphillips@gsblaw.com
Science Advisor
TEL 202 965 7880 x1785

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 0.25 hours per response for registration and 0.25 hours per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the completed form to this address.

SELF-CERTIFICATION STATEMENT FOR THE PHYSICAL/CHEMICAL PROPERTIES (PR NOTICE 98-1)

Product Name:	**RESULTIX™**
Reg. No./File Symbol No. (if known) or Company No.	**86865-R**

SELF-CERTIFICATION STATEMENT:

I certify that the reported information on the "Summary Form" represents a true and accurate record of the test results of studies generated or owned by (Company Name): Piedmont Animal Health LLC and that the values of the properties reported are reliable. I further certify that such data was generated in substantial conformity with OPPTS Test Guidelines Series 830 Product Properties, applicable to my product, and in effect at the time of submission.

As a condition of registration, EPA may, by order, (1) withdraw a pending registration, (2) suspend the registration of this product without opportunity for hearing, or (3) assess civil penalties provided for in section 14 of FIFRA for violations of section 12(a)(2)(N) of FIFRA without opportunity for hearing, if I have not submitted to EPA within thirty (30) days of receipt of a request by the Agency, or within a specified time agreed to by the Agency, test results of studies summarized in the "Summary Form."

As a condition of registration, EPA may, by order, (1) withdraw a pending registration, (2) suspend the registration of this product without opportunity for hearing, or (3) assess civil penalties provided for in section 14 of FIFRA for violations of sections 12(a)(2)(N), 12(a)(2)(Q), or 12(a)(2)(R) of FIFRA without opportunity for hearing, if I fail to provide to EPA within thirty (30) days of receipt of a notification of error, or within a specified time agreed to by the Agency, information that EPA determines is required to correct the error.

Applicant's Name:	**Kathleen G. Palma, Ph.D.**		
Title:	**Vice President of Research & Development**	Telephone No.:	**336-544-0320 x 202**
Applicant's Signature: Kathleen G. Palma, Ph.D.		Date: 02 Dec 2009	

EPA Form 8570-37 (07/JAN/1998)

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

Paperwork Reduction Act Notice: The public reporting burden for this collection of information is estimated to average 1 hour per response for registration activities and 1 hour per response for reregistration and special review activities, including time for reading the instructions and completing the necessary forms. Send comments regarding burden estimate or any other aspect of this collection of information, including suggestions for reducing the burden to: Director, OPPE Information Management Division (2137), U.S. Environmental Protection Agency, 401 M Street, S.W., Washington, DC 20460. Do not send the completed form to this address.

SUMMARY OF THE PHYSICAL/CHEMICAL PROPERTIES (PR Notice 98-1)

1. Product Name: RESULTIX™		2. Reg. No. 86865-R
3. Company Name: Piedmont Animal Health LLC		4. Submission Date: December 3, 2009
5. First Submission [X] 6. Resubmission [ ]	7. Pesticide Type: Biochemical	10. Registration [X]
8. Formulated Manufacturing-Use Product [X] Or 9. End-Use Product [X]		11. Reregistration [ ]
13. Product Manager or Chemical Review Manager #/Name (If Known): L. Hollis, PM #91		12. Rereg Case #

14. Guideline Reference No.(Grn)/ Title	15. Value Or Qualitative Description / Method(s) Used Where Applicable and References	16. MRID or Report No.
Group B. Series 830-Physical and Chemical Properties (40 CFR 158.190)		
.6302 Color	TGAI: colorless	Volume 2
.6303 Physical State	TGAI & EP: liquid	Volume 2
.6304 Odor	TGAI: Practically odorless	Volume 2
.6313 Stability to normal & elevated temperature, metals	TGAI & EP: stable under elevated temperatures, acid, base, oxidation & light; TGAI stable to carbon steel containers.	Volumes 4, 5
.6315 Flammability/ Flame Extension	TGAI: flashpoint by closed cup164°C. EP: flash point by closed cup 85 deg C.	Volumes 2, 6
.6317 Storage Stability	TGAI and EP: stable up to 48 months	Volumes 2, 4, 5, 7, 8
.6320 Corrosion Characteristics	TGAI & EP: product containers stable	Volumes 2, 4, 5, 7
.7050 UV/Visible absorption	Very little or no absorbance exhibited with the UV-A and UV-B regions of the spectrum	Volumes 8, 9
.7100 Viscosity	TGAI: low viscosity; EP: 3.5 – 3.7 cP	Volume 2
.7200 Melting point/ range	TGAI: -3-5 deg C	Volume 2
.7220 Boiling point/ range	TGAI: 192.6 deg C at 20 mm Hg	Volume 2
.7300 Density/Relative Density/Bulk Density	TGAI: 0.85 g/mL at 25 deg C; EP: 0.85-0.86 g/mL	Volume 2
.7550 .7560 .7570 Partition Coefficient (n-octanol /water)	TGAI: 7.17 - 7.43	Volume 2
.7840 Water solubility	TGAI: Insoluble	Volume 2
.7950 Vapor Pressure	TGAI: <1 Torr at 20°C	Volume 2

EPA Form 8570-36 (07/JAN/1998)

JUSTIFICATION FOR SUBSTITUTIONS AND NOT CONDUCTING VARIOUS TESTS

Based on the results from the meeting at the EPA, only Tier I data requirements are to be fulfilled or otherwise justified as to why the data requirements were not fulfilled. Justifications are presented below; additional information is in the Volumes designated for each set.

Part 158.2030. Biochemical Pesticides Product Chemistry Data Requirements

Three requirements are NOT APPLICABLE; see table below. See Volume 2 for additional information.

Guideline Number	Test	Test Material	Justification for Not Applicable
830.6319	Miscibility	EP	The product is NOT an emulsifiable liquid to be diluted with petroleum solvents.
830.7000	pH	Both	Both the MP and the EP are NOT soluble or dispersible in water.
830.7520	Particle size, fiber length, and diameter distribution	MP	The MP is NOT a solid substance with a density of $<10^{-6}$ g/L or a fibrous test substance with a diameter of ≤ 0.1 um.

Part 158.2040. Biochemical Pesticides Residue Data Requirements

All required residue data are listed; however, all are NOT APPLICABLE because RESULTIX™ is not for food uses.

Part 158.2050. Biochemical Pesticides Human Health Assessment Data Requirements

Acute oral and inhalation toxicity studies utilizing the EP, RESULTIX™, as the test substance are not included in this pesticide registration submission package. In addition, studies utilizing IPM as the test substance were not found for some Tier I toxicology requirements. These guideline requirements are listed in the table below. The rationales for substituting other studies or for not conducting studies are either presented in the table (when brief) or presented in the body of text beginning on the next page. In addition, any study for which there is questionable relevancy, such as what "significant" exposure is, will also be discussed in this section.

Guideline Studies Not Submitted		
Gdln No.	**Description**	**Rationale**
RESULTIX™ as the Test Substance		
870.1100	Acute Oral Toxicity	See discussion below.
870.1300	Acute Inhalation Toxicity	See discussion below.
IPM as the Test Substance		
870.3100	90-Day Oral Toxicity	The use of RESULTIX™ will NOT result in repeated oral exposure to humans (From Test Note #6 in 40CFR Part §158.2050).
870.3250	90-Day Dermal Toxicity	See discussion below.
870.3465	90-Day Inhalation	See discussion below.
870.3700	Prenatal Developmental	See discussion below.
870.5300, 5375	*In Vitro* Mammalian Cell	See discussion below.

Acute Oral Toxicity - EP

Available IPM and [redacted] acute oral toxicity data and a subchronic 28-day repeat dose oral toxicity study with IPM in rats can be used to fulfill the requirements for an EP acute oral toxicity study.

Both IPM and [redacted] are minimally or nontoxic by the oral route of exposure (>13.6 g/kg bw and 4800 mg/kg bw, respectively). These two substances are not expected to chemically react together and each substance is not expected to potentiate the toxicological effects of the other. Consequently, a mixture of these two substances together would expect to result in an oral LD50 value that would be comparable to each individual oral LD50 value; the worst case is the LD50

value of [redacted] (4800 mg/kg bw), which would result in a Toxicity Category III for acute oral exposures. In addition, a 28-day repeat-dose oral toxicity study utilizing the EP resulted in minimal adverse effects at all doses of 3-15 mL/kg bw reversing after a 14-day recovery period.

Acute Inhalation Toxicity - EP

Available IPM and [redacted] acute inhalation toxicity data can be used to fulfill the requirements for an EP acute inhalation study. IPM is essentially nontoxic by the inhalation route of exposure (>33 mg/L; See Table 3). [redacted] is minimally toxic (LC50 = 2.7 – 8.7 mg/L) based on the results from a review and a 25 year old study[redacted]

IPM and [redacted] are not expected to chemically react together and each substance is not expected to potentiate the toxicological effects of the other. Consequently, a mixture of these two substances together would expect to result in an inhalation LC50 value that would be comparable to each individual inhalation LC50 value; the worst case would be the LC50 value of 2.7 mg/L from an old not-well documented study utilizing [redacted] as the test substance; this would result in a Toxicity Category III for acute inhalation exposures.

90-Day Dermal Toxicity - TGAI

Two 28-day dermal toxicity studies (CIR, 1982) and two dermal carcinogenicity studies were conducted with IPM as the test substance; in addition a 28-day dermal toxicity study in pigs was conducted with the EP. Localized lesions and inflammation were found at the dose sites of animals administered IPM for 28 days. However, there were no adverse effects, including dermal lesions at the dose site, observed in pigs administered the EP for 28 days or for mice administered IPM for lifespan. A 90-day dermal toxicity study would be intermediate in length to these two study types and consequently, the results would bracket the results from 90 days of exposure to IPM undiluted and localized dermal effects would likely be found after 90 days of exposure, but not systemic adverse effects. In addition, the pharmacokinetic study conducted in children (See summary in Physiological Fate section and Volume 20) indicates that absorption of IPM or [redacted] after potential dermal exposure from the typical use of RESULTIX™ is likely to be minimal or nonexistent.

90-Day Inhalation Toxicity – TGAI

A 90-day inhalation toxicity study testing a formulation containing IPM was reported in CIR (1982; see Table 4). The only reported adverse effects were increased absolute and relative lung weights. In addition, IPM is essentially nontoxic by the inhalation route of exposure (>33 mg/L).

This guideline study is required if there is a likelihood of significant levels of repeated inhalation exposure to the pesticide as a gas, vapor, or aerosol (From Test Note #8 in 40CFR Part §158.2050). Examples of significant levels of exposure (Test Note #9 of the table in 40CFR Part §158.2050) include occupational exposure or repeated application of insect repellents directly to the skin. The frequency of exposure (excluding route) for these examples can be used for determining whether the use of RESULTIX™ would result in significant levels of exposure to humans. The use of RESULTIX™ to control ticks on dogs and cats would not be considered significant because the use is intermittent and often seasonal, the brief application is only to observed ticks, not generally to the skin of the dog or cat, and the applicator is not deliberately exposed to the product as would be the case for an insect repellent. Consequently, because the use of RESULTIX™ will NOT result in significant levels of repeated inhalation exposures (and IPM is acutely nontoxic) this guideline study is NOT APPLICABLE for this submission.

Prenatal Developmental Toxicity – TGAI

The use of RESULTIX™ under widespread and commonly recognized practice is NOT expected to result in significant exposure to female humans, based on the examples given in Test Note #9 of the table in 40CFR Part §158.2050 (occupational exposure or repeated application of insect repellents directly to the skin). Consequently, the submission of this guideline study is NOT APPLICABLE for this pesticide registration submission.

In Vitro Mammalian Cell Assays - TGAI

The criteria for determining the relevancy of conducting the two *in vitro* mammalian cell assays are both NOT APPLICABLE. The active ingredient (or its metabolites) is NOT structurally related to a known mutagen or belongs to any chemical class of compounds containing a known mutagen. AND the use of RESULTIX™ is NOT likely to result in significant human exposure (See discussions above for the 90-Day Inhalation and Prenatal Developmental Toxicity guideline studies).

Two carcinogenicity studies, which are Tier III biochemical pesticide data requirements, were conducted in rabbits and mice utilizing IPM as the test substance. In addition, a reverse mutation

Acute Toxicity Fish – TGAI & EP

One acute 96-hour LC50 in fish was reported for IPM. Otherwise, there are no acute toxicity data available for IPM. The environmental fate data available indicate that IPM would be readily metabolized by aquatic organisms, although it is highly lipophilic and may potentially bioaccumulate. IPM is also semivolatile and would not persist in aquatic environments.

This study would be required for the EP because the inert ingredient, [redacted], has the potential for aquatic toxicity; although it is highly volatile. Data available for [redacted] concluded that [redacted] is expected to be toxic to fish.

Consequently, in lieu of conducting this study utilizing either the active ingredient or the EP, the Environmental Hazards statement on the draft label for both the active and the EP will have the following statement:

> "This pesticide is toxic to invertebrates and fish. Do not discharge this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage authority. For guidance, contact your State Water Board or Regional Office of the EPA."

Acute Oral and Dietary Toxicity Avian – TGAI & EP

These two studies are NOT APPLICABLE for the following reasons:

- The potential routes of exposure to birds from the commercial use of RESULTIX™ would be inhalation, dermal, and oral. The route of exposure for these two studies is oral (gavage and dietary); the other routes are not applicable. Because the EP is a colorless and practically odorless liquid product, it is unlikely that the EP would be gastronomically attractive for birds to ingest. Usually toxicity to birds is from ingestion of solid pesticide products that resemble seeds (e.g., granular formulation) or from ingestion of pesticide-coated seeds.
- The EP container is small (20 mL) and spillage of the colorless fluid would result in minimal amounts present on soil or plant surfaces. Birds are also unlikely to mistake accidental spillage of RESULTIX™ as water, particularly because of the small volume and rapid volatilization of IPM and [redacted].
- If perchance birds accidentally ingested RESULTIX™, they would likely exhale the [redacted] and metabolize the IPM rapidly.

- There were no citations found from a search of the Dialog database system for either IPM or [redacted] on avian species. This indicates that IPM and [redacted] appear not to be of concern relative to the toxicity of these two substances to avian species. Although [redacted] has the potential to be toxic to nontarget organisms, its bioavailability to birds from the use of RESULTIX™ is unlikely not bioavailable directly to birds through ingestion or dermal absorption, although it may be inhaled because [redacted] is volatile there are no available data indicating the [redacted] has an effect on or is even bioavailable to birds other than as part of the food chain; probably because of its high volatility and lack of gastronomic attraction to birds. That these two substances are not of concern to avian species is a reasonable assumption for environmental concerns for the EP because [redacted] is volatile and the EP is a liquid product.

Therefore, this study is NOT APPLICABLE.

Terrestrial Plant Toxicity Seedling Emergence and Vegetative Vigor – TGAI & EP

The target species fortRESULTIX™ is an insect and it is not for use on plants; the mode of action, the general use pattern, and the small size of the container preclude its effects on terrestrial plant toxicity. There were no citations found from a search of the Dialog database system for either IPM or [redacted]. This indicates that IPM and [redacted] appear not to be of concern relative to the toxicity of these two substances to vascular plants. Therefore, this study is NOT APPLICABLE.

Nontarget Insect Testing – TGAI

Because RESULTIX™ is used to kill ticks by desiccating them (solubilizing the cuticle), it is likely to have this affect on all insects and other arthropods. However, its use pattern and the small size of the container preclude its general use for the killing of indoor or outdoor arthropods, particularly honeybees. Therefore, this study is NOT APPLICABLE.

See Volume 21 for additional information.

From: paygovadmin@mail.doc.twai.gov [mailto:paygovadmin@mail.doc.twai.gov]
Sent: Tuesday, November 24, 2009 5:01 PM
To: kathy.palma@piedmontpharma.com
Subject: Pay.Gov Payment Confirmation

THIS IS AN AUTOMATED MESSAGE. PLEASE DO NOT REPLY.

Your transaction has been successfully completed.

Payment Summary

Application Name: PRIA Service Fees
Pay.gov Tracking ID: 2501PVHJ
Agency Tracking ID: 74090085940

Account Holder Name: jackie plemmons
Transaction Type: Sale
Billing Address: 204 muirs chapel rd
Billing Address 2: ste 200
City: greensboro
State/Province: NC
Zip/Postal Code: 27410
Country: USA
Card Type: Visa
Card Number: **********5806
Payment Amount: $4,135.00
Transaction Date: Nov 24, 2009 5:01:24 PM

Decision Number:
Registration Number:
Company Name: Piedmont Animal Health
Company Number: 86865
Action Code: B600

90-Day Inhalation Toxicity – TGAI

A 90-day inhalation toxicity study testing a formulation containing IPM was reported in CIR (1982; see Table 4). The only reported adverse effects were increased absolute and relative lung weights. In addition, IPM is essentially nontoxic by the inhalation route of exposure (>33 mg/L).

This guideline study is required if there is a likelihood of significant levels of repeated inhalation exposure to the pesticide as a gas, vapor, or aerosol (From Test Note #8 in 40CFR Part §158.2050). Examples of significant levels of exposure (Test Note #9 of the table in 40CFR Part §158.2050) include occupational exposure or repeated application of insect repellents directly to the skin. The frequency of exposure (excluding route) for these examples can be used for determining whether the use of RESULTIX™ would result in significant levels of exposure to humans. The use of RESULTIX™ to control ticks on dogs and cats would not be considered significant because the use is intermittent and often seasonal, the brief application is only to observed ticks, not generally to the skin of the dog or cat, and the applicator is not deliberately exposed to the product as would be the case for an insect repellent. Consequently, because the use of RESULTIX™ will NOT result in significant levels of repeated inhalation exposures (and IPM is acutely nontoxic) this guideline study is NOT APPLICABLE for this submission.

Prenatal Developmental Toxicity – TGAI

The use of RESULTIX™ under widespread and commonly recognized practice is NOT expected to result in significant exposure to female humans, based on the examples given in Test Note #9 of the table in 40CFR Part §158.2050 (occupational exposure or repeated application of insect repellents directly to the skin). Consequently, the submission of this guideline study is NOT APPLICABLE for this pesticide registration submission.

In Vitro Mammalian Cell Assays - TGAI

The criteria for determining the relevancy of conducting the two *in vitro* mammalian cell assays are both NOT APPLICABLE. The active ingredient (or its metabolites) is NOT structurally related to a known mutagen or belongs to any chemical class of compounds containing a known mutagen. AND the use of RESULTIX™ is NOT likely to result in significant human exposure (See discussions above for the 90-Day Inhalation and Prenatal Developmental Toxicity guideline studies).

Two carcinogenicity studies, which are **Tier III** biochemical pesticide data requirements, were conducted in rabbits and mice utilizing IPM as the test substance. In addition, a reverse mutation

assay was also conducted with IPM. The results from these three studies were negative. Consequently, conducting the two *in vitro* mammalian genotoxicity studies are not necessary because these *in vitro* studies are, in essence, screening studies to determine whether the test substance has the potential to be a carcinogen. In conclusion, based on available data and that relevancy criteria are both NOT APPLICABLE, the conduction of the two Tier I *in vitro* mammalian cell guideline studies is NOT APPLICABLE for this pesticide registration submission.

See Volume 10 for additional information.

Part 158.2060, Biochemical Pesticides Nontarget Organisms And Environmental Fate Data Requirements

Acute Toxicity Daphnids – TGAI & EP

No acute toxicity data for daphnids were available for IPM. The environmental fate data available indicate that IPM would be readily metabolized by aquatic organisms, although it is highly lipophilic and may potentially bioaccumulate. IPM is also semivolatile and would not persist in aquatic environments.

This study would be required for the EP because the inert ingredient, [redacted], has the potential for aquatic toxicity; although it is highly volatile. Data available for [redacted] concluded that [redacted] is expected to be toxic to daphnids.

Consequently, in lieu of conducting this study utilizing either the active ingredient or the EP, the Environmental Hazards statement on the draft label for both the active and the EP (See Volume 1) will have the following statement:

> "This pesticide is toxic to invertebrates and fish. Do not discharge this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage authority. For guidance, contact your State Water Board or Regional Office of the EPA."

Acute Toxicity Fish – TGAI & EP

One acute 96-hour LC50 in fish was reported for IPM. Otherwise, there are no acute toxicity data available for IPM. The environmental fate data available indicate that IPM would be readily metabolized by aquatic organisms, although it is highly lipophilic and may potentially bioaccumulate. IPM is also semivolatile and would not persist in aquatic environments.

This study would be required for the EP because the inert ingredient, [redacted], has the potential for aquatic toxicity; although it is highly volatile. Data available for [redacted] concluded that [redacted] is expected to be toxic to fish.

Consequently, in lieu of conducting this study utilizing either the active ingredient or the EP, the Environmental Hazards statement on the draft label for both the active and the EP will have the following statement:

> "This pesticide is toxic to invertebrates and fish. Do not discharge this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage authority. For guidance, contact your State Water Board or Regional Office of the EPA."

Acute Oral and Dietary Toxicity Avian – TGAI & EP

These two studies are NOT APPLICABLE for the following reasons:

- The potential routes of exposure to birds from the commercial use of RESULTIX™ would be inhalation, dermal, and oral. The route of exposure for these two studies is oral (gavage and dietary); the other routes are not applicable. Because the EP is a colorless and practically odorless liquid product, it is unlikely that the EP would be gastronomically attractive for birds to ingest. Usually toxicity to birds is from ingestion of solid pesticide products that resemble seeds (e.g., granular formulation) or from ingestion of pesticide-coated seeds.
- The EP container is small (20 mL) and spillage of the colorless fluid would result in minimal amounts present on soil or plant surfaces. Birds are also unlikely to mistake accidental spillage of RESULTIX™ as water, particularly because of the small volume and rapid volatilization of IPM and [redacted].
- If perchance birds accidentally ingested RESULTIX™, they would likely exhale the [redacted] and metabolize the IPM rapidly.

- There were no citations found from a search of the Dialog database system for either IPM or [redacted] on avian species. This indicates that IPM and [redacted] appear not to be of concern relative to the toxicity of these two substances to avian species. Although [redacted] has the potential to be toxic to nontarget organisms, its bioavailability to birds from the use of RESULTIX™ is unlikely not bioavailable directly to birds through ingestion or dermal absorption, although it may be inhaled because [redacted] is volatile there are no available data indicating the [redacted] has an effect on or is even bioavailable to birds other than as part of the food chain; probably because of its high volatility and lack of gastronomic attraction to birds. That these two substances are not of concern to avian species is a reasonable assumption for environmental concerns for the EP because [redacted] is volatile and the EP is a liquid product.

Therefore, this study is NOT APPLICABLE.

Terrestrial Plant Toxicity Seedling Emergence and Vegetative Vigor – TGAI & EP

The target species fortRESULTIX™ is an insect and it is not for use on plants; the mode of action, the general use pattern, and the small size of the container preclude its effects on terrestrial plant toxicity. There were no citations found from a search of the Dialog database system for either IPM or [redacted] This indicates that IPM and [redacted] appear not to be of concern relative to the toxicity of these two substances to vascular plants. Therefore, this study is NOT APPLICABLE.

Nontarget Insect Testing – TGAI

Because RESULTIX™ is used to kill ticks by desiccating them (solubilizing the cuticle), it is likely to have this affect on all insects and other arthropods. However, its use pattern and the small size of the container preclude its general use for the killing of indoor or outdoor arthropods, particularly honeybees. Therefore, this study is NOT APPLICABLE.

See Volume 21 for additional information.

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

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SUMMARY OF THE PHYSICAL/CHEMICAL PROPERTIES (PR Notice 98-1)

1. Product Name: RESULTIX™		2. Reg. No. 86865-R
3. Company Name: Piedmont Animal Health LLC		4. Submission Date: December 3, 2009
5. First Submission [X] 6. Resubmission [ ]	7. Pesticide Type: Biochemical	10. Registration [X]
8. Formulated Manufacturing-Use Product [X] Or 9. End-Use Product [X]		11. Reregistration [ ]
13. Product Manager or Chemical Review Manager #/Name (If Known): L. Hollis, PM #91		12. Rereg Case #

14. Guideline Reference No.(Grn)/ Title	15. Value Or Qualitative Description / Method(s) Used Where Applicable and References	16. MRID or Report No.
Group B. Series 830-Physical and Chemical Properties (40 CFR 158.190)		
.6302 Color	TGAI: colorless	Volume 2
.6303 Physical State	TGAI & EP: liquid	Volume 2
.6304 Odor	TGAI: Practically odorless	Volume 2
.6313 Stability to normal & elevated temperature, metals	TGAI & EP: stable under elevated temperatures, acid, base, oxidation & light; TGAI stable to carbon steel containers.	Volumes 4, 5
.6315 Flammability/ Flame Extension	TGAI: flashpoint by closed cup164°C. EP: flash point by closed cup 85 deg C.	Volumes 2, 6
.6317 Storage Stability	TGAI and EP: stable up to 48 months	Volumes 2, 4, 5, 7, 8
.6320 Corrosion Characteristics	TGAI & EP: product containers stable	Volumes 2, 4, 5, 7
.7050 UV/Visible absorption	Very little or no absorbance exhibited with the UV-A and UV-B regions of the spectrum	Volumes 8, 9
.7100 Viscosity	TGAI: low viscosity; EP: 3.5 – 3.7 cP	Volume 2
.7200 Melting point/ range	TGAI: -3-5 deg C	Volume 2
.7220 Boiling point/ range	TGAI: 192.6 deg C at 20 mm Hg	Volume 2
.7300 Density/Relative Density/Bulk Density	TGAI: 0.85 g/mL at 25 deg C; EP: 0.85-0.86 g/mL	Volume 2
.7550 .7560 .7570 Partition Coefficient (n-octanol /water)	TGAI: 7.17 - 7.43	Volume 2
.7840 Water solubility	TGAI: Insoluble	Volume 2
.7950 Vapor Pressure	TGAI: <1 Torr at 20°C	Volume 2

EPA Form 8570-36 (07/JAN/1998)

Form Approved OMB No. 2070-0060

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SELF-CERTIFICATION STATEMENT FOR THE PHYSICAL/CHEMICAL PROPERTIES (PR NOTICE 98-1)

Product Name:	**RESULTIX™**
Reg. No./File Symbol No. (if known) or Company No.	**86865-R**

SELF-CERTIFICATION STATEMENT:

I certify that the reported information on the "Summary Form" represents a true and accurate record of the test results of studies generated or owned by (Company Name): Piedmont Animal Health LLC and that the values of the properties reported are reliable. I further certify that such data was generated in substantial conformity with OPPTS Test Guidelines Series 830 Product Properties, applicable to my product, and in effect at the time of submission.

As a condition of registration, EPA may, by order, (1) withdraw a pending registration, (2) suspend the registration of this product without opportunity for hearing, or (3) assess civil penalties provided for in section 14 of FIFRA for violations of section 12(a)(2)(N) of FIFRA without opportunity for hearing, if I have not submitted to EPA within thirty (30) days of receipt of a request by the Agency, or within a specified time agreed to by the Agency, test results of studies summarized in the "Summary Form."

As a condition of registration, EPA may, by order, (1) withdraw a pending registration, (2) suspend the registration of this product without opportunity for hearing, or (3) assess civil penalties provided for in section 14 of FIFRA for violations of sections 12(a)(2)(N), 12(a)(2)(Q), or 12(a)(2)(R) of FIFRA without opportunity for hearing, if I fail to provide to EPA within thirty (30) days of receipt of a notification of error, or within a specified time agreed to by the Agency, information that EPA determines is required to correct the error.

Applicant's Name:	**Kathleen G. Palma, Ph.D.**		
Title:	**Vice President of Research & Development**	Telephone No.:	**336-544-0320 x 202**
Applicant's Signature: Kathleen G. Palma, Ph.D.		Date: 02 Dec 2009	

EPA Form 8570-37 (07/JAN/1998)

Form Approved OMB No. 2070-0060; 2070-0057; 2070-0107; 2070-0122; 2070-0164

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
1200 Pennsylvania Avenue, N.W.
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Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number	EPA Registration Number/File Symbol
Piedmont Animal Health LLC. 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410 Telephone: 336-544-0320 x 202	86865-R
Active Ingredient(s) and/or representative test compound(s) Isopropyl myristate	**Date** December 11, 2009
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Residential Outdoor Use, Nonfood	**Product Name** RESULTIX™

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

☒ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses.

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (i) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
Kathleen G. Palma, Ph.D.	12/14/09	Kathleen G. Palma, Ph.D. Vice President of Research & Development

EPA Form 8570-34 (12-2003) Electronic and Paper versions available. Submit only Paper version.

NOTES FOR DATA MATRIX

The data guidelines on the data matrix and summarized below are from those sections listed in 40CFR Part 158.2010 (Biochemical pesticides data requirements).

Part 158.2030. Biochemical Pesticides Product Chemistry Data Requirements

All required chemistry data for both the technical grade active ingredient/manufacturing-use product (TGAI/MP) and the end-use product (EP) are listed; relevant volume numbers are so indicated. If not applicable (NA), reasoning will be discussed in the Miscellaneous Chemistry Information Volume 2.

Part 158.2040. Biochemical Pesticides Residue Data Requirements

All required residue data are listed; however, all are NOT APPLICABLE because this product is NOT for food uses.

Part 158.2050. Biochemical Pesticides Human Health Assessment Data Requirements

All Tier I data requirements are listed; relevant volume numbers are so indicated. If not applicable (NA) or there is a substitution of one or more studies for a guideline study, the rationale for this will be discussed in the Miscellaneous Toxicology Information Volume 10. All Tier II and III data requirements are not listed as per the meeting between the EPA and Piedmont Animal Health.

Part 158.2060. Biochemical Pesticides Nontarget Organisms and Environmental Fate Data Requirements

All Tier I data requirements are listed; the relevant volume number is so indicated. If not applicable (NA) or there is a substitution of published information for a guideline study, the rationale for this will be discussed in the Environmental Fate Information Volume 21. All Tier II and III data requirements are not listed as per the meeting between the EPA and Piedmont Animal Health.

Part 158.2070. Biochemical Pesticides Product Performance Data Requirements

Because this is a specialized section, there is only one listing that is pertinent; relevant volume numbers are so indicated.

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 1 of 6
December 3, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	As listed under 40CFR Part 158.2030				
880.1100	Product identity and composition	47811701	Piedmont Animal Health		Also Volume 2
880.1200	Description of starting materials, production and formulation process	47811701	Piedmont Animal Health		Also Volume 2
880.1400	Discussion of formation of impurities	47811701	Piedmont Animal Health		Also Volume 2
830.1700	Preliminary analysis		Piedmont Animal Health		Volumes 2, 3
830.1750	Certified limits		Piedmont Animal Health		Volumes 2, 3
830.1800	Enforcement analytical method		Piedmont Animal Health		Volumes 2, 3
830.1900	Submittal of samples				Not Applicable (NA)
830.6302	Color		Piedmont Animal Health		Volume 2
830.6303	Physical state		Piedmont Animal Health		Volume 2
830.6304	Odor		Piedmont Animal Health		Volume 2
830.6313	Stability to normal and elevated temperature, metals & metal ions		Piedmont Animal Health		Volumes 4, 5
830.6315	Flammability		Piedmont Animal Health		Volumes 2, 6

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 Dec 2009

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

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DATA MATRIX

Date December 3, 2009	EPA Reg. No./File Symbol 86865-R	Page 2 of 6
Applicant's / Registrant's Name & Address Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	**Product** RESULTIX™	

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.6317	Storage stability		Piedmont Animal Health		Volumes 2, 4, 5, 7, 8
830.6319	Miscibility		Piedmont Animal Health		Volume 2
830.6320	Corrosion characteristics		Piedmont Animal Health		Volumes 4, 5, 7
830.7000	pH		Piedmont Animal Health		Volume 2
830.7050	UV/Visible absorption		Piedmont Animal Health		Volumes 8, 9
830.7100	Viscosity		Piedmont Animal Health		Volume 2
830.7200	Melting point/melting range		Piedmont Animal Health		Volume 2
830.7220	Boiling point/boiling range		Piedmont Animal Health		Volume 2
830.7300	Density/relative density/bulk density		Piedmont Animal Health		Volume 2
830.7520	Particle size, fiber length, and diameter distribution		Piedmont Animal Health		Volume 2
830.7550, 7560, 7570	Partition coefficient (octanol-water)		Piedmont Animal Health		Volume 2
830.7840	Water solubility; Column elution method; shake flask		Piedmont Animal Health		Volume 2
830.7950	Vapor pressure		Piedmont Animal Health		Volume 2

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 Dec 2009

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 3 of 6
December 3, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	As listed under 40CFR Part 158.2040				
860.1100	Chemical identity				All data requirements are NOT APPLICABLE because this EP is not for food uses.
860.1200	Directions for Use				
860.1300	Nature of the residue in --plants, livestock				
860.1340	Residue analytical method				
860.1360	Multiresidue method				
860.1400	Magnitude of the residue – potable water, fish, irrigated crops				
860.1460	Food handling				
860.1480	Meat/milk/poultry/eggs				
860.1500	Crop field trials				
860.1520	Processed food/feed				
860.1540	Anticipated Residues				
860.1550	Proposed tolerances				
860.1560	Reasonable grounds in support of the petition				
860.1650	Submittal of analytical reference standards				

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 Dec 2009

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 4 of 6
December 3, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Tier I	**As listed under 40CFR Part 158.2050**				
870.1100	Acute oral toxicity		Piedmont Animal Health		Volume 10
870.1200	Acute dermal toxicity		Piedmont Animal Health		Volumes 10, 11, 12
870.1300	Acute inhalation toxicity		Piedmont Animal Health		Volume 10
870.2400	Acute eye irritation		Piedmont Animal Health		Volumes 10, 13
870.2500	Acute dermal irritation		Piedmont Animal Health		Volumes 10, 14
870.2600	Skin sensitization		Piedmont Animal Health		Volumes 10, 15
None	Hypersensitivity Incidents		Piedmont Animal Health		Volume 10
870.3050	Repeated dose 28-day oral toxicity		Piedmont Animal Health		Volumes 10, 16
870.3100	90-day oral toxicity		Piedmont Animal Health		Volume 10

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 Dec 2009

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DATA MATRIX

Date December 3, 2009	EPA Reg. No./File Symbol 86865-R	Page 5 of 6
Applicant's / Registrant's Name & Address Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	**Product** RESULTIX™	

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.3200	21/28-day dermal toxicity		Piedmont Animal Health		Volumes 10, 17
870.3250	90-day dermal toxicity		Piedmont Animal Health		Volume 10
870.3465	90-day inhalation toxicity		Piedmont Animal Health		Volume 10
870.3700	Prenatal developmental toxicity		Piedmont Animal Health		Volume 10
870.4200	Carcinogenicity		Piedmont Animal Health		Volume 10
870.5100	Bacterial reverse mutation test		Piedmont Animal Health		Volume 10
870.5300	*In vitro* mammalian cell gene mutation test		Piedmont Animal Health		Volume 10
870.5375	*In vitro* mammalian chromosome aberration test		Piedmont Animal Health		Volume 10
Special Testing					
870.7200	Companion animal safety		Piedmont Animal Health		Volumes 18, 19
870.7485	Metabolism and pharmacokinetics		Piedmont Animal Health		Volumes 10, 20

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 DEC 2009

EPA MEETING MINUTES FOR APRIL 30, 2009 AND EPA RESPONSE LETTER

On April 30, 2009, three Piedmont Animal Health representatives met with two EPA representatives of the Biochemical Pesticides Branch. The meeting minutes were drafted by Piedmont and reviewed by the EPA, which in return responded with a letter. Copies of these two documents begin on the next page.

Inert ingredient information may be entitled to confidential treatment

Meeting Minutes

EPA Meeting April 30, 2009

Attendees:

Angela Gonzales
Leonard Cole
Kathy Palma
Doug Hepler
Bert Clayton

Members of Piedmont Animal Health (PAH) met with EPA representatives Leonard Cole and Angela Gonzales on April 30, 2009 at 2:00p.m. EST at the EPA facility in Crystal City, MD. The purpose of the meeting was to discuss the registration path forward for PAH's new nonpesticidal tick spray (50% Isopropyl Myristate). The meeting lasted approximately 1 hour and the following points were discussed:

Introductions

1. EPA will accept a reduced data set approach for this registration
2. Biochemical classification has been obtained by Piedmont
3. Product description:

   Active – 50% IPM

   Excipient – 50%[redacted]

4. No label yet, no CSF. Could be "as needed" tick spray
5. Dr. Kathy Palma provides history of Resultz development
   a. Have safety profile in humans from clinical
   b. Mechanism – dissolves cuticular wax
   c. < 4 hrs ticks die, some may be moribund but will die soon after

Product ingredient source information may be entitled to confidential treatment

Inert ingredient information may be entitled to confidential treatment

6. Source – Active derived from [redacted], [redacted]

   [redacted]

7. Piedmont should clear [redacted] under ECFR – check 40CFR 189-30 and contact PV Shaw or Kerry Grenstad - can replace with other Excipient or go to "inerts" branch
8. Leonard reports that inert branch is fast, because it's non-food use
9. Data Requirements – see handout provided by Angela Gonzales
   a. Satisfy technical and end-use date requirement
   b. Address all data requirements – say "why" if N/A
   c. Include units in CSFs
   d. Supplier needs to send all "impurities" even if proprietary
   e. We can use references – be specific
10. 86-5 – Formatted data requirement to pass administrative screen
11. Non-food use :
12. Address Tier I only – Tox end use – "six pack"
13. If literature is used, use info doc – guidance to use literature references
    a. Peer-reviewed
    b. Scientific credible data
    c. Site MRID
14. There are fees involved now (B6)
15. Tox discussion – provide "exposure" discussion if endpoints identified. EPA will do risk assessment.
16. No studies are waived unless

a. No exposure

b. Very acidic or basic

c. We will not be "granted" waiver

17. Can use PK studies form Resultz

18. Talk about global use of RESULTZ™ and safety profile

19. Eco-requirements – use environmental assessment

    a. Write a rationale to not require a bird study

    b. Address fish and invertebrate studies because dogs do swim

    c. Concern is endangered species

20. Tier 2 probably not required

21. Study proposal – makes sure data shows 90% reduction. (efficacy)

22. Study outline – how to address wet dogs. Label may need to say "apply to dry dog".

23. Companion animal studies – requirement, Angela will look into this and respond to PAH.

    Can we tie into efficacy

24. Register end-use only

25. No requirement to submit a protocol – use typical protocol format

26. B-600 non food use new product up to 12 months for an answer

    a. $15,700 apply waiver/ under PRIA2 – pest- reg. act

    b. Fill out walver for small business

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

JUN 17 2009

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Kathleen G. Palma, Ph.D.
Regulatory Affairs, Consultant
Piedmont Animal Health
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

Dear Dr. Palma:

Subject: Response to Notes dated June 8, 2009
Meeting with Piedmont Animal Health

The Agency is in receipt of the meeting notes from the April 30 pre-registration meeting with Piedmont Animal Health concerning a new product containing the unregistered biochemical, isopropyl myristate. The following is the Agency's official response to the meeting notes per the action items as listed in your letter:

1) Piedmont Animal Health Note:

Piedmont Animal Health received a biochemical classification for this product. Consequently the EPA will accept a reduced safety data set for registration which would only include Tier I safety requirements as outlined in 158.2030, the Biochemical pesticides product chemistry data requirements table. Tier II safety requirements will probably not required.

Agency Response

There are no Tiers for product chemistry. All product chemistry data guidelines must be satisfied for both the Technical Grade Active Ingredient (TGAI) and the End Use Product (EP). As you stated in your note above, please refer to 40 CFR § 158.2030 for biochemical pesticides product chemistry data requirements.

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Inert ingredient information may be entitled to confidential treatment

Product ingredient source information may be entitled to confidential treatment

2) Piedmont Animal Health Note:

The tick spray consists of 50% Isopropyl myristate, the active and 50% [redacted], the excipient. There is no label or Confidential Certificate of Formulation (CSF). The spray could be used on an "as needed" basis. EPA instructed PAH that [redacted] should be cleared as the excipient under 40 CFR § 189.30 and contact PV Shaw or Kerry Grenstad. PAH can replace with another excipient or go to the "inerts" branch if necessary. EPA acknowledged that the "inerts" branch would be fast since this tick spray is a non-food use.

Agency Response

All pesticide products must bear a label with all of the required labeling language. Please refer to 40 CFR § 156-Labeling Requirements for Pesticides and Devices. You must have a Confidential Statement of Formula (CSF) for your product, and it must be completely filled out. The CSF EPA form 8570-4. Tips for avoiding Confidential Statement of Formula or Product Chemistry issues with Biopesticides can be found via the following internet link: www.epa.gov/pesticides/biopesticides/regtools/index.htm. This aforementioned link is also a good source for all issues related to registering biopesticides. The Agency is in agreement with your understanding that you must have your inert ingredients cleared by the "Inerts Assessment Branch". You may contact Prakashchandra (PV) Shah at 703.308.1846. For clarification purposes, BPPD cannot speak as to the speed of clearance of any inert ingredients. Inert Assessment Branch is in a different division.

3 Piedmont Animal Health Note:

Piedmont Animal Health gave a brief history of the tick spray's development. The tick spray has a safe profile in humans because Phase 3 clinical trials with CDER/FDA under INAD 66,651 were conducted with the same product as a head lice product for humans. The clinical studies with the safety profiles will be submitted to support safety with humans for the tick product. Once the product is sprayed on a tick, death begins less than 4 hours after the tick is sprayed. Some ticks may be moribund but will die within 24 hours. The isopropyl myristate, a fatty acid ester [redacted] EPA provided PAH with a handout listing the data requirements. EPA mentioned some of those requirements. Technical and end-use data requirements should be satisfied. All data requirements should be addressed even if those requirements are not applicable. An explanation as to why the data requirement is not applicable should be provided. Units should be included with the CSF. All "impurities should be sent by the supplier even if that information is proprietary. As long as reference are specific, EPA can use them.

Agency Reponse

The Agency is in agreement with you note above with the exception that all data requirements MUST be addressed, and the references that you have MUST be submitted with your application for registration.

4 Piedmont Animal Health Note:

Per 86.5, formatted data requirements must pass administrative screen for formatting. If literature is used in the submission, use info doc as guidance to use literature references. The type of acceptable cited literature would be peer-reviewed articles, scientifically credible data and a citation from the MRID.

Agency Response

The Agency is in agreement with the discussion as outlined above. All data submitted must be formatted according to PR Notice 86-5.

5 Piedmont Animal Health Note:

Since this tick product is considered a B-600 (non-food use new product) the cost is $15,700 however PAH may qualify for a small business waiver under PRIA2 (Pesticide Registration Act). No studies are waived unless there is no exposure or the product is very acidic or basic. Given these criteria, PAH will not be granted a waiver for the tick spray.

Agency Reponse

The Agency is in agreement with the discussion that your product is a new active ingredient non-food use and would be classified as a B600 under Pesticide Registration Improvement Act (PRIA 2). PAH stated that the fee would be $15,700. The Agency is in agreement with your note that PAH may qualify for a small business waiver. The Agency is in agreement that no guideline studies are waived unless there is no exposure.

6 Piedmont Animal Health Note:

For the toxicology discussion, exposure should be discussed provided endpoints are identified. EPA will do the risk assessment. The pharmacokinetic studies done for the development of the human head louse product (Resultz™) can be used to support the tick spray product for dogs. The global use of Resultz™ and the post-marketing safety profile can also be used to support the safety of the tick spray.

Agency Response

It is important to note that all Tier I data requirements MUST be addressed individually. The safety profile is contingent upon Biopesticide and Pollution Prevention Division's review of the data and the acceptability of those data.

7) Piedmont Animal Health Note:

The Environmental Assessment completed for Resultz™ should address the ecological requirements. A rationale should be written why a bird study is not required given that birds should not come into contact with this product. Fish and aquatic invertebrate studies should be addressed because dogs do swim. EPA is concerned for endangered species.

Agency Response

The Agency is in agreement with the note above.

8) PRIA Category

In the efficacy study there should be a 90% reduction in ticks. Given that the tick spray is most efficacious when sprayed on dry dogs, the label may need to read "apply to dry dog". Ms. Gonzales stated that she would look into the requirement for companion animal safety and respond back to PAH. PAH stated that the safety could be tied into the efficacy study with possible physical exams and clinical blood chemistries. There is no requirement to submit the efficacy protocol but the typical protocol format should be used. The end use product is the only thing to be registered.

Agency Response

The Agency is in agreement with the note above. Also you must address companion animal study according to 40 CFR § 158.2050.

Should you have any questions regarding this response to your meeting notes, you may contact Leonard Cole directly at 703.305.5412 or via email at cole.leonard@epa.gov . We hope that you find this information helpful.

Sincerely,

Linda A. Hollis, Chief
Biochemical Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)

TRANSMITTAL DOCUMENT

1. Name and Address of Submitter

Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

Agent

Kathleen G. Palma, Ph.D.
Vice President of Research & Development
Email: kpalma@piedmontpharma.com
Telephone: 336-544-0320 x 202

2. Regulatory Action for which this Package is Submitted

Pesticide Registration Submission
RESULTIX™
EPA File Symbol No. 86865-R
Registration for the End-Use Product

3. Transmittal Date

December 3, 2009

4. List of Submitted Documents

Volume 1 Administrative Materials

- Transmittal Document
- EPA Form 8570-1 (Application for Pesticide Registration)
- EPA Form 8570-4 (Confidential Statement of Formula) – one for the active, one for the EP
- Draft labels, 2 sets (5 copies each; one set for the active, one set for the EP)
- EPA Form 8570-35 (Data Matrix) (with Notes)
- EPA Form 8570-36 (Summary of the Physical/Chemical Properties)
- EPA Form 8570-37 (Self-Certification Statement for the Physical/Chemical Properties)
- EPA Form 3540-8 (Application for Registration of Pesticide-Producing and Device-Producing Establishment) (2 pages)
- Justification for Substitutions and not Conducting Various Tests
- EPA Meeting Minutes for April 30, 2009 and EPA Response Letter

- PRIA2 Fee Waiver Documentation, including EPA Small Business Certification Form and verification of online payment of 25% of registration fee

Volume 2	Miscellaneous Chemistry Information
Volume 3	Determination of the Percent Active Ingredient and Impurities in Five Batches of Isopropyl Myristate Technical Grade Material (EN-CAS Project #09-0033)
Volume 4	Report for the Forced Degradation Study on Isopropyl Myristate Drug Substance and Isopropyl Myristate Solution (50% w/w) by GC (Document Control No. PED-AR-014-0105-R0)
Volume 5	Storage Stability of Isopropyl Myristate Manufacturing-Use Product at 25 and 40° C in Carbon Steel Containers for up to 48 Months (Document Control No. PED-SP-019-0706-R1)
Volume 6	Flammability / Flashpoint (Study No. 10633-07)
Volume 7	Analysis of Extractables and Leachables in HDPE Bottles and PP Caps Used to Package the Isopropyl Myristate [redacted] Formulation (Feasibility Study) (Report No. R061229B)
Volume 8	Photostability Protocol, Testing Schedule and Results for Isopropyl Myristate Solution (50% w/w), ANDA (Document Control No. PED-SP-022-0107-R0)
Volume 9	An Investigation of the UV/Visible Absorbance Properties of Isopropyl Myristate 50% Solution, Isopropyl Myristate and [redacted] (Document Control No.: PED-MIS-024-0307-R0)
Volume 10	Miscellaneous Toxicology Information.
Volume 11	Acute Dermal Toxicity Study in Rabbits (Study No. 7205-02)
Volume 12	Acute Dermal Toxicity Study in Rats (Study No. 7204-02)
Volume 13	Acute Eye Irritation Study in Rabbits (Study No. 7089-02)
Volume 14	Acute Dermal Irritation Study in Rabbits (Study No. 7090-02)
Volume 15	Skin Sensitization Study in Guinea Pigs (Study No. 13304-09)
Volume 16	28-Day Oral Toxicity Study in Rats with a 14-Day Recovery (Study No. 1016-001)
Volume 17	28-Day Dermal Toxicity Study in Pigs with a 14-Day Recovery (Study No.1016-002)
Volume 18	Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against *Rhipicephalus sanguineus* and *Dermacentor variabilis* on Dogs (Study No. PAH-09-0036)

Inert ingredient information may be entitled to confidential treatment

Volume 19	Pivotal Study to Determine Safety and Efficacy of Isopropyl Myristate (IPM) Tick Spray against *Rhipicephalus sanguineus* and *Dermacentor variabilis* on Cats (Study No. PAH-09-0065)
Volume 20	Pharmacokinetic, Safety and Tolerance Study of Resultz Pediculicide Rinse in Pediatric Subjects with *Pediculosis Capitis* (HTR Study No. 04-123941-108)
Volume 21	Environmental Fate Information

5. Company Contacts

MATTHEW R. SCHNEIDER

mschneider@gsblaw.com

GARVEY SCHUBERT BARER
fifth floor
1000 potomac street nw
washington, dc 20007-3501

TEL 202 965 7880 x1787

SUSAN PHILLIPS
sphillips@gsblaw.com
Science Advisor
TEL 202 965 7880 x1785

JUSTIFICATION FOR SUBSTITUTIONS AND NOT CONDUCTING VARIOUS TESTS

Based on the results from the meeting at the EPA, only Tier 1 data requirements are to be fulfilled or otherwise justified as to why the data requirements were not fulfilled. Justifications are presented below; additional information is in the Volumes designated for each set.

Part 158.2030. Biochemical Pesticides Product Chemistry Data Requirements

Three requirements are NOT APPLICABLE; see table below. See Volume 2 for additional information.

Guideline Number	Test	Test Material	Justification for Not Applicable
830.6319	Miscibility	EP	The product is NOT an emulsifiable liquid to be diluted with petroleum solvents.
830.7000	pH	Both	Both the MP and the EP are NOT soluble or dispersible in water.
830.7520	Particle size, fiber length, and diameter distribution	MP	The MP is NOT a solid substance with a density of $<10^{-6}$ g/L or a fibrous test substance with a diameter of $\leq$0.1 um.

Part 158.2040. Biochemical Pesticides Residue Data Requirements

All required residue data are listed; however, all are NOT APPLICABLE because RESULTIX™ is not for food uses.

Part 158.2050. Biochemical Pesticides Human Health Assessment Data Requirements

Acute oral and inhalation toxicity studies utilizing the EP, RESULTIX™, as the test substance are not included in this pesticide registration submission package. In addition, studies utilizing IPM as the test substance were not found for some Tier I toxicology requirements. These guideline requirements are listed in the table below. The rationales for substituting other studies or for not conducting studies are either presented in the table (when brief) or presented in the body of text beginning on the next page. In addition, any study for which there is questionable relevancy, such as what "significant" exposure is, will also be discussed in this section.

Guideline Studies Not Submitted		
Gdln No.	**Description**	**Rationale**
RESULTIX™ as the Test Substance		
870.1100	Acute Oral Toxicity	See discussion below.
870.1300	Acute Inhalation Toxicity	See discussion below.
IPM as the Test Substance		
870.3100	90-Day Oral Toxicity	The use of RESULTIX™ will NOT result in repeated oral exposure to humans (From Test Note #6 in 40CFR Part §158.2050).
870.3250	90-Day Dermal Toxicity	See discussion below.
870.3465	90-Day Inhalation	See discussion below.
870.3700	Prenatal Developmental	See discussion below.
870.5300, 5375	*In Vitro* Mammalian Cell	See discussion below.

Acute Oral Toxicity - EP

Available IPM and [redacted] acute oral toxicity data and a subchronic 28-day repeat dose oral toxicity study with IPM in rats can be used to fulfill the requirements for an EP acute oral toxicity study.

Both IPM and [redacted] are minimally or nontoxic by the oral route of exposure (>13.6 g/kg bw and 4800 mg/kg bw, respectively). These two substances are not expected to chemically react together and each substance is not expected to potentiate the toxicological effects of the other. Consequently, a mixture of these two substances together would expect to result in an oral LD50 value that would be comparable to each individual oral LD50 value; the worst case is the LD50

value of [redacted] (4800 mg/kg bw), which would result in a Toxicity Category III for acute oral exposures. In addition, a 28-day repeat-dose oral toxicity study utilizing the EP resulted in minimal adverse effects at all doses of 3-15 mL/kg bw reversing after a 14-day recovery period.

Acute Inhalation Toxicity - EP

Available IPM and [redacted] acute inhalation toxicity data can be used to fulfill the requirements for an EP acute inhalation study. IPM is essentially nontoxic by the inhalation route of exposure (>33 mg/L; See Table 3). [redacted] is minimally toxic (LC50 = 2.7 – 8.7 mg/L) based on the results from a review and a 25 year old study; [redacted]

IPM and [redacted] are not expected to chemically react together and each substance is not expected to potentiate the toxicological effects of the other. Consequently, a mixture of these two substances together would expect to result in an inhalation LC50 value that would be comparable to each individual inhalation LC50 value; the worst case would be the LC50 value of 2.7 mg/L from an old not-well documented study utilizing [redacted] as the test substance; this would result in a Toxicity Category III for acute inhalation exposures.

90-Day Dermal Toxicity - TGAI

Two 28-day dermal toxicity studies (CIR, 1982) and two dermal carcinogenicity studies were conducted with IPM as the test substance; in addition a 28-day dermal toxicity study in pigs was conducted with the EP. Localized lesions and inflammation were found at the dose sites of animals administered IPM for 28 days. However, there were no adverse effects, including dermal lesions at the dose site, observed in pigs administered the EP for 28 days or for mice administered IPM for lifespan. A 90-day dermal toxicity study would be intermediate in length to these two study types and consequently, the results would bracket the results from 90 days of exposure to IPM undiluted and localized dermal effects would likely be found after 90 days of exposure, but not systemic adverse effects. In addition, the pharmacokinetic study conducted in children (See summary in Physiological Fate section and Volume 20) indicates that absorption of IPM or after potential dermal exposure from the typical use of RESULTIX™ is likely to be minimal or nonexistent.

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Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Tier I	**As listed under 40CFR Part 158.2060**				
850.1010	Aquatic invertebrate acute toxicity, freshwater daphnids		Piedmont Animal Health		Volume 21
850.1075	Fish acute toxicity test, freshwater and marine		Piedmont Animal Health		Volume 21
850.2100	Avian acute oral toxicity		Piedmont Animal Health		Volume 21
850.2200	Avian dietary toxicity		Piedmont Animal Health		Volume 21
850.4100	Terrestrial plant toxicity, seedling emergence		Piedmont Animal Health		Volume 21
850.4150	Terrestrial plant toxicity, vegetative vigor		Piedmont Animal Health		Volume 21
880.4350	Nontarget insect testing		Piedmont Animal Health		Volume 21
	As listed under 40CFR Part 158.2070				
810.3300	Treatments to Control Pests of Humans and Pets		Piedmont Animal Health		Volumes 18, 19

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 DEC 2009

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DATA MATRIX

Date December 11, 2009	**EPA Reg. No./File Symbol** 86865-R	**Page 1 of 6**
Applicant's / Registrant's Name & Address Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	**Product** RESULTIX™	

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	As listed under 40CFR Part 158.2030				
880.1100	Product identity and composition	47811701	Piedmont Animal Health	Own	Also Volume 2
880.1200	Description of starting materials, production and formulation process	47811701	Piedmont Animal Health	Own	Also Volume 2
880.1400	Discussion of formation of impurities	47811701	Piedmont Animal Health	Own	Also Volume 2
830.1700	Preliminary analysis		Piedmont Animal Health	Own	Volumes 2, 3
830.1750	Certified limits		Piedmont Animal Health	Own	Volumes 2, 3
830.1800	Enforcement analytical method		Piedmont Animal Health	Own	Volumes 2, 3
830.1900	Submittal of samples				Not Applicable (NA)
830.6302	Color		Piedmont Animal Health	Own	Volume 2
830.6303	Physical state		Piedmont Animal Health	Own	Volume 2
830.6304	Odor		Piedmont Animal Health	Own	Volume 2
830.6313	Stability to normal and elevated temperature, metals & metal ions		Piedmont Animal Health	Own	Volumes 4, 5
830.6315	Flammability		Piedmont Animal Health	Own	Volumes 2, 6

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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DATA MATRIX

Date December 11, 2009	EPA Reg. No./File Symbol 86865-R	Page 2 of 6
Applicant's / Registrant's Name & Address Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	**Product** RESULTIX™	

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.6317	Storage stability		Piedmont Animal Health	Own	Volumes 2, 4, 5, 7, 8
830.6319	Miscibility		Piedmont Animal Health	Own	Volume 2
830.6320	Corrosion characteristics		Piedmont Animal Health	Own	Volumes 4, 5, 7
830.7000	pH		Piedmont Animal Health	Own	Volume 2
830.7050	UV/Visible absorption		Piedmont Animal Health	Own	Volumes 8, 9
830.7100	Viscosity		Piedmont Animal Health	Own	Volume 2
830.7200	Melting point/melting range		Piedmont Animal Health	Own	Volume 2
830.7220	Boiling point/boiling range		Piedmont Animal Health	Own	Volume 2
830.7300	Density/relative density/bulk density		Piedmont Animal Health	Own	Volume 2
830.7520	Particle size, fiber length, and diameter distribution		Piedmont Animal Health	Own	Volume 2
830.7550, 7560, 7570	Partition coefficient (octanol-water)		Piedmont Animal Health	Own	Volume 2
830.7840	Water solubility; Column elution method; shake flask		Piedmont Animal Health	Own	Volume 2
830.7950	Vapor pressure		Piedmont Animal Health	Own	Volume 2

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 3 of 6
December 11, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	As listed under 40CFR Part 158.2040				
860.1100	Chemical identity				All data requirements are NOT APPLICABLE because this EP is not for food uses.
860.1200	Directions for Use				
860.1300	Nature of the residue in --plants, livestock				
860.1340	Residue analytical method				
860.1360	Multiresidue method				
860.1400	Magnitude of the residue – potable water, fish, irrigated crops				
860.1460	Food handling				
860.1480	Meat/milk/poultry/eggs				
860.1500	Crop field trials				
860.1520	Processed food/feed				
860.1540	Anticipated Residues				
860.1550	Proposed tolerances				
860.1560	Reasonable grounds in support of the petition				
860.1650	Submittal of analytical reference standards				

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 4 of 6
December 11, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Tier I	**As listed under 40CFR Part 158.2050**				
870.1100	Acute oral toxicity		Piedmont Animal Health	Own	Volume 10
870.1200	Acute dermal toxicity		Piedmont Animal Health	Own	Volumes 10, 11, 12
870.1300	Acute inhalation toxicity		Piedmont Animal Health	Own	Volume 10
870.2400	Acute eye irritation		Piedmont Animal Health	Own	Volumes 10, 13
870.2500	Acute dermal irritation		Piedmont Animal Health	Own	Volumes 10, 14
870.2600	Skin sensitization		Piedmont Animal Health	Own	Volumes 10, 15
None	Hypersensitivity Incidents		Piedmont Animal Health	Own	Volume 10
870.3050	Repeated dose 28-day oral toxicity		Piedmont Animal Health	Own	Volumes 10, 16
870.3100	90-day oral toxicity		Piedmont Animal Health	Own	Volume 10

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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Date	EPA Reg. No./File Symbol	Page 5 of 6
December 11, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.3200	21/28-day dermal toxicity		Piedmont Animal Health	Own	Volumes 10, 17
870.3250	90-day dermal toxicity		Piedmont Animal Health	Own	Volume 10
870.3465	90-day inhalation toxicity		Piedmont Animal Health	Own	Volume 10
870.3700	Prenatal developmental toxicity		Piedmont Animal Health	Own	Volume 10
870.4200	Carcinogenicity		Piedmont Animal Health	Own	Volume 10
870.5100	Bacterial reverse mutation test		Piedmont Animal Health	Own	Volume 10
870.5300	*In vitro* mammalian cell gene mutation test		Piedmont Animal Health	Own	Volume 10
870.5375	*In vitro* mammalian chromosome aberration test		Piedmont Animal Health	Own	Volume 10
Special Testing					
870.7200	Companion animal safety		Piedmont Animal Health	Own	Volumes 18, 19
870.7485	Metabolism and pharmacokinetics		Piedmont Animal Health	Own	Volumes 10, 20

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 6 of 6
December 11, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Tier I	**As listed under 40CFR Part 158.2060**				
850.1010	Aquatic invertebrate acute toxicity, freshwater daphnids		Piedmont Animal Health	Own	Volume 21
850.1075	Fish acute toxicity test, freshwater and marine		Piedmont Animal Health	Own	Volume 21
850.2100	Avian acute oral toxicity		Piedmont Animal Health	Own	Volume 21
850.2200	Avian dietary toxicity		Piedmont Animal Health	Own	Volume 21
850.4100	Terrestrial plant toxicity, seedling emergence		Piedmont Animal Health	Own	Volume 21
850.4150	Terrestrial plant toxicity, vegetative vigor		Piedmont Animal Health	Own	Volume 21
880.4350	Nontarget insect testing		Piedmont Animal Health	Own	Volume 21
	As listed under 40CFR Part 158.2070				
810.3300	Treatments to Control Pests of Humans and Pets		Piedmont Animal Health	Own	Volumes 18, 19

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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Biochemical Pesticide Human Health Assessment Data Requirements
(From 40CFR §158.2050 and Listed on Data Matrix in Volume 1)

As per the meeting minutes that Piedmont Animal Health and the EPA agreed to, the registration of RESULTIX™ end-use product (EP) requires fulfillment of requirements for both the EP and the technical-grade active ingredient/manufacturing-use product (TGAI/MP). Below are the Tier I toxicology requirements for supporting the registration of this EP as a biochemical pesticide. This table describes the material (TGAI, EP, or both) tested to fulfill these requirements, whether the study is required (R) or conditionally required (C) for the general use pattern for RESULTIX™ (Residential Outdoor Non-Food Use), the corresponding test note number (based on footnotes for the table in 40CFR §158.2050), and the volume containing pertinent information.

Table 1. Toxicity Data Requirements

Gdln No.	Description	Material Tested	Required (R) or Conditional (C) & Note #[a]		Volume
870.1100	Acute Oral Toxicity	Both	R	1	10
870.1200	Acute Dermal Toxicity	Both	R	1, 2	10, 11, 12
870.1300	Acute Inhalation Toxicity	Both	R	3	10
870.2400	Acute Eye Irritation	Both	R	2	10, 13
870.2500	Acute Dermal Irritation	Both	R	1, 2	10, 14
870.2600	Skin Sensitization	Both	R	2, 4	10, 15
None	Hypersensitivity Incidents	Both	R	5	10
870.3100	90-Day Oral Toxicity	TGAI	C	6	10
870.3250	90-Day Dermal Toxicity	TGAI	C	7	10
870.3465	90-Day Inhalation Toxicity	TGAI	C	8	10
870.3700	Prenatal Developmental Toxicity	TGAI	C	9	10
870.5100	Bacterial Reverse Mutation Test	TGAI	C	10	10
870.5300, 5375	*In Vitro* Mammalian Cell Assay	TGAI	C	10	10
870.7200	Companion Animal Safety	EP	R	11	18, 19

(a) See next page for notes.

The following Test Notes are taken directly from 40CFR Part §158.2050. Relevancy pertains to the EPA general use pattern, actual use and properties of IPM or RESULTIX™. If considered not relevant or if relevancy is questionable (?), further discussion is presented in this Volume 10.

Table 2. Test Notes to Determine Relevancy

Description	Relevant	Study
1. Required unless the test material is a gas or highly volatile.	Yes	Acute oral/dermal
2. Required unless test material is corrosive to skin or has pH <2 or >11.5.	Yes	Acute dermal
3. Required when the pesticide, under conditions of use, would result in respirable material (e.g., gas, volatile substance or aerosol/particulate)...	Yes	Acute inhalation
4. Required if repeated contact with human skin is likely to occur under conditions of use.	Yes	Dermal, Sensitization
5. Hypersensitivity (HS) incidents must be reported as adverse effects data.	Yes	HS
6. Required for non-food uses that are likely to result in repeated oral exposure to humans.	No	90-day oral
7. Required to support uses involving purposeful application to the human skin or which would result in comparable prolonged human exposure to product ...and if any of the following criteria are met:	Yes	90-day dermal
i. Data from a 90-day oral study are not required.	Met	
ii. The active ingredient is known or expected to be metabolized differently by the dermal route of exposure than by the oral route and the metabolite is of toxicological concern.	NA[a]	
iii. The use pattern is such that the dermal route would be the primary route of exposure.	NA[b]	
8. Required if there is a likelihood of significant levels of repeated inhalation exposure to the pesticide as a gas, vapor, or aerosol.	?[c]	90-day inhalation
9. Required if the use of the product under widespread and commonly recognized practice may reasonably be expected to result in significant exposure to female humans (e.g., occupational exposure or repeated application of insect repellents directly to the skin).	?[c]	Prenatal developmental
10. Required to support nonfood uses if either:		Bacterial reverse mutation; *In vitro* mammalian
i. The use is likely to result in significant human exposure; or	?[c]	
ii. The active ingredient (or its metabolites) is structurally related to a known mutagen or belongs to any chemical class of compounds containing a known mutagen.	NA	
11. May be required if the product's use will result in exposure to domestic animals through, but not limited to, direct application or consumption of treated feed (No. 20 in 40CFR §158.2050 table).	Yes	Companion Animal Safety

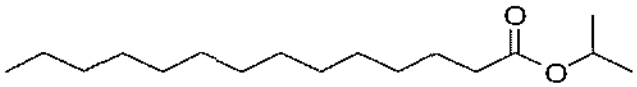
(a) NA = Not Applicable.
(b) Whether inhalation or dermal is major route of exposure is not relevant; the first criterion was met.
(c) Relevancy depends upon what is considered significant (the frequency of use?); see Justification section for further discussion.

Introduction

Isopropyl Myristate

The active ingredient (TGAI) is isopropyl myristate (IPM; CAS No.110-27-0), an esterified fatty acid. Isopropyl myristate is its IUPAC name; synonyms include 1-methylethyl tetradecanoate, tetradecanoic acid, 1-methylethyl ester, and myristic acid isopropyl ester.

IPM is synthesized from the reaction of myristic acid and isopropyl alcohol (See Volume 2); purity and impurity composition are further described in Volume 3. The molecular weight of IPM is 270.5 Daltons. Its empirical formula is $C_{17}H_{34}O_2$, and its structure is:



EPA FIFRA Regulatory Information

Isopropyl myristate (IPM) is unique in that it has been an approved active ingredient and it is currently an approved inert ingredient for food uses (qualifying it for non-food uses as well). IPM was one of a mixture of active ingredients in three EPs (EPA Reg. Nos. 7745-3, 8082-2, 9799-1), which were cancelled in 1986-87; however, there has never been a TGAI/MP registration for IPM (See Information Searches and Results section).

More importantly, IPM, as an inert ingredient, is exempted from the requirement of a tolerance under 40CFR §180.910 and it is being proposed for addition to the minimal risk pesticide inerts list under FIFRA 25(b). As of October 2009 (via e-CFR), IPM has a tolerance exemption as an solvent in pesticide formulations applied to growing crops or to raw agricultural commodities after harvest. It is on a list of "Inert Ingredients Eligible for FIFRA 25(b) Pesticide Products" (Updated March 3, 2009; AT: http://www.epa.gov/opprd001/inerts/section25b_inerts.pdf). To be exempted from FIFRA requirements under FIFRA 25(b), actives and inerts have to be of minimal risk to humans and the environment. Thus, because IPM is being considered for addition to this list and also that IPM is exempt from tolerances on all pre- and postharvest food crops and commodities, the EPA acknowledges that IPM is of minimal or no toxicological or environmental concern.

EPA TSCA Regulatory Information

IPM is extensively-produced as an industrial or fragrance chemical in the United States, as regulated under TSCA. In 2006 (the most recent reporting period for the EPA TSCA inventory), more than 1 million pounds of IPM were manufactured in or imported to the United States, which makes IPM an HPV (high-production volume) chemical.

FDA Regulatory Information

IPM is used as an excipient in many drug products particularly for transdermal applications and also as a cosmetic ingredient. IPM is in numerous otic and topical preparations at concentrations up to 50% of the formulation and in vaginal products at concentrations up to 5% of the formulation (FDA Inactive Ingredients Database; updated October 2009). It is also one of most frequently used cosmetic ingredients (FDA VCRP Cosmetic Ingredient Listing; updated May 2009).

RESULTIX™ End-Use Product

The EP, RESULTIX™, is a 50% w/w solution of IPM and [redacted] is the only inert ingredient in this formulation; it is on the non-food inert ingredients list (page [redacted] of 72 of the updated January 27, 2009 list; AT: http://www.epa.gov/opprd001/inerts/inert_nonfooduse.pdf). In addition, it is used extensively as a [redacted]. The molecular weight of [redacted] is [redacted]

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

JUN 17 2009

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Kathleen G. Palma, Ph.D.
Regulatory Affairs, Consultant
Piedmont Animal Health
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

Dear Dr. Palma:

Subject: Response to Notes dated June 8, 2009
Meeting with Piedmont Animal Health

The Agency is in receipt of the meeting notes from the April 30 pre-registration meeting with Piedmont Animal Health concerning a new product containing the unregistered biochemical, isopropyl myristate. The following is the Agency's official response to the meeting notes per the action items as listed in your letter:

I) Piedmont Animal Health Note:

Piedmont Animal Health received a biochemical classification for this product. Consequently the EPA will accept a reduced safety data set for registration which would only include Tier I safety requirements as outlined in 158.2030, the Biochemical pesticides product chemistry data requirements table. Tier II safety requirements will probably not required.

Agency Response

There are no Tiers for product chemistry. All product chemistry data guidelines must be satisfied for both the Technical Grade Active Ingredient (TGAI) and the End Use Product (EP). As you stated in your note above, please refer to 40 CFR § 158.2030 for biochemical pesticides product chemistry data requirements.

Inert ingredient information may be entitled to confidential treatment

Product ingredient source information may be entitled to confidential treatment

2) Piedmont Animal Health Note:

The tick spray consists of 50% Isopropyl myristate, the active and 50% [redacted], the excipient. There is no label or Confidential Certificate of Formulation (CSF). The spray could be used on an "as needed" basis. EPA instructed PAH that [redacted] should be cleared as the excipient under 40 CFR § 189.30 and contact PV Shaw or Kerry Grenstad. PAH can replace with another excipient or go to the "inerts" branch if necessary. EPA acknowledged that the "inerts" branch would be fast since this tick spray is a non-food use.

Agency Response

All pesticide products must bear a label with all of the required labeling language. Please refer to 40 CFR § 156-Labeling Requirements for Pesticides and Devices. You must have a Confidential Statement of Formula (CSF) for your product, and it must be completely filled out. The CSF EPA form 8570-4. Tips for avoiding Confidential Statement of Formula or Product Chemistry issues with Biopesticides can be found via the following internet link: www.epa.gov/pesticides/biopesticides/regtools/index.htm. This aforementioned link is also a good source for all issues related to registering biopesticides. The Agency is in agreement with your understanding that you must have your inert ingredients cleared by the "Inerts Assessment Branch". You may contact Prakashchandra (PV) Shah at 703.308.1846. For clarification purposes, BPPD cannot speak as to the speed of clearance of any inert ingredients. Inert Assessment Branch is in a different division.

3 Piedmont Animal Health Note:

Piedmont Animal Health gave a brief history of the tick spray's development. The tick spray has a safe profile in humans because Phase 3 clinical trials with CDER/FDA under INAD 66,651 were conducted with the same product as a head lice product for humans. The clinical studies with the safety profiles will be submitted to support safety with humans for the tick product. Once the product is sprayed on a tick, death begins less than 4 hours after the tick is sprayed. Some ticks may be moribund but will die within 24 hours. The isopropyl myristate, a fatty acid ester, [redacted] EPA provided PAH with a handout listing the data requirements. EPA mentioned some of those requirements. Technical and end-use data requirements should be satisfied. All data requirements should be addressed even if those requirements are not applicable. An explanation as to why the data requirement is not applicable should be provided. Units should be included with the CSF. All "impurities should be sent by the supplier even if that information is proprietary. As long as reference are specific, EPA can use them.

Agency Reponse

The Agency is in agreement with you note above with the exception that all data requirements MUST be addressed, and the references that you have MUST be submitted with your application for registration.

4 Piedmont Animal Health Note:

Per 86.5, formatted data requirements must pass administrative screen for formatting. If literature is used in the submission, use info doc as guidance to use literature references. The type of acceptable cited literature would be peer-reviewed articles, scientifically credible data and a citation from the MRID.

Agency Response

The Agency is in agreement with the discussion as outlined above. All data submitted must be formatted according to PR Notice 86-5.

5 Piedmont Animal Health Note:

Since this tick product is considered a B-600 (non-food use new product) the cost is $15,700 however PAH may qualify for a small business waiver under PRIA2 (Pesticide Registration Act). No studies are waived unless there is no exposure or the product is very acidic or basic. Given these criteria, PAH will not be granted a waiver for the tick spray.

Agency Reponse

The Agency is in agreement with the discussion that your product is a new active ingredient non-food use and would be classified as a B600 under Pesticide Registration Improvement Act (PRIA 2). PAH stated that the fee would be $15,700. The Agency is in agreement with your note that PAH may qualify for a small business waiver. The Agency is in agreement that no guideline studies are waived unless there is no exposure.

6 Piedmont Animal Health Note:

For the toxicology discussion, exposure should be discussed provided endpoints are identified. EPA will do the risk assessment. The pharmacokinetic studies done for the development of the human head louse product (Resultz™) can be used to support the tick spray product for dogs. The global use of Resultz™ and the post-marketing safety profile can also be used to support the safety of the tick spray.

Agency Response

It is important to note that all Tier 1 data requirements MUST be addressed individually. The safety profile is contingent upon Biopesticide and Pollution Prevention Division's review of the data and the acceptability of those data.

7) Piedmont Animal Health Note:

The Environmental Assessment completed for Resultz™ should address the ecological requirements. A rationale should be written why a bird study is not required given that birds should not come into contact with this product. Fish and aquatic invertebrate studies should be addressed because dogs do swim. EPA is concerned for endangered species.

Agency Response

The Agency is in agreement with the note above.

8) PRIA Category

In the efficacy study there should be a 90% reduction in ticks. Given that the tick spray is most efficacious when sprayed on dry dogs, the label may need to read "apply to dry dog". Ms. Gonzales stated that she would look into the requirement for companion animal safety and respond back to PAH. PAH stated that the safety could be tied into the efficacy study with possible physical exams and clinical blood chemistries. There is no requirement to submit the efficacy protocol but the typical protocol format should be used. The end use product is the only thing to be registered.

Agency Response

The Agency is in agreement with the note above. Also you must address companion animal study according to 40 CFR § 158.2050.

Should you have any questions regarding this response to your meeting notes, you may contact Leonard Cole directly at 703.305.5412 or via email at cole.leonard@epa.gov . We hope that you find this information helpful.

Sincerely,

Linda A. Hollis, Chief
Biochemical Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)

ENVIRONMENTAL PROTECTION AGENCY

[EPA–HQ–OPP–2010–0096; FRL–8811–6]

Pesticide Products; Registration Applications

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: EPA has received applications to register pesticide products containing active ingredients not included in any previously registered pesticide products. Pursuant to the provisions of section 3(c)(4) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), EPA is hereby providing notice of receipt and opportunity to comment on these applications.

DATES: Comments must be received on or before April 9, 2010.

ADDRESSES: Submit your comments, identified by docket identification (ID) number and the File Symbol(s) of interest as shown in the body of this document, by one of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the on-line instructions for submitting comments.
- *Mail:* Office of Pesticide Programs (OPP) Regulatory Public Docket (7502P), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001.
- *Delivery:* OPP Regulatory Public Docket (7502P), Environmental Protection Agency, Rm. S–4400, One Potomac Yard (South Bldg.), 2777 S. Crystal Dr., Arlington, VA. Deliveries are only accepted during the Docket Facility's normal hours of operation (8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays). Special arrangements should be made for deliveries of boxed information. The Docket Facility telephone number is (703) 305–5805.

Instructions: Direct your comments to the docket Identification (ID) number and the File Symbol(s) for the application(s) of interest as shown in the body of this document. EPA's policy is that all comments received will be included in the docket without change and may be made available on-line at *http://www.regulations.gov*, including any personal information provided, unless the comment includes information claimed to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Do not submit information that you consider to be CBI or otherwise protected through regulations.gov or e-mail. The regulations.gov website is an "anonymous access" system, which means EPA will not know your identity or contact information unless you provide it in the body of your comment. If you send an e-mail comment directly to EPA without going through regulations.gov, your e-mail address will be automatically captured and included as part of the comment that is placed in the docket and made available on the Internet. If you submit an electronic comment, EPA recommends that you include your name and other contact information in the body of your comment and with any disk or CD-ROM you submit. If EPA cannot read your comment due to technical difficulties and cannot contact you for clarification, EPA may not be able to consider your comment. Electronic files should avoid the use of special characters, any form of encryption, and be free of any defects or viruses.

Docket: All documents in the docket are listed in the docket index available at *http://www.regulations.gov.* Although listed in the index, some information is not publicly available, e.g., CBI or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, is not placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available either in the electronic docket at *http://www.regulations.gov*, or, if only available in hard copy, at the OPP Regulatory Public Docket in Rm. S–4400, One Potomac Yard (South Bldg.), 2777 S. Crystal Dr., Arlington, VA. The hours of operation of this Docket Facility are from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The Docket Facility telephone number is (703) 305–5805.

FOR FURTHER INFORMATION CONTACT: The Regulatory Action Leader, Biopesticides and Pollution Prevention Division (7511P), listed in the following table:

Regulatory Action Leader	Telephone Number and E-mail Address	Mailing Address	File Symbol(s)
Driss Benmhend	(703) 308–9525 *benmhend.driss@epa.gov*	Biopesticides and Pollution Prevention Division (7511P) Office of Pesticide Programs Environmental Protection Agency 1200 Pennsylvania Ave., NW. Washington, DC 20460–0001	5481–LAI 5481–LAO 5481–LTN 5481–LTR
Susanne Cerrelli	(703) 308–8077 *cerrelli.susanne@epa.gov*	Do.	86174–E 86174–G 86174–R 86174–U
Cheryl Greene	(703) 308–0352 *greene.cheryl@epa.gov*	Do.	86865–R
Denise Greenway	(703) 308–8263 *greenway.denise@epa.gov*	Do.	7005t–RNL 84888–E 84888–R
Anna Gross	(703) 305–5614 *gross.anna@epa.gov*	Do.	67986–A

Regulatory Action Leader	Telephone Number and E-mail Address	Mailing Address	File Symbol(s)
Jeannine Kausch	(703) 347–8920 *kausch.jeannine@epa.gov*	Do.	68539–I 68539–O 68539–RN 81179–E 84059–O 84059–RN
Kathleen Martin	(703) 308–2857 *martin.kathleen@epa.gov*	Do.	239–ETNE 239–ETNG 239–ETNU 73314–A 73314–T
Chris Pfeifer	(703) 308–0031 *pfeifer.chris@epa.gov*	Do.	83028–RN
Ann Sibold	(703) 305–6502 *sibold.ann@epa.gov*	Do.	84059–RR
Menyon Adams	(703) 347-8496 *adams.menyon@epa.gov*	Do.	80286-RA 80286-RT

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. Potentially affected entities may include, but are not limited to:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed in this unit could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether this action might apply to certain entities. If you have any questions regarding the applicability of this action to a particular entity, consult the person associated with the File Symbol of interest and listed under **FOR FURTHER INFORMATION CONTACT.**

B. What Should I Consider as I Prepare My Comments for EPA?

1. *Submitting CBI.* Do not submit this information to EPA through regulations.gov or e-mail. Clearly mark the part or all of the information that you claim to be CBI. For CBI information in a disk or CD-ROM that you mail to EPA, mark the outside of the disk or CD-ROM as CBI and then identify electronically within the disk or CD-ROM the specific information that is claimed as CBI. In addition to one complete version of the comment that includes information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public docket. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2.

2. *Tips for preparing your comments.* When submitting comments, remember to:

i. Identify the document by docket ID number and other identifying information (subject heading, Federal Register date, and page number). If you are commenting on a docket that addresses multiple products, please indicate to which File Symbol(s) your comment applies.

ii. Follow directions. The Agency may ask you to respond to specific questions or organize comments by referencing a Code of Federal Regulations (CFR) part or section number.

iii. Explain why you agree or disagree; suggest alternatives and substitute language for your requested changes.

iv. Describe any assumptions and provide any technical information and/or data that you used.

v. If you estimate potential costs or burdens, explain how you arrived at your estimate in sufficient detail to allow for it to be reproduced.

vi. Provide specific examples to illustrate your concerns and suggest alternatives.

vii. Explain your views as clearly as possible, avoiding the use of profanity or personal threats.

viii. Make sure to submit your comments by the comment period deadline identified.

II. Registration Applications

EPA received applications to register pesticide products containing active ingredients not included in any previously registered products. Pursuant to the provision of section 3(c)(4) of FIFRA, EPA is hereby providing notice of receipt and opportunity to comment on these applications. Notice of receipts of these applications does not imply a decision by the Agency on the applications.

1. *File Symbol:* 239–ETNE. *Docket Number:* EPA–HQ–OPP–2010–0094. *Applicant:* OMC Consulting, 828 Tanglewood Lane, East Lansing, MI 48823 (on behalf of The Scotts Company LLC, d/b/a The Ortho Group, P.O. Box 190, Marysville, OH 43040). *Product Name:* Phoma Tech. *Active Ingredient: Phomo macrostomo* strain 94–44B at 92%. *Proposed Classification/Use:* Manufacturing-use product. (K. Martin).

2. *File Symbol:* 239–ETNG. *Docket Number:* EPA–HQ–OPP–2010–0094. *Applicant:* OMC Consulting, 828 Tanglewood Lane, East Lansing, MI 48823 (on behalf of The Scotts Company LLC, d/b/a The Ortho Group, P.O. Box 190, Marysville, OH 43040). *Product Name:* Phoma H. *Active Ingredient: Phomo macrostomo* strain 94–44B at 92%. *Proposed Classification/Use:* Terrestrial (nonfood, residential outdoor). (K. Martin).

3. *File Symbol:* 239–ETNU. *Docket Number:* EPA–HQ–OPP–2010–0094. *Applicant:* OMC Consulting, 828 Tanglewood Lane, East Lansing, MI 48823 (on behalf of The Scotts Company LLC, d/b/a The Ortho Group, P.O. Box

190, Marysville, OH 43040). *Product Name*: Phoma P. *Active Ingredient*: *Phomo macrostomo* strain 94-44B at 92%. *Proposed Classification/Use*: Terrestrial (nonfood, residential outdoor, nurseries, greenhouses). (K. Martin).

4. *File Symbol*: 5481–LAI. *Docket Number*: EPA–HQ–OPP–2010–0064. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of AMVAC Chemical Corporation, 4695 Macarthur Court, Suite 1250, Newport Beach, CA 92660–1706). *Product Name*: AMV-1018 Technical. *Active Ingredient*: 3-decen-2-one at 98%. *Proposed Classification/Use*: Manufacturing-use product. (D. Benmhend).

5. *File Symbol*: 5481–LAO. *Docket Number*: EPA–HQ–OPP–2010–0064. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of AMVAC Chemical Corporation, 4695 Macarthur Court, Suite 1250, Newport Beach, CA 92660–1706). *Product Name*: AMV-1018 67.5 EC. *Active Ingredient*: 3-decen-2-one at 67.5%. *Proposed Classification/Use*: Potato sprout inhibitor for indoor use only. (D. Benmhend).

6. *File Symbol*: 5481–LTN. *Docket Number*: EPA–HQ–OPP–2010–0064. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of AMVAC Chemical Corporation, 4695 Macarthur Court, Suite 1250, Newport Beach, CA 92660–1706). *Product Name*: AMV-1018 90 EC. *Active Ingredient*: 3-decen-2-one at 90%. *Proposed Classification/Use*: Potato sprout inhibitor for indoor use only. (D. Benmhend).

7. *File Symbol*: 5481–LTR. *Docket Number*: EPA–HQ–OPP–2010–0064. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of AMVAC Chemical Corporation, 4695 Macarthur Court, Suite 1250, Newport Beach, CA 92660–1706). *Product Name*: AMV-1018 EP. *Active Ingredient*: 3-decen-2-one at 98%. *Proposed Classification/Use*: Potato sprout inhibitor for indoor use only. (D. Benmhend).

8. *File Symbol*: 67986–A. *Docket Number*: EPA–HQ–OPP–2009–0539. *Applicant*: Interregional Research Project Number 4 (IR-4), Rutgers University, 500 College Road East, Suite 201W, Princeton, NJ 08540 (on behalf of OmniLytics, 5450 W. Wiley Post Way, Salt Lake City, UT 84116). *Product Name*: AgriPhage CMM. *Active Ingredient*: Bacteriophage of *Clovibacter michigonensis* subsp. *michigonensis* at 0.05%. *Proposed Classification/Use*: Bactericide for use against canker on tomato. (A. Gross).

9. *File Symbol*: 68539–I. *Docket Number*: EPA–HQ–OPP–2010–0057. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of BioWorks Incorporated, 100 Rawson Road, Suite 205, Victor, NY 14564). *Product Name*: G-41 Technical. *Active Ingredient*: *Trichodermo virens* strain G-41 at 12.1%. *Proposed Classificotion/Use*: Manufacturing-use product. (J. Kausch).

10. *File Symbol*: 68539–O. *Docket Number*: EPA–HQ–OPP–2010–0057. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of BioWorks Incorporated, 100 Rawson Road, Suite 205, Victor, NY 14564). *Product Name*: BW240 WP. *Active Ingredient*: *Trichoderma virens* strain G-41 at 0.61%. *Proposed Classificotian/Use*: Preventative fungicide for control of disease organisms such as *Pythium*, *Phytophthoro*, *Rhizoctonia*, and *Fusarium* on various crops. (J. Kausch)

11. *File Symbol*: 68539–RN. *Docket Number*: EPA–HQ–OPP–2010–0057. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of BioWorks Incorporated, 100 Rawson Road, Suite 205, Victor, NY 14564). *Product Name*: BW240 G. *Active Ingredient*: *Trichodermo virens* strain G-41 at 0.61%. *Proposed Classificotian/Use*: Preventative fungicide for control of disease organisms such as *Pythium*, *Phytophthora*, *Rhizoctonia*, and *Fusorium* on various crops. (J. Kausch).

12. *File Symbol*: 70051–RNL. *Docket Number*: EPA–HQ–OPP–2010–0103. *Applicant*: Certis USA LLC, 9145 Guilford Road, Suite 175, Columbia, MD 21046. *Product Name*: CX-9090. *Active Ingredient*: *Bocillus subtilis* strain CX-9060 at 25.0%. *Proposed Classification/Use*: For the control or suppression of fungal and bacterial diseases of horticultural crops. (D. Greenway).

13. *File Symbol*: 73314–A. *Docket Number*: EPA–HQ–OPP–2010–0093. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of Natural Industries Incorporated, 6223 Theall Road, Houston, TX 77066). *Product Name*: NoFly(tm). *Active Ingredient*: *Paecilomyces fumosoroseus* strain FE 9901 at 18%. *Proposed Classification/Use*: Greenhouse (only) for control of whiteflies, aphids, thrips, psyllids, mealybugs, leaf hoppers, plant bugs, weevils, grasshoppers, mormon crickets, locust, and beetles on all greenhouse and nursery crops including ornamentals, vegetables, and herbs. (K. Martin).

14. *File Symbol*: 73314–T. *Docket Number*: EPA–HQ–OPP–2010–0093. *Applicant*: Technology Sciences Group Incorporated, 1150 18th Street NW., Suite 1000, Washington, DC 20036 (on behalf of Natural Industries Incorporated, 6223 Theall Road, Houston, TX 77066). *Product Name*: NoFly(tm) Technical. *Active Ingredient*: *Paecilomyces fumosoroseus* strain FE 9901 at 69%. *Proposed Classificotion/Use*: Manufacturing-use product. (K. Martin).

15. *File Symbol*: 81179–E. *Docket Number*: EPA–HQ–OPP–2010–0056. *Applicant*: Interregional Research Project Number 4 (IR-4), Rutgers University, 500 College Road East, Suite 201W, Princeton, NJ 08540 (on behalf of BioProdex Incorporated, 8520 NW 2 Place, Gainesville, FL 32607–1423). *Product Name*: SolviNix. *Active Ingredient*: *Tobacco Mild Green Mosoic Tobomovirus* at 3%. *Proposed Classification/Use*: Post-emergent herbicide for control of tropical soda apple (*Solonum viorum*) in citrus, forestry, grass pastures, rangeland, sod-production fields, roadsides, sugarcane, temperate fruits and nuts, tropical fruits and nuts, turf, Conservation Reserve Program and other natural areas, and rights-of-way. (J. Kausch).

16. *File Symbol*: 83028–RN. *Docket Number*: EPA–HQ–OPP–2010–0080. *Applicant*: NCA Biotech Incorporated, 3406 Pomona Boulevard, Pomona, CA 91768. *Product Name*: Technical Salicylic Acid. *Active Ingredient*: Salicylic Acid at 98.7%. *Proposed Classificotion/Use*: Manufacturing-use product for formulation into plant growth regulator end-use products. (J. Pfeifer).

17. *File Symbol*: 84059–O. *Docket Number*: EPA–HQ–OPP–2010–0058. *Applicont*: Marrone Bio Innovations Incorporated, 2121 Second Street, Suite B-107, Davis, CA 95618. *Product Nome*: MBI-203 TGAI. *Active Ingredient*: *Chromobocterium subtsugae* strain PRAA4-1^T at 100.00%. *Proposed Classification/Use*: Manufacturing-use product. (J. Kausch).

18. *File Symbol*: 84059–RN. *Docket Number*: EPA–HQ–OPP–2010–0058. *Applicant*: Marrone Bio Innovations Incorporated, 2121 Second Street, Suite B-107, Davis, CA 95618. *Product Name*: MBI-203 EP. *Active Ingredient*: *Chromobacterium subtsugoe* strain PRAA4-1^T at 94.50%. *Proposed Classification/Use*: Insecticide for use in the control or suppression of many

foliar-feeding pests such as caterpillars, foliage-feeding coleopteran, aphids, whiteflies, and plant-sucking mites on ornamental plants, turf, and various edible crops. (J. Kausch).

19. *File Symbol*: 84059–RR. *Docket Number*: EPA–HQ–OPP–2010–0079. *Applicant*: Marrone Bio Innovations Incorporated, 2121 Second Street, Suite B-107, Davis, CA 95618. *Product Name*: MBI-005. *Active Ingredient*: *Streptomyces ocidiscabies* strain RL-110T at 100%. *Proposed Classification/Use*: Manufacturing-use product. (A. Sibold).

20. *File Symbol*: 84888–E. *Docket Number*: EPA–HQ–OPP–2010–0090. *Applicant*: Technology Sciences Group Incorporated, 712 Fifth Street, Suite A, Davis, CA 95616 (on behalf of Agrium Advanced Technologies RP Incorporated, 10 Craig Street, Brantford, Ontario Canada N3R 7J1). *Product Name*: Nivalis. *Active Ingredient*: *Typhulo phacorrhiza* strain 94671 at 4.00%. *Proposed Classification/Use*: Biofungicide for turf. (D. Greenway).

21. *File Symbol*: 84888–R. *Docket Number*: EPA–HQ–OPP–2010–0090. *Applicont*: Technology Sciences Group Incorporated, 712 Fifth Street, Suite A, Davis, CA 95616 (on behalf of Agrium Advanced Technologies RP Incorporated, 10 Craig Street, Brantford, Ontario Canada N3R 7J1). *Product Nome*: Nivalis Technical. *Active Ingredient*: *Typhula phacorrhiza* strain 94671 at 4.00%. *Proposed Classificotion/Use*: Manufacturing-use product. (D. Greenway).

22. *File Symbol*: 86174–E. *Docket Number*: EPA–HQ–OPP–2010–0100. *Applicont*: SciReg Incorporated, 12733 Director's Loop, Woodbridge, VA 22192 (on behalf of Bio-Ferm GmbH, Konrad Lorenz Strasse 20, A-3430, Tulln, Austria). *Product Nome*: *Aureobosidium pullulons* strain DSM 14940 Technical. *Active Ingredient*: *Aureobosidium pullulons* strain DSM 14940 at 80%. *Proposed Classificotion/Use*: Manufacturing-use product. (S. Cerrelli).

23. *File Symbol*: 86174–G. *Docket Numbers*: EPA–HQ–OPP–2010–0100 and EPA–HQ–OPP–2010–0106. *Applicont*: SciReg Incorporated, 12733 Director's Loop, Woodbridge, VA 22192 (on behalf of Bio-Ferm GmbH, Konrad Lorenz Strasse 20, A-3430, Tulln, Austria). *Product Name*: Botector. *Active Ingredients*: *Aureobasidium pullulans* strain DSM 14940 at 50% and *Aureobasidium pullulans* strain DSM 14941 at 50%. *Proposed Classificotion/Use*: Fungicide for agricultural, commercial, and residential use on citrus, grapes, pome fruits, stone fruits, and strawberries. (S. Cerrelli).

24. *File Symbol*: 86174–R. *Docket Number*: EPA–HQ–OPP–2010–0106. *Applicont*: SciReg Incorporated, 12733 Director's Loop, Woodbridge, VA 22192 (on behalf of Bio-Ferm GmbH, Konrad Lorenz Strasse 20, A-3430, Tulln, Austria). *Product Nome*: *Aureobasidium pullulans* strain DSM 14941 Technical. *Active Ingredient*: *Aureobosidium pullulons* strain DSM 14941 at 80%. *Proposed Classification/Use*: Manufacturing-use product. (S. Cerrelli).

25. *File Symbol*: 86174–U. *Docket Numbers*: EPA–HQ–OPP–2010–0100 and EPA–HQ–OPP–2010–0106. *Applicont*: SciReg Incorporated, 12733 Director's Loop, Woodbridge, VA 22192 (on behalf of Bio-Ferm GmbH, Konrad Lorenz Strasse 20, A-3430, Tulln, Austria). *Product Name*: Blossom Protect. *Active Ingredients*: *Aureobasidium pullulans* strain DSM 14940 at 32.25% and *Aureobosidium pullulans* strain DSM 14941 at 32.25%. *Proposed Classification/Use*: Fungicide for agricultural, commercial, and residential use to prevent fire blight on pome fruits. (S. Cerrelli).

26. *File Symbol*: 86865–R. *Docket Number*: EPA–HQ–OPP–2010–0082. *Applicont*: Piedmont Animal Health, 204 Muirs Chapel Road, Suite 200, Greensboro, NC 27410. *Product Name*: Resultix(tm). *Active Ingredient*: Isopropyl Myristate at 50%. *Proposed Classificotion/Use*: Insecticide for use against ticks on cats and dogs. (C. Greene).

27. *File Symbol*: 80286-RT. *Docket Number*: EPA-HQ-OPP-2010-0040. *Applicont*: ISCA Technologies Incorporated, 1230 Spring Street, Riverside, CA 92507. *Product Name*: ISCA TuTa MP. *Active Ingredient*: (E,Z,Z)-3,8,11-Tetradecatrienyl Acetate at 96.31%. *Proposed Classification/Use*: Manufacturing-use product. (M. Adams).

28. *File Symbol*: 80286-RA. *Docket Number*: EPA-HQ-OPP-2010-0040. *Applicont*: ISCA Technologies Incorporated, 1230 Spring Street, Riverside, CA 92507. *Product Name*: SPLAT TuTa(tm). *Active Ingredient*: (E,Z,Z)-3,8,11-Tetradecatrienyl Acetate at 0.3%. *Proposed Classification/Use*: Straight-carbon-chain Lepidoptera pheromone (SCLP) for use against tomato leafminer on all crops and in non-crop areas. (M. Adams).

List of Subjects

Environmental protection, Pesticides and pests.

Dated: March 1, 2010.

Keith A. Matthews,

Acting Director, Biopesticides and Pollution Prevention Division, Office of Pesticide Programs.

[FR Doc. 2010–4835 Filed 3–9–10; 8:45 am]

BILLING CODE 6560–50–S

FEDERAL DEPOSIT INSURANCE CORPORATION

Agency Information Collection Activities: Submission for OMB Review; Comment Request

AGENCY: Federal Deposit Insurance Corporation (FDIC).

ACTION: Notice of information collections to be submitted to OMB for review and approval under the Paperwork Reduction Act of 1995.

SUMMARY: In accordance with the requirements of the Paperwork Reduction Act of 199 (44 U.S.C. chapter 35), the FDIC hereby gives notice that it plans to submit to the Office of Management and Budget (OMB) a request for OMB review and renewal of its "Foreign Banks" information collection (OMB No. 3064–0114).

DATES: Comments must be submitted on or before April 9, 2010.

ADDRESSES: Interested parties are invited to submit written comments. All comments should refer to the name of the collection. Comments may be submitted by any of the following methods:

- *http://www.FDIC.gov/regulotions/lows/federal/propose.html.*
- *E-mail: comments@fdic.gov.*
- *Moil:* Leneta G. Gregorie (202.898.3719), Counsel, Federal Deposit Insurance Corporation, PA1730–3000, 550 17th Street, NW., Washington, DC 20429.
- *Hand Delivery:* Comments may be hand-delivered to the guard station at the rear of the 550 17th Street Building (located on F Street), on business days between 7 a.m. and 5 p.m.

All comments should refer to the relevant OMB control number. A copy of the comments may also be submitted to the FDIC Desk Officer, Office of Information and Regulatory Affairs, Office of Management and Budget, New Executive Office Building, Room 10235, Washington, DC 20503.

FOR FURTHER INFORMATION CONTACT: For further information about the information collection discussed in this notice, please contact Leneta G. Gregorie, by telephone at (202) 898–3719 or by mail at the address identified above.

Meeting Minutes

EPA Meeting April 30, 2009

Attendees:

Angela Gonzales
Leonard Cole
Kathy Palma
Doug Hepler
Bert Clayton

Members of Piedmont Animal Health (PAH) met with EPA representatives Leonard Cole and Angela Gonzales on April 30, 2009 at 2:00p.m. EST at the EPA facility in Crystal City, MD. The purpose of the meeting was to discuss the registration path forward for PAH's new nonpesticidal tick spray (50% Isopropyl Myristate). The meeting lasted approximately 1 hour and the following points were discussed:

Introductions

1. EPA will accept a reduced data set approach for this registration

2. Biochemical classification has been obtained by Piedmont

3. Product description:

   Active – 50% IPM

   Excipient – 50%[redacted]

4. No label yet, no CSF. Could be "as needed" tick spray

5. Dr. Kathy Palma provides history of Resultz development

   a. Have safety profile in humans from clinical

   b. Mechanism – dissolves cuticular wax

   c. < 4 hrs ticks die, some may be moribund but will die soon after

Inert ingredient information may be entitled to confidential treatment

Product ingredient source information may be entitled to confidential treatment

6. Source – Active derived from [redacted], [redacted]

   [redacted]

7. Piedmont should clear [redacted] under ECFR – check 40CFR 189-30 and contact PV Shaw or Kerry Grenstad - can replace with other Excipient or go to "inerts" branch

8. Leonard reports that inert branch is fast, because it's non-food use

9. Data Requirements – see handout provided by Angela Gonzales

   a. Satisfy technical and end-use date requirement

   b. Address all data requirements – say "why" if N/A

   c. Include units in CSFs

   d. Supplier needs to send all "impurities" even if proprietary

   e. We can use references – be specific

10. 86-5 – Formatted data requirement to pass administrative screen

Kathy? — 11. ~~Non-food use does not require~~?

Kathy? — 12. Address tier 1 only – ~~Tox end use~~ – "six pack"

13. If literature is used, use info doc – guidance to use literature references

    a. Peer-reviewed

    b. Scientific credible data

    c. Site MRID

14. There are fees involved now (B6)

15. Tox discussion – provide "exposure" discussion if endpoints identified. EPA will do risk assessment.

16. No studies are waived unless

a. No exposure

b. Very acidic or basic

c. We will not be "granted" waiver

17. Can use PK studies form Resultz

18. Talk about global use of Resultz and safety profile.

19. Eco-requirements – use environmental assessment

a. Write a rationale to not require a bird study

b. Address fish and invertebrate studies because dogs do swim

c. Concern is endangered species

20. Tier 2 probably not required

21. Study proposal – makes sure data shows 90% reduction. (efficacy)

22. Study outline – how to address wet dogs. Label may need to say "apply to dry dog".

23. Companion animal studies – requirement, Angela will look into this and respond to PAH.

Can we tie into efficacy ?

24. Register end-use only

25. No requirement to submit a protocol – use typical protocol format

26. B-600 non food use new product up to 12 months for an answer

a. $15,700 apply waiver/ under PRIA2 – pest- reg. act

b. Fill out waiver for small business

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

JUN 17 2009

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Kathleen G. Palma, Ph.D.
Regulatory Affairs, Consultant
Piedmont Animal Health
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

Dear Dr. Palma:

Subject: Response to Notes dated June 8, 2009
Meeting with Piedmont Animal Health

The Agency is in receipt of the meeting notes from the April 30 pre-registration meeting with Piedmont Animal Health concerning a new product containing the unregistered biochemical, isopropyl myristate. The following is the Agency's official response to the meeting notes per the action items as listed in your letter:

1) Piedmont Animal Health Note:

Piedmont Animal Health received a biochemical classification for this product. Consequently the EPA will accept a reduced safety data set for registration which would only include Tier I safety requirements as outlined in 158.2030, the Biochemical pesticides product chemistry data requirements table. Tier II safety requirements will probably not required.

Agency Response

There are no Tiers for product chemistry. All product chemistry data guidelines must be satisfied for both the Technical Grade Active Ingredient (TGAI) and the End Use Product (EP). As you stated in your note above, please refer to 40 CFR § 158.2030 for biochemical pesticides product chemistry data requirements.

Inert ingredient information may be entitled to confidential treatment

Product ingredient source information may be entitled to confidential treatment

2) Piedmont Animal Health Note:

The tick spray consists of 50% Isopropyl myristate, the active and 50% [redacted], the excipient. There is no label or Confidential Certificate of Formulation (CSF). The spray could be used on an "as needed" basis. EPA instructed PAH that [redacted] should be cleared as the excipient under 40 CFR § 189.30 and contact PV Shaw or Kerry Grenstad. PAH can replace with another excipient or go to the "inerts" branch if necessary. EPA acknowledged that the "inerts" branch would be fast since this tick spray is a non-food use.

Agency Response

All pesticide products must bear a label with all of the required labeling language. Please refer to 40 CFR § 156-Labeling Requirements for Pesticides and Devices. You must have a Confidential Statement of Formula (CSF) for your product, and it must be completely filled out. The CSF EPA form 8570-4. Tips for avoiding Confidential Statement of Formula or Product Chemistry issues with Biopesticides can be found via the following internet link: www.epa.gov/pesticides/biopesticides/regtools/index.htm. This aforementioned link is also a good source for all issues related to registering biopesticides. The Agency is in agreement with your understanding that you must have your inert ingredients cleared by the "Inerts Assessment Branch". You may contact Prakashchandra (PV) Shah at 703.308.1846. For clarification purposes, BPPD cannot speak as to the speed of clearance of any inert ingredients. Inert Assessment Branch is in a different division.

3 Piedmont Animal Health Note:

Piedmont Animal Health gave a brief history of the tick spray's development. The tick spray has a safe profile in humans because Phase 3 clinical trials with CDER/FDA under INAD 66,651 were conducted with the same product as a head lice product for humans. The clinical studies with the safety profiles will be submitted to support safety with humans for the tick product. Once the product is sprayed on a tick, death begins less than 4 hours after the tick is sprayed. Some ticks may be moribund but will die within 24 hours. The isopropyl myristate, a fatty acid ester [redacted] EPA provided PAH with a handout listing the data requirements. EPA mentioned some of those requirements. Technical and end-use data requirements should be satisfied. All data requirements should be addressed even if those requirements are not applicable. An explanation as to why the data requirement is not applicable should be provided. Units should be included with the CSF. All "impurities should be sent by the supplier even if that information is proprietary. As long as reference are specific, EPA can use them.

Agency Reponse

The Agency is in agreement with you note above with the exception that all data requirements MUST be addressed, and the references that you have MUST be submitted with your application for registration.

4 Piedmont Animal Health Note:

Per 86.5, formatted data requirements must pass administrative screen for formatting. If literature is used in the submission, use info doc as guidance to use literature references. The type of acceptable cited literature would be peer-reviewed articles, scientifically credible data and a citation from the MRID.

Agency Response

The Agency is in agreement with the discussion as outlined above. All data submitted must be formatted according to PR Notice 86-5.

5 Piedmont Animal Health Note:

Since this tick product is considered a B-600 (non-food use new product) the cost is $15,700 however PAH may qualify for a small business waiver under PRIA2 (Pesticide Registration Act). No studies are waived unless there is no exposure or the product is very acidic or basic. Given these criteria, PAH will not be granted a waiver for the tick spray.

Agency Reponse

The Agency is in agreement with the discussion that your product is a new active ingredient non-food use and would be classified as a B600 under Pesticide Registration Improvement Act (PRIA 2). PAH stated that the fee would be $15,700. The Agency is in agreement with your note that PAH may qualify for a small business waiver. The Agency is in agreement that no guideline studies are waived unless there is no exposure.

6 Piedmont Animal Health Note:

For the toxicology discussion, exposure should be discussed provided endpoints are identified. EPA will do the risk assessment. The pharmacokinetic studies done for the development of the human head louse product (Resultz™) can be used to support the tick spray product for dogs. The global use of Resultz™ and the post-marketing safety profile can also be used to support the safety of the tick spray.

Agency Response

It is important to note that all Tier I data requirements MUST be addressed individually. The safety profile is contingent upon Biopesticide and Pollution Prevention Division's review of the data and the acceptability of those data.

7) Piedmont Animal Health Note:

The Environmental Assessment completed for Resultz™ should address the ecological requirements. A rationale should be written why a bird study is not required given that birds should not come into contact with this product. Fish and aquatic invertebrate studies should be addressed because dogs do swim. EPA is concerned for endangered species.

Agency Response

The Agency is in agreement with the note above.

8) PRIA Category

In the efficacy study there should be a 90% reduction in ticks. Given that the tick spray is most efficacious when sprayed on dry dogs, the label may need to read "apply to dry dog". Ms. Gonzales stated that she would look into the requirement for companion animal safety and respond back to PAH. PAH stated that the safety could be tied into the efficacy study with possible physical exams and clinical blood chemistries. There is no requirement to submit the efficacy protocol but the typical protocol format should be used. The end use product is the only thing to be registered.

Agency Response

The Agency is in agreement with the note above. Also you must address companion animal study according to 40 CFR § 158.2050.

Should you have any questions regarding this response to your meeting notes, you may contact Leonard Cole directly at 703.305.5412 or via email at cole.leonard@epa.gov . We hope that you find this information helpful.

Sincerely,

Linda A. Hollis, Chief
Biochemical Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)

FRONT PANEL

RESULTIX™

Kills Ticks on Dogs and Cats

ACTIVE INGREDIENT	
Isopropyl Myristate	50.0%
OTHER INGREDIENT	50.0%
TOTAL	100.0%

KEEP OUT OF REACH OF CHILDREN

CAUTION

See Side/Back Panel for First Aid

STOP - READ LABEL BEFORE USE

EPA Reg. No. 86865-R

EPA Est. No. 71979-SC-001

Manufactured for
Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410
1-336-544-0320 x 207

NET CONTENTS
20 mL (0.65 oz.)

ACCEPTED

AUG 24 2011
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 86865-1

SIDE PANEL

FIRST AID

If on skin:	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor immediately for treatment advice.
If in eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. • Call a poison control center or doctor immediately for treatment advice.
If inhaled:	• Move person to fresh air. • If person is not breathing, call 911 or an ambulance; then give artificial respiration, preferably mouth-to-mouth if possible. • Call a poison control center or doctor immediately for treatment advice.
If swallowed:	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by a poison control center or doctor. • Do not give anything by mouth to an unconscious person.

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-222-1222 (American Association of Poison Control Centers) any time day or night for emergency medical treatment information.

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION. May cause dermal and eye irritation. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet.

ENVIRONMENTAL HAZARDS

This pesticide is toxic to invertebrates and fish. Do not discharge this product into lakes, streams, ponds, estuaries, oceans, or other waters where aquatic invertebrates or fish may be found.

BACK PANEL

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

RESULTIX™, when used as instructed below, will dissolve the outer wax layer coving the hard shell (cuticle) of the tick resulting in uncontrollable water loss and death of the tick.

For the removal and killing of attached and crawling ticks on dogs and cats

APPLICATION AND USE INSTRUCTIONS

For external use only.

Do not use near dog's or cat's eyes.

Do not use on irritated skin.

Stop treatment with this product and consult a veterinarian if skin irritation or skin infection develops during use of product.

- Use when you see a tick or ticks on your dog or cat.
- Remove cap and hold bottle upright. Direct nozzle at tick and spray until tick is covered with solution (2 sprays).
- The tick will be dead within 3 hours; it will fall off of the dog or cat or will be immobile when removed.
- If tick falls off indoors within 3 hours of application, carefully pick up and dispose of tick using gloves or tweezers.
- After 3 hours, if the tick has not fallen off, remove carefully with gloves or tweezers and dispose of tick.
- Dispose of ticks by placing in sealable plastic bag, sealing the bag, and placing it in an outdoor garbage can.
- Wash hands after accidental exposure to any ticks.

STORAGE AND DISPOSAL

Do not contaminate water, food, or feed by storage and disposal.

Pesticide Storage:

Store in a dry place away from extreme heat and cold (tightly closed between 59° F – 86° F (15° C – 30° C). Keep container closed when not in use. Always store pesticide in the original container. Store away from food and pet food. Keep away from open flames.

In case of fire or other emergency, report at once by toll-free telephone to CHEMTREC (800-424-9300).

Pestieide Disposal and Container Handling:

Nonrefillable container. Do not reuse or refill this container.
When empty: place in trash or offer for recycling if available.
Never place unused product down any indoor or outdoor drain.

NOTICE: Seller warrants that the product conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use. To the extent permitted by applicable law, this warranty or any other warranty of merchantability or fitness for a particular purpose, express or implied, does not extend to the use of this product contrary to label instructions, or under abnormal conditions, or under conditions not reasonably foreseeable to Seller. To the extent permitted by applicable law, buyer assumes the risk of any such use.

ANY PANEL (Do not substitute these for required statements)

Label Claims (one or more in various combinations, located in various places throughout the box and bottle/insert labels)

Breakthrough in tick killing for attached and crawling ticks

Convenient and easy to apply

For the Killing of Ticks on Dogs and Cats

Free of conventional pesticides

Patented spray formula softens the waterproof outer waxy layer of the tick's body, resulting in dehydration

Direct spray formula is safe to use on pets

Can be used as often as needed

Can be part of your tick prevention regimen

Tick Killing Solution™

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division
(7511P)
1200 Pennsylvania Avenue NW
Washington, DC 20460

EPA Reg. Number:	Date of Issuance:
86865-1	AUG 25 2011
Term of Issuance:	**UNCONDITIONAL**
Name of Pesticide Product:	Resultix™

NOTICE OF PESTICIDE:

__XX___ Registration ____ Re-registration
(under FIFRA, as amended)

Name and Address of Registrant (include ZIP Code):

Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Biopesticides and Pollution Prevention Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered under the Federal Insecticide, Fungicide and Rodenticide Act.

Registration is in no way to be construed as an endorsement or recommendation of this product by the Agency. In order to protect health and the environment, the Administrator, on his motion, may at any time suspend or cancel the registration of a pesticide in accordance with the Act. The acceptance of any name in connection with the registration of a product under this Act is not to be construed as giving the registrant a right to exclusive use of the name or to its use if it has been covered by others.

This product is unconditionally registered in accordance with FIFRA Sec. 3(c) provided you:

1. Submit and/or cite all data required for registration/ reregistration of your product under FIFRA section 3(c)(5) and section 4 when the Agency requires all registrants of similar products to submit such data.

2. Make the following label change before you release the product for shipment: Revise the EPA Registration Number to read, **"EPA Reg. No. 86865-1".**

3. Submit three (3) copies of the revised final printed labeling before you release the product for shipment.

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA Section 6(e). Your release for shipment of the product constitutes acceptance of these conditions. A stamped copy of the label is enclosed for your records.

Signature of Approving Official:	Date:
Keith A. Matthews, Director Biopesticides and Pollution Prevention Division	25 August 2011

EPA Form 8570-6

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs
Biopesticides and Pollution Prevention Division
(7511P)
1200 Pennsylvania Avenue NW
Washington, DC 20460

EPA Reg. Number:	Date of Issuance:
86865-1	AUG 25 2011
Term of Issuance:	UNCONDITIONAL
Name of Pesticide Product:	Resiltix™

NOTICE OF PESTICIDE:

__XX___ Registration ____ Re-registration
(under FIFRA, as amended)

Name and Address of Registrant (include ZIP Code):

Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

Note: Changes in labeling differing in substance from that accepted in connection with this registration must be submitted to and accepted by the Biopesticides and Pollution Prevention Division prior to use of the label in commerce. In any correspondence on this product always refer to the above EPA registration number.

On the basis of information furnished by the registrant, the above named pesticide is hereby registered under the Federal Insecticide, Fungicide and Rodenticide Act.

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2. Make the following label change before you release the product for shipment: Revise the EPA Registration Number to read, **"EPA Reg. No. 86865-1".**

3. Submit three (3) copies of the revised final printed labeling before you release the product for shipment.

If these conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA Section 6(e). Your release for shipment of the product constitutes acceptance of these conditions. A stamped copy of the label is enclosed for your records.

Signature of Approving Official:

Keith A. Matthews, Director
Biopesticides and Pollution Prevention Division

Date: 25 August 2011

CONCURRENCES

SYMBOL		7511P	7511P				
SURNAME		Cole	Hollis				
DATE		8/17/11	8/25/11				

EPA Form 8570-6

EPA Form 1320-1A (1/90) *Printed on Recycled Paper* OFFICIAL FILE COPY

Pages 354-355 – * Product ingredient source information may be entitled to confidential treatment*

Biochemical Pesticide Human Health Assessment Data Requirements
(From 40CFR §158.2050 and Listed on Data Matrix in Volume 1)

As per the meeting minutes that Piedmont Animal Health and the EPA agreed to, the registration of RESULTIX™ end-use product (EP) requires fulfillment of requirements for both the EP and the technical-grade active ingredient/manufacturing-use product (TGAI/MP). Below are the Tier I toxicology requirements for supporting the registration of this EP as a biochemical pesticide. This table describes the material (TGAI, EP, or both) tested to fulfill these requirements, whether the study is required (R) or conditionally required (C) for the general use pattern for RESULTIX™ (Residential Outdoor Non-Food Use), the corresponding test note number (based on footnotes for the table in 40CFR §158.2050), and the volume containing pertinent information.

Table 1. Toxicity Data Requirements

Gdln No.	Description	Material Tested	Required (R) or Conditional (C) & Note #[(a)]		Volume
870.1100	Acute Oral Toxicity	Both	R	1	10
870.1200	Acute Dermal Toxicity	Both	R	1, 2	10, 11, 12
870.1300	Acute Inhalation Toxicity	Both	R	3	10
870.2400	Acute Eye Irritation	Both	R	2	10, 13
870.2500	Acute Dermal Irritation	Both	R	1, 2	10, 14
870.2600	Skin Sensitization	Both	R	2, 4	10, 15
None	Hypersensitivity Incidents	Both	R	5	10
870.3100	90-Day Oral Toxicity	TGAI	C	6	10
870.3250	90-Day Dermal Toxicity	TGAI	C	7	10
870.3465	90-Day Inhalation Toxicity	TGAI	C	8	10
870.3700	Prenatal Developmental Toxicity	TGAI	C	9	10
870.5100	Bacterial Reverse Mutation Test	TGAI	C	10	10
870.5300, 5375	*In Vitro* Mammalian Cell Assay	TGAI	C	10	10
870.7200	Companion Animal Safety	EP	R	11	18, 19

(a) See next page for notes.

The following Test Notes are taken directly from 40CFR Part §158.2050. Relevancy pertains to the EPA general use pattern, actual use and properties of IPM or RESULTIX™. If considered not relevant or if relevancy is questionable (?), further discussion is presented in this Volume 10.

Table 2. Test Notes to Determine Relevancy

Description	Relevant	Study
1. Required unless the test material is a gas or highly volatile.	Yes	Acute oral/dermal
2. Required unless test material is corrosive to skin or has pH <2 or >11.5.	Yes	Acute dermal
3. Required when the pesticide, under conditions of use, would result in respirable material (e.g., gas, volatile substance or aerosol/particulate)...	Yes	Acute inhalation
4. Required if repeated contact with human skin is likely to occur under conditions of use.	Yes	Dermal, Sensitization
5. Hypersensitivity (HS) incidents must be reported as adverse effects data.	Yes	HS
6. Required for non-food uses that are likely to result in repeated oral exposure to humans.	No	90-day oral
7. Required to support uses involving purposeful application to the human skin or which would result in comparable prolonged human exposure to product ...and if any of the following criteria are met:	Yes	90-day dermal
i. Data from a 90-day oral study are not required.	Met	
ii. The active ingredient is known or expected to be metabolized differently by the dermal route of exposure than by the oral route and the metabolite is of toxicological concern.	NA[(a)]	
iii. The use pattern is such that the dermal route would be the primary route of exposure.	NA[(b)]	
8. Required if there is a likelihood of significant levels of repeated inhalation exposure to the pesticide as a gas, vapor, or aerosol.	?[(c)]	90-day inhalation
9. Required if the use of the product under widespread and commonly recognized practice may reasonably be expected to result in significant exposure to female humans (e.g., occupational exposure or repeated application of insect repellents directly to the skin).	?[(c)]	Prenatal developmental
10. Required to support nonfood uses if either:		Bacterial reverse mutation; *In vitro* mammalian
i. The use is likely to result in significant human exposure; or	?[(c)]	
ii. The active ingredient (or its metabolites) is structurally related to a known mutagen or belongs to any chemical class of compounds containing a known mutagen.	NA	
11. May be required if the product's use will result in exposure to domestic animals through, but not limited to, direct application or consumption of treated feed (No. 20 in 40CFR §158.2050 table).	Yes	Companion Animal Safety

(a) NA = Not Applicable.
(b) Whether inhalation or dermal is major route of exposure is not relevant; the first criterion was met.
(c) Relevancy depends upon what is considered significant (the frequency of use?); see Justification section for further discussion.

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DATA MATRIX

Date December 11, 2009	EPA Reg. No./File Symbol 86865-R	Page 1 of 6
Applicant's / Registrant's Name & Address Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	**Product** RESULTIX™	

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	As listed under 40CFR Part 158.2030				
880.1100	Product identity and composition	47811701	Piedmont Animal Health	Own	Also Volume 2
880.1200	Description of starting materials, production and formulation process	47811701	Piedmont Animal Health	Own	Also Volume 2
880.1400	Discussion of formation of impurities	47811701	Piedmont Animal Health	Own	Also Volume 2
830.1700	Preliminary analysis		Piedmont Animal Health	Own	Volumes 2, 3
830.1750	Certified limits		Piedmont Animal Health	Own	Volumes 2, 3
830.1800	Enforcement analytical method		Piedmont Animal Health	Own	Volumes 2, 3
830.1900	Submittal of samples				Not Applicable (NA)
830.6302	Color		Piedmont Animal Health	Own	Volume 2
830.6303	Physical state		Piedmont Animal Health	Own	Volume 2
830.6304	Odor		Piedmont Animal Health	Own	Volume 2
830.6313	Stability to normal and elevated temperature, metals & metal ions		Piedmont Animal Health	Own	Volumes 4, 5
830.6315	Flammability		Piedmont Animal Health	Own	Volumes 2, 6

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 2 of 6
December 11, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.6317	Storage stability		Piedmont Animal Health	Own	Volumes 2, 4, 5, 7, 8
830.6319	Miscibility		Piedmont Animal Health	Own	Volume 2
830.6320	Corrosion characteristics		Piedmont Animal Health	Own	Volumes 4, 5, 7
830.7000	pH		Piedmont Animal Health	Own	Volume 2
830.7050	UV/Visible absorption		Piedmont Animal Health	Own	Volumes 8, 9
830.7100	Viscosity		Piedmont Animal Health	Own	Volume 2
830.7200	Melting point/melting range		Piedmont Animal Health	Own	Volume 2
830.7220	Boiling point/boiling range		Piedmont Animal Health	Own	Volume 2
830.7300	Density/relative density/bulk density		Piedmont Animal Health	Own	Volume 2
830.7520	Particle size, fiber length, and diameter distribution		Piedmont Animal Health	Own	Volume 2
830.7550, 7560, 7570	Partition coefficient (octanol-water)		Piedmont Animal Health	Own	Volume 2
830.7840	Water solubility; Column elution method; shake flask		Piedmont Animal Health	Own	Volume 2
830.7950	Vapor pressure		Piedmont Animal Health	Own	Volume 2

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 3 of 6
December 11, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	As listed under 40CFR Part 158.2040				
860.1100	Chemical identity				All data requirements are NOT APPLICABLE because this EP is not for food uses.
860.1200	Directions for Use				
860.1300	Nature of the residue in --plants, livestock				
860.1340	Residue analytical method				
860.1360	Multiresidue method				
860.1400	Magnitude of the residue – potable water, fish, irrigated crops				
860.1460	Food handling				
860.1480	Meat/milk/poultry/eggs				
860.1500	Crop field trials				
860.1520	Processed food/feed				
860.1540	Anticipated Residues				
860.1550	Proposed tolerances				
860.1560	Reasonable grounds in support of the petition				
860.1650	Submittal of analytical reference standards				

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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DATA MATRIX

Date December 11, 2009	EPA Reg. No./File Symbol 86865-R	Page 4 of 6
Applicant's / Registrant's Name & Address Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	**Product** RESULTIX™	

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Tier I	**As listed under 40CFR Part 158.2050**				
870.1100	Acute oral toxicity		Piedmont Animal Health	Own	Volume 10
870.1200	Acute dermal toxicity		Piedmont Animal Health	Own	Volumes 10, 11, 12
870.1300	Acute inhalation toxicity		Piedmont Animal Health	Own	Volume 10
870.2400	Acute eye irritation		Piedmont Animal Health	Own	Volumes 10, 13
870.2500	Acute dermal irritation		Piedmont Animal Health	Own	Volumes 10, 14
870.2600	Skin sensitization		Piedmont Animal Health	Own	Volumes 10, 15
None	Hypersensitivity Incidents		Piedmont Animal Health	Own	Volume 10
870.3050	Repeated dose 28-day oral toxicity		Piedmont Animal Health	Own	Volumes 10, 16
870.3100	90-day oral toxicity		Piedmont Animal Health	Own	Volume 10

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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WASHINGTON, D.C. 20460

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 5 of 6
December 11, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.3200	21/28-day dermal toxicity		Piedmont Animal Health	Own	Volumes 10, 17
870.3250	90-day dermal toxicity		Piedmont Animal Health	Own	Volume 10
870.3465	90-day inhalation toxicity		Piedmont Animal Health	Own	Volume 10
870.3700	Prenatal developmental toxicity		Piedmont Animal Health	Own	Volume 10
870.4200	Carcinogenicity		Piedmont Animal Health	Own	Volume 10
870.5100	Bacterial reverse mutation test		Piedmont Animal Health	Own	Volume 10
870.5300	*In vitro* mammalian cell gene mutation test		Piedmont Animal Health	Own	Volume 10
870.5375	*In vitro* mammalian chromosome aberration test		Piedmont Animal Health	Own	Volume 10
Special Testing					
870.7200	Companion animal safety		Piedmont Animal Health	Own	Volumes 18, 19
870.7485	Metabolism and pharmacokinetics		Piedmont Animal Health	Own	Volumes 10, 20

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 6 of 6
December 11, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Tier I	**As listed under 40CFR Part 158.2060**				
850.1010	Aquatic invertebrate acute toxicity, freshwater daphnids		Piedmont Animal Health	Own	Volume 21
850.1075	Fish acute toxicity test, freshwater and marine		Piedmont Animal Health	Own	Volume 21
850.2100	Avian acute oral toxicity		Piedmont Animal Health	Own	Volume 21
850.2200	Avian dietary toxicity		Piedmont Animal Health	Own	Volume 21
850.4100	Terrestrial plant toxicity, seedling emergence		Piedmont Animal Health	Own	Volume 21
850.4150	Terrestrial plant toxicity, vegetative vigor		Piedmont Animal Health	Own	Volume 21
880.4350	Nontarget insect testing		Piedmont Animal Health	Own	Volume 21
	As listed under 40CFR Part 158.2070				
810.3300	Treatments to Control Pests of Humans and Pets		Piedmont Animal Health	Own	Volumes 18, 19

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	12/14/09

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Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number	EPA Registration Number/File Symbol
Piedmont Animal Health LLC. 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410 Telephone: 336-544-0320 x 202	86865-R
Active Ingredient(s) and/or representative test compound(s) Isopropyl myristate	**Date** December 11, 2009
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) Residential Outdoor Use, Nonfood	**Product Name** RESULTIX™

NOTE: If your product is a 100% repackaging of another purchased EPA-registered product labeled for all the same uses on your label, you do not need to submit this form. You must submit the Formulator's Exemption Statement (EPA Form 8570-27).

☐ I am responding to a Data-Call-In Notice, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

SECTION I: METHOD OF DATA SUPPORT (Check one method only)

☐ I am using the cite-all method of support, and have included with this form a list of companies sent offers of compensation (the Data Matrix form should be used for this purpose).

☒ I am using the selective method of support (or cite-all option under the selective method), and have included with this form a completed list of data requirements (the Data Matrix form must be used).

SECTION II: GENERAL OFFER TO PAY

[Required if using the cite-all method or when using the cite-all option under the selective method to satisfy one or more data requirements]

☐ I hereby offer and agree to pay compensation, to other persons, with regard to the approval of this application, to the extent required by FIFRA.

SECTION III: CERTIFICATION

I certify that this application for registration, this form for reregistration, or this Data-Call-In response is supported by all data submitted or cited in the application for registration, the form for reregistration, or the Data-Call-In response. In addition, if the cite-all option or cite-all option under the selective method is indicated in Section I, this application is supported by all data in the Agency's files that (1) concern the properties or effects of this product or an identical or substantially similar product, or one or more of the ingredients in this product; and (2) is a type of data that would be required to be submitted under the data requirements in effect on the date of approval of this application if the application sought the initial registration of a product of identical or similar composition and uses.

I certify that for each exclusive use study cited in support of this registration or reregistration, that I am the original data submitter or that I have obtained the written permission of the original data submitter to cite that study.

I certify that for each study cited in support of this registration or reregistration that is not an exclusive use study, either: (a) I am the original data submitter; (b) I have obtained the permission of the original data submitter to use the study in support of this application; (c) all periods of eligibility for compensation have expired for the study; (d) the study is in the public literature; or (e) I have notified in writing the company that submitted the study and have offered (i) to pay compensation to the extent required by sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA; and (ii) to commence negotiations to determine the amount and terms of compensation, if any, to be paid for the use of the study.

I certify that in all instances where an offer of compensation is required, copies of all offers to pay compensation and evidence of their delivery in accordance with sections 3(c)(1)(F) and/or 3(c)(2)(B) of FIFRA are available and will be submitted to the Agency upon request. Should I fail to produce such evidence to the Agency upon request, I understand that the Agency may initiate action to deny, cancel or suspend the registration of my product in conformity with FIFRA.

I certify that the statements I have made on this form and all attachments to it are true, accurate, and complete. I acknowledge that any knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

Signature	Date	Typed or Printed Name and Title
Kathleen G. Palma, Ph.D.	12/14/09	Kathleen G. Palma, Ph.D. Vice President of Research & Development

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NOTES FOR DATA MATRIX

The data guidelines on the data matrix and summarized below are from those sections listed in 40CFR Part 158.2010 (Biochemical pesticides data requirements).

Part 158.2030. Biochemical Pesticides Product Chemistry Data Requirements

All required chemistry data for both the technical grade active ingredient/manufacturing-use product (TGAI/MP) and the end-use product (EP) are listed; relevant volume numbers are so indicated. If not applicable (NA), reasoning will be discussed in the Miscellaneous Chemistry Information Volume 2.

Part 158.2040. Biochemical Pesticides Residue Data Requirements

All required residue data are listed; however, all are NOT APPLICABLE because this product is NOT for food uses.

Part 158.2050. Biochemical Pesticides Human Health Assessment Data Requirements

All Tier I data requirements are listed; relevant volume numbers are so indicated. If not applicable (NA) or there is a substitution of one or more studies for a guideline study, the rationale for this will be discussed in the Miscellaneous Toxicology Information Volume 10. All Tier II and III data requirements are not listed as per the meeting between the EPA and Piedmont Animal Health.

Part 158.2060. Biochemical Pesticides Nontarget Organisms and Environmental Fate Data Requirements

All Tier I data requirements are listed; the relevant volume number is so indicated. If not applicable (NA) or there is a substitution of published information for a guideline study, the rationale for this will be discussed in the Environmental Fate Information Volume 21. All Tier II and III data requirements are not listed as per the meeting between the EPA and Piedmont Animal Health.

Part 158.2070. Biochemical Pesticides Product Performance Data Requirements

Because this is a specialized section, there is only one listing that is pertinent; relevant volume numbers are so indicated.

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DATA MATRIX

Date December 3, 2009	EPA Reg. No./File Symbol 86865-R	Page 1 of 6
Applicant's / Registrant's Name & Address Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	**Product** RESULTIX™	

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	As listed under 40CFR Part 158.2030				
880.1100	Product identity and composition	47811701	Piedmont Animal Health		Also Volume 2
880.1200	Description of starting materials, production and formulation process	47811701	Piedmont Animal Health		Also Volume 2
880.1400	Discussion of formation of impurities	47811701	Piedmont Animal Health		Also Volume 2
830.1700	Preliminary analysis		Piedmont Animal Health		Volumes 2, 3
830.1750	Certified limits		Piedmont Animal Health		Volumes 2, 3
830.1800	Enforcement analytical method		Piedmont Animal Health		Volumes 2, 3
830.1900	Submittal of samples				Not Applicable (NA)
830.6302	Color		Piedmont Animal Health		Volume 2
830.6303	Physical state		Piedmont Animal Health		Volume 2
830.6304	Odor		Piedmont Animal Health		Volume 2
830.6313	Stability to normal and elevated temperature, metals & metal ions		Piedmont Animal Health		Volumes 4, 5
830.6315	Flammability		Piedmont Animal Health		Volumes 2, 6

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 Dec 2009

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 2 of 6
December 3, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
830.6317	Storage stability		Piedmont Animal Health		Volumes 2, 4, 5, 7, 8
830.6319	Miscibility		Piedmont Animal Health		Volume 2
830.6320	Corrosion characteristics		Piedmont Animal Health		Volumes 4, 5, 7
830.7000	pH		Piedmont Animal Health		Volume 2
830.7050	UV/Visible absorption		Piedmont Animal Health		Volumes 8, 9
830.7100	Viscosity		Piedmont Animal Health		Volume 2
830.7200	Melting point/melting range		Piedmont Animal Health		Volume 2
830.7220	Boiling point/boiling range		Piedmont Animal Health		Volume 2
830.7300	Density/relative density/bulk density		Piedmont Animal Health		Volume 2
830.7520	Particle size, fiber length, and diameter distribution		Piedmont Animal Health		Volume 2
830.7550, 7560, 7570	Partition coefficient (octanol-water)		Piedmont Animal Health		Volume 2
830.7840	Water solubility; Column elution method; shake flask		Piedmont Animal Health		Volume 2
830.7950	Vapor pressure		Piedmont Animal Health		Volume 2

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 Dec 2009

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DATA MATRIX

Date	EPA Reg. No./File Symbol	Page 3 of 6
December 3, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
	As listed under 40CFR Part 158.2040				
860.1100	Chemical identity				All data requirements are NOT APPLICABLE because this EP is not for food uses.
860.1200	Directions for Use				
860.1300	Nature of the residue in --plants, livestock				
860.1340	Residue analytical method				
860.1360	Multiresidue method				
860.1400	Magnitude of the residue – potable water, fish, irrigated crops				
860.1460	Food handling				
860.1480	Meat/milk/poultry/eggs				
860.1500	Crop field trials				
860.1520	Processed food/feed				
860.1540	Anticipated Residues				
860.1550	Proposed tolerances				
860.1560	Reasonable grounds in support of the petition				
860.1650	Submittal of analytical reference standards				

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 Dec. 2009

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DATA MATRIX

Date December 3, 2009	EPA Reg. No./File Symbol 86865-R	Page 4 of 6
Applicant's / Registrant's Name & Address Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	**Product** RESULTIX™	

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Tier I	**As listed under 40CFR Part 158.2050**				
870.1100	Acute oral toxicity		Piedmont Animal Health		Volume 10
870.1200	Acute dermal toxicity		Piedmont Animal Health		Volumes 10, 11, 12
870.1300	Acute inhalation toxicity		Piedmont Animal Health		Volume 10
870.2400	Acute eye irritation		Piedmont Animal Health		Volumes 10, 13
870.2500	Acute dermal irritation		Piedmont Animal Health		Volumes 10, 14
870.2600	Skin sensitization		Piedmont Animal Health		Volumes 10, 15
None	Hypersensitivity Incidents		Piedmont Animal Health		Volume 10
870.3050	Repeated dose 28-day oral toxicity		Piedmont Animal Health		Volumes 10, 16
870.3100	90-day oral toxicity		Piedmont Animal Health		Volume 10

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 Dec 2009

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Date	EPA Reg. No./File Symbol	Page 5 of 6
December 3, 2009	86865-R	

Applicant's / Registrant's Name & Address	Product
Piedmont Animal Health LLC 204 Muirs Chapel Road, Suite 200 Greensboro, NC 27410	RESULTIX™

Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
870.3200	21/28-day dermal toxicity		Piedmont Animal Health		Volumes 10, 17
870.3250	90-day dermal toxicity		Piedmont Animal Health		Volume 10
870.3465	90-day inhalation toxicity		Piedmont Animal Health		Volume 10
870.3700	Prenatal developmental toxicity		Piedmont Animal Health		Volume 10
870.4200	Carcinogenicity		Piedmont Animal Health		Volume 10
870.5100	Bacterial reverse mutation test		Piedmont Animal Health		Volume 10
870.5300	*In vitro* mammalian cell gene mutation test		Piedmont Animal Health		Volume 10
870.5375	*In vitro* mammalian chromosome aberration test		Piedmont Animal Health		Volume 10
Special Testing					
870.7200	Companion animal safety		Piedmont Animal Health		Volumes 18, 19
870.7485	Metabolism and pharmacokinetics		Piedmont Animal Health		Volumes 10, 20

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 DEC 2009

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Ingredient

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
Tier I	**As listed under 40CFR Part 158.2060**				
850.1010	Aquatic invertebrate acute toxicity, freshwater daphnids		Piedmont Animal Health		Volume 21
850.1075	Fish acute toxicity test, freshwater and marine		Piedmont Animal Health		Volume 21
850.2100	Avian acute oral toxicity		Piedmont Animal Health		Volume 21
850.2200	Avian dietary toxicity		Piedmont Animal Health		Volume 21
850.4100	Terrestrial plant toxicity, seedling emergence		Piedmont Animal Health		Volume 21
850.4150	Terrestrial plant toxicity, vegetative vigor		Piedmont Animal Health		Volume 21
880.4350	Nontarget insect testing		Piedmont Animal Health		Volume 21
	As listed under 40CFR Part 158.2070				
810.3300	Treatments to Control Pests of Humans and Pets		Piedmont Animal Health		Volumes 18, 19

Signature	Name and Title	Date
Kathleen G. Palma, Ph.D.	Kathleen G. Palma, Ph.D. Vice President of Research & Development	02 DEC 2009

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JUN 17 2009

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Kathleen G. Palma, Ph.D.
Regulatory Affairs, Consultant
Piedmont Animal Health
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

Dear Dr. Palma:

Subject: Response to Notes dated June 8, 2009
Meeting with Piedmont Animal Health

The Agency is in receipt of the meeting notes from the April 30 pre-registration meeting with Piedmont Animal Health concerning a new product containing the unregistered biochemical, isopropyl myristate. The following is the Agency's official response to the meeting notes per the action items as listed in your letter:

1) Piedmont Animal Health Note:

Piedmont Animal Health received a biochemical classification for this product. Consequently the EPA will accept a reduced safety data set for registration which would only include Tier I safety requirements as outlined in 158.2030, the Biochemical pesticides product chemistry data requirements table. Tier II safety requirements will probably not required.

Agency Response

There are no Tiers for product chemistry. All product chemistry data guidelines must be satisfied for both the Technical Grade Active Ingredient (TGAI) and the End Use Product (EP). As you stated in your note above, please refer to 40 CFR § 158.2030 for biochemical pesticides product chemistry data requirements.

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Inert ingredient information may be entitled to confidential treatment

Product ingredient source information may be entitled to confidential treatment

2) Piedmont Animal Health Note:

The tick spray consists of 50% Isopropyl myristate, the active and 50% [redacted], the excipient. There is no label or Confidential Certificate of Formulation (CSF). The spray could be used on an "as needed" basis. EPA instructed PAH that [redacted] should be cleared as the excipient under 40 CFR § 189.30 and contact PV Shaw or Kerry Grenstad. PAH can replace with another excipient or go to the "inerts" branch if necessary. EPA acknowledged that the "inerts" branch would be fast since this tick spray is a non-food use.

Agency Response

All pesticide products must bear a label with all of the required labeling language. Please refer to 40 CFR § 156-Labeling Requirements for Pesticides and Devices. You must have a Confidential Statement of Formula (CSF) for your product, and it must be completely filled out. The CSF EPA form 8570-4. Tips for avoiding Confidential Statement of Formula or Product Chemistry issues with Biopesticides can be found via the following internet link: www.epa.gov/pesticides/biopesticides/regtools/index.htm. This aforementioned link is also a good source for all issues related to registering biopesticides. The Agency is in agreement with your understanding that you must have your inert ingredients cleared by the "Inerts Assessment Branch". You may contact Prakashchandra (PV) Shah at 703.308.1846. For clarification purposes, BPPD cannot speak as to the speed of clearance of any inert ingredients. Inert Assessment Branch is in a different division.

3 Piedmont Animal Health Note:

Piedmont Animal Health gave a brief history of the tick spray's development. The tick spray has a safe profile in humans because Phase 3 clinical trials with CDER/FDA under INAD 66,651 were conducted with the same product as a head lice product for humans. The clinical studies with the safety profiles will be submitted to support safety with humans for the tick product. Once the product is sprayed on a tick, death begins less than 4 hours after the tick is sprayed. Some ticks may be moribund but will die within 24 hours. The isopropyl myristate, a fatty acid ester, [redacted] EPA provided PAH with a handout listing the data requirements. EPA mentioned some of those requirements. Technical and end-use data requirements should be satisfied. All data requirements should be addressed even if those requirements are not applicable. An explanation as to why the data requirement is not applicable should be provided. Units should be included with the CSF. All "impurities should be sent by the supplier even if that information is proprietary. As long as reference are specific, EPA can use them.

Agency Repouse

The Agency is in agreement with you note above with the exception that all data requirements MUST be addressed, and the references that you have MUST be submitted with your application for registration.

4 Piedmont Animal Health Note:

Per 86.5, formatted data requirements must pass administrative screen for formatting. If literature is used in the submission, use info doc as guidance to use literature references. The type of acceptable cited literature would be peer-reviewed articles, scientifically credible data and a citation from the MRID.

Agency Response

The Agency is in agreement with the discussion as outlined above. All data submitted must be formatted according to PR Notice 86-5.

5 Piedmont Animal Health Note:

Since this tick product is considered a B-600 (non-food use new product) the cost is $15,700 however PAH may qualify for a small business waiver under PRIA2 (Pesticide Registration Act). No studies are waived unless there is no exposure or the product is very acidic or basic. Given these criteria, PAH will not be granted a waiver for the tick spray.

Agency Reponse

The Agency is in agreement with the discussion that your product is a new active ingredient non-food use and would be classified as a B600 under Pesticide Registration Improvement Act (PRIA 2). PAH stated that the fee would be $15,700. The Agency is in agreement with your note that PAH may qualify for a small business waiver. The Agency is in agreement that no guideline studies are waived unless there is no exposure.

6 Piedmont Animal Health Note:

For the toxicology discussion, exposure should be discussed provided endpoints are identified. EPA will do the risk assessment. The pharmacokinetic studies done for the development of the human head louse product (Resultz™) can be used to support the tick spray product for dogs. The global use of Resultz™ and the post-marketing safety profile can also be used to support the safety of the tick spray.

Agency Response

It is important to note that all Tier I data requirements MUST be addressed individually. The safety profile is contingent upon Biopesticide and Pollution Prevention Division's review of the data and the acceptability of those data.

7) Piedmont Animal Health Note:

The Environmental Assessment completed for Resultz™ should address the ecological requirements. A rationale should be written why a bird study is not required given that birds should not come into contact with this product. Fish and aquatic invertebrate studies should be addressed because dogs do swim. EPA is concerned for endangered species.

Agency Response

The Agency is in agreement with the note above.

8) PRIA Category

In the efficacy study there should be a 90% reduction in ticks. Given that the tick spray is most efficacious when sprayed on dry dogs, the label may need to read "apply to dry dog". Ms. Gonzales stated that she would look into the requirement for companion animal safety and respond back to PAH. PAH stated that the safety could be tied into the efficacy study with possible physical exams and clinical blood chemistries. There is no requirement to submit the efficacy protocol but the typical protocol format should be used. The end use product is the only thing to be registered.

Agency Response

The Agency is in agreement with the note above. Also you must address companion animal study according to 40 CFR § 158.2050.

Should you have any questions regarding this response to your meeting notes, you may contact Leonard Cole directly at 703.305.5412 or via email at cole.leonard@epa.gov . We hope that you find this information helpful.

Sincerely,

Linda A. Hollis, Chief
Biochemical Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)

EPA MEETING MINUTES FOR APRIL 30, 2009 AND EPA RESPONSE LETTER

On April 30, 2009, three Piedmont Animal Health representatives met with two EPA representatives of the Biochemical Pesticides Branch. The meeting minutes were drafted by Piedmont and reviewed by the EPA, which in return responded with a letter. Copies of these two documents begin on the next page.

Inert ingredient information may be entitled to confidential treatment
Product ingredient source information may be entitled to confidential treatment

6. Source – Active derived from [redacted], [redacted]

   [redacted]

7. Piedmont should clear [redacted] under ECFR – check 40CFR 189-30 and contact PV Shaw or Kerry Grenstad - can replace with other Excipient or go to "inerts" branch
8. Leonard reports that inert branch is fast, because it's non-food use
9. Data Requirements – see handout provided by Angela Gonzales
   a. Satisfy technical and end-use date requirement
   b. Address all data requirements – say "why" if N/A
   c. Include units in CSFs
   d. Supplier needs to send all "impurities" even if proprietary
   e. We can use references – be specific
10. 86-5 – Formatted data requirement to pass administrative screen
11. Non-food use
12. Address Tier I only – Tox end use – "six pack"
13. If literature is used, use info doc – guidance to use literature references
    a. Peer-reviewed
    b. Scientific credible data
    c. Site MRID
14. There are fees involved now (B6)
15. Tox discussion – provide "exposure" discussion if endpoints identified. EPA will do risk assessment.
16. No studies are waived unless

a. No exposure

b. Very acidic or basic

c. We will not be "granted" waiver

17. Can use PK studies form Resultz

18. Talk about global use of RESULTZ™ and safety profile

19. Eco-requirements – use environmental assessment

    a. Write a rationale to not require a bird study

    b. Address fish and invertebrate studies because dogs do swim

    c. Concern is endangered species

20. Tier 2 probably not required

21. Study proposal – makes sure data shows 90% reduction. (efficacy)

22. Study outline – how to address wet dogs. Label may need to say "apply to dry dog".

23. Companion animal studies – requirement, Angela will look into this and respond to PAH.

    Can we tie into efficacy

24. Register end-use only

25. No requirement to submit a protocol – use typical protocol format

26. B-600 non food use new product up to 12 months for an answer

    a. $15,700 apply waiver/ under PRIA2 – pest- reg. act

    b. Fill out waiver for small business

FRONT PANEL

RESULTIX™

End-Use Product
Kills Ticks on Dogs and Cats

ACTIVE INGREDIENT	
Isopropyl Myristate	50.0%
OTHER INGREDIENT	50.0%
TOTAL	100.0%

KEEP OUT OF REACH OF CHILDREN

CAUTION

See Side/Back Panel for First Aid

STOP - READ LABEL BEFORE USE

EPA Reg. No. 86865-R

EPA Est. No. 71979-SC-001

Manufactured for
Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

NET CONTENTS
20 mL (0.65 oz.)

SIDE PANEL

FIRST AID

Hot Line Number

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-222-1222 for emergency medical treatment information.

If on skin:	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor immediately for treatment advice.
If in eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. • Call a poison control center or doctor immediately for treatment advice.
If inhaled:	• Move person to fresh air. • If person is not breathing, call 911 or an ambulance; then give artificial respiration, preferably mouth-to-mouth if possible. • Call a poison control center or doctor immediately for treatment advice.
If swallowed:	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by a poison control center or doctor. • Do not give anything by mouth to an unconscious person.

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION. May cause eye and dermal irritation. Avoid contact with eyes, skin, or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet. Remove contaminated clothing and wash clothing before reuse. Wear appropriate protective equipment, such as protective eyewear, rubber gloves, and long-sleeved shirts.

ENVIRONMENTAL HAZARDS

This pesticide is toxic to invertebrates and fish. Do not discharge this product into lakes, streams, ponds, estuaries, oceans, or other waters unless in accordance with the National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the local sewage authority. For guidance, contact your State Water Board or Regional Office of the EPA.

BACK PANEL

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

For the treatment of ticks on dogs and cats.

- Use when you see a tick or ticks on your dog or cat.
- Remove cap and hold bottle upright, direct nozzle at tick and spray until tick is covered with solution (2 sprays).
- Dispose of dead ticks.

For external use only.
Do not use near dog's or cat's eyes.
Stop and ask a vet if skin irritation or infection is present or develops during use of product.
Keep away from open flames
Store at 59° F – 86° F (15° C – 30° C)

STORAGE AND DISPOSAL

Do not contaminate water, food, or feed by storage and disposal.

Pesticide Storage:
Store in a dry place away from extreme heat and cold (tightly closed at or below +30°C). Keep container closed when not in use. Always store pesticide in the original container. Store away from food and pet food.
In case of fire or other emergency, report at once by toll-free telephone to CHEMTREC (800-424-9300).

Pesticide Disposal and Container Handling:
Nonrefillable container. Do not reuse or refill this container.
If empty: place in trash or offer for recycling if available.
If partly filled: call your local solid waste agency for disposal instructions.
Never place unused product down any indoor or outdoor drain.

NOTICE: Seller warrants that the product conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use. Neither this warranty nor any other warranty of merchantability or fitness for a particular purpose, express or implied, extends to the use of this product contrary to label instructions, or under abnormal conditions, or under conditions not reasonably foreseeable to Seller, and Buyer assumes the risk of any such use.

ANY PANEL (Do not substitute these for required statements)

Label Claims (one or more in various combinations, located in various places throughout the box and bottle/insert labels)

Breakthrough in tick treatments

Clinically proven

Convenient and easy to apply as soon as you see a tick on your pet

Even kills "super ticks", the ones that have built up resistance to traditional pesticide treatments

For the Treatment of Ticks on Dogs and Cats

Free of conventional pesticides

Guaranteed effective

Kills 100% of ticks, even Super Ticks

Kills ticks on pets

No conventional pesticides

Non pesticide, direct spray formula starts killing ticks in seconds

Patented spray formula softens the waterproof outer waxy layer of the tick's body, resulting in rapid dehydration

Recommended to use on its own or in conjunction with other flea and tick control medications

Safe for you and your family

Safe to use on pets

Simple way to kill 100% of ticks on your pet that's completely non-toxic to animals, odorless and pesticide-free

Tick Killing Solution™

Works to reduce human exposure to tick-borne diseases (when used in conjunction with safe tick removal practices)

Pages 383-385 Product ingredient source information may be entitled to confidential treatment

Product ingredient source information may be entitled to confidential treatment

Product Reviewer: Russell Jones/DC/USEPA/US Date of initial draft review 03/26/2009 11:15:56 AM
Date reviewed by the Classification Committee

Active ingredients: Isopropyl Myristate

Company: Piedmont Animal Health Address: 204 Muirs Chapel Road, Suite 200, Greensboro, NC 27410

Company contact: Kathleen Palma, Ph.D., Vice Peresident of Research & Development
Phone: 336-544-0320 x-202 FAX number: 336-544-0322 eMail: kpalma@piedmontpharma.com

Company Representative: Address:
Phone: FAX number: eMail:

Use Patterns:

The activity of this product indicates that it is a Insecticide

Natural Occurrence: Not naturally occurring. It is a fatty acid ester of myristyl alcohol and myristic acid. Myristic acid is produced via the saponification and fractionation of animal/vegetable oils and fats; or via esterfication of isopropyl alcohol and myristic acid. Source of myristic acid for this product is [redacted]

Mode of Action: Solubilizes cuticle - leads to dehydration of target insect

Proposed Use Rates:

Toxicity survey: Acute oral LD50 >16 mL/kg (rat) to >49.7 mL/kg (mouse); Acute dermal LD50 > 5 g/kg; no subchronic dermal tox;

Product is widely used in cosmetics, up to 50% conc. Cosmetic Ingredient Review (CIR) Expert Panel evaluation in 2002 showed that up to 58% isopropyl myristate was not a human skin irritant & not a sensitizer. Minimal skin and eye irritant. Not a carcinogen, but enhanced carcinogenicity of benzo(a)pyrene on human skin.

In Europe is approved for use as an artificial lalvoring at 5 ppm

Decision: Not naturally-occurring, but has non-toxic mode of action similar to sucrose octanoate

Committee Classification: Not a Biochemical but eligible for reduced data set

Management Approval:
- ● Approve
- ○ Approve with comment
- ○ Needs revision - see comments
- ○ Janet L Andersen Director BPPD
- ○ Associate Director BPPD

Comments: Approved by Linda Hollis, Biochemical Pesticides Branch Chief on 03/27/2009

Review Division:
- ● BPPD
- ○ Registration Division
- ○ Antimicrobial Division

Candidate for 25(b) exemption:
- ○ Yes
- ● No

21-Day Screen Completed by Contractor

21-Day Expires on 12-24-09

Jacket # 86865-R
MRID# 479253

Content Screen: Recommended to Pass/Fail

86-5 Review: Passed/Failed/NA

Transfer This Jacket to:

LINDA HOLLIS

PRIA 2 – 21 Day Content Screen Review Worksheet

(EPA/OPP Use Only)

3/23/09

21 Day Screen Start Date: 12-3-09

Experts In-Processing Signature: MF HARRINGTON Date 12-7-09 Fee Paid: Yes ✓

Division management contacted on issues No_____ Yes _____ Date _____

EPA Reg. Number: 86865-R	EPA Receipt Date: 12-3-09

	Items for Review			Yes	No	N/A*
1	**Application Form** (EPA Form 8570-1)(link to form) signed & complete including package type			X		
2	**Confidential Statement of Formula** all boxes completed, form signed, and dated (EPA Form 8570-4) (Link to form)			X		
	a) All inerts (link to http://www.epa.gov/opprd001/inerts/), including fragrances, approved for the proposed uses (see Footnote A)	yes	no			
		X				
3	**Certification with Respect to Citation of Data** (EPA Form 8570-34) (Link to form) completed and signed (N/A if 100% repack)			X		
	Certificate and data matrix consistent			X		
	If applicant is relying on data that are compensable, is the offer to pay statement included. (see Footnote B)	yes	no			
	If applicable, is there a letter of Authorization for exclusive use only.					
4	**Formulator's Exemption Statement** (EPA Form 8570-27) (Link to form) completed and signed (N/A if source is unregistered or applicant owns the technical)					X
5	**Data Matrix** (EPA Form 8570-35) (Link to form) both internal and external copies (PR 98-5) (Link to PR 98-5) completed and signed (N/A if 100% repack)			X		
		yes	no			
	a) Selective Method (Fee category experts use)	X				
	b) Cite-All (Fee category experts use)					
	c) Applicant owns all data (Fee category experts use)					
6	**5 Copies of Label (link to http://www.epa.gov/oppfead1/labeling/lrm/) (Electronic labels on CD are encouraged and guidance is available)(link to** http://www.epa.gov/pesticides/regulating/registering/submissions/index.htm#labels)			X		

7	**Is the data package consistent with PR Notice 86-5** (link to PRN 86-5)	X		
8	**Notice of Filing (link to http://www.epa.gov/pesticides/regulating/tolerance_petitions.htm) included with petitions (link to http://www.epa.gov/pesticides/regulating/tolerances.htm)**			X
9	**If applicable for conventional applications, reduced risk rationale (link to http://www.epa.gov/opprd001/workplan/reducedrisk.html)**			X
10	**Required Data (link to http://www.epa.gov/pesticides/regulating/data_requirements.htm) and/or data waivers. See Footnote C.**			
	a) List study (or studies) not included with application			

Comments:

- Inerts approved for non-food use only
- Studies associated w/ jacket have passed 86-5 review

Jacket Passed

MRID 479253

* N/A – Not Applicable

Footnotes

A. During the 21 day initial content review, all CSFs will be reviewed to determine whether all inerts listed, including fragrances, are approved for the proposed uses. If an unapproved inert is identified, the applicant must either 1) resolve the inert issue by, for example, removing the inert, substituting it with an approved inert, submitting documentation that EPA approved the inert for the proposed pesticidal uses, correcting mistakes on the CSF, etc. or 2) provide the data to support OPP approval of the inert or 3) withdraw the application. Removing or substituting an inert ingredient will require a new CSF and may require submission of data. All information, forms, data and documentation resolving the inert issue must have been received by the Agency or the application withdrawn within the 21 day period, otherwise, the Agency will reject the application as described below.

To successfully complete this aspect of the 21 day initial content screen, applicants are **strongly encouraged** to verify that all inert ingredients have been approved for the application's uses even if **a product is currently registered** by consulting the inert Web

site [link to http://www.epa.gov/opprd001/inerts/lists.html] and if the inert is not approved, to **obtain the necessary inert approval prior to submitting an application to register a pesticide product containing that inert ingredient.** Some inert ingredients are no longer approved for food uses or certain types of uses. The name and/or CAS number on a CSF must match the name and CAS number on this web site. Simple typographical errors in the name or CAS number have resulted in processing delays.

If an inert is not listed on the inert ingredient web site and the applicant believes that the inert has been approved, the applicant should contact the Inert Ingredient Assessment Branch (IIAB) at inertsbranch@epa.gov and resolve the issue. Copies of the correspondence with IIAB resolving the issue should accompany the application. All new inerts except PIP inerts are reviewed by IIAB. The IIAB should also be contacted for any questions on what supporting data needs to be submitted for and the Agency's inert review process. Questions on PIP inerts should be directed to the Chief of Microbial Pesticides Branch [Link to http://www.epa.gov/oppbppd1/biopesticides/contacts_bppd.htm].

When a brand, trade, or proprietary name of an inert ingredient is listed on a CSF, additional information such as an alternate name of the inert, CAS number or other information [link to http://www.epa.gov/opprd001/inerts/tips.pdf] must also be included to enable the Agency to determine if it has been approved. Each component of an inert mixture (including a fragrance) must be identified. In some cases, the supplier of the mixture or fragrance may need to provide this information to the Agency. Prior to the Agency's receipt of an application, applicants must arrange with a proprietary mixture or fragrance supplier to provide the component information to the Agency or promptly upon EPA's request. If the inert ingredients in a proprietary blend (including fragrances) cannot or are not identified or provided within the 21-day content review period, the Agency will reject the application.

During the 21 day content review, applicants should submit information to the individual identified by the Agency when the applicant is informed of an unapproved inert.

Unapproved Inerts Identified on CSFs

All applications except conventional new products and PIPs

Once an unapproved inert is identified on a CSF, the Agency will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If this option is selected and implemented, the Agency may request an extension in the PRIA decision review timeframe to accommodate the inert review/approval process;

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of these options is selected and implemented by the applicant within the 21 day content review period, the Agency will reject the application and retain 25% of the full fee of the category identified.

Conventional New Product Applications

When the Registration Division identifies an unapproved inert on a CSF with an application for a new product that the applicant has not identified as requiring an inert approval (R311, R312 or R313), it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert, including any required petition to establish or amend a tolerance or exemption from a tolerance. (This option may change the PRIA category for the application, which could require a longer decision review time and a larger fee. If additional fees are due, they must be received by the Agency within the 21 day content review period.)

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21-day content-review period, the Agency will reject the application and retain 25% of the appropriate fee for the new product-inert approval category.

PIP Applications

When the Biopesticide and Pollution Prevention Division identifies an unapproved inert on a PIP CSF and a request to approve the inert does not accompany the application, it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the spelling or name of the inert to that in 40 CFR 174, or providing documentation that the inert has been approved; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If an inert ingredient tolerance exemption petition is required, the petition must be received by the Agency and the B903 fee paid within the 21 day period. If this option is selected and implemented, the Agency will discuss harmonizing the timeframe for both actions.

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21 day content review period, the Agency will reject the application and retain 25% of the fee.

B. A policy on documentation of offers to pay is still being developed, however, for a me-too or fast track (similar/identical) new product, R300 or A530, an application without the necessary authorizations of offers to pay will be placed into either R301 or A531. The Agency recommends that authorizations of offers to pay be submitted with other PRIA applications to avoid delays in the Agency's decision.

C. Biopesticide applicants are advised to contact the Agency and discuss study waivers prior to submitting their application to the Agency. Documentation of such discussions should be submitted with the study waiver.

Script for Rejection Phone calls

Contact Name: Susan Phillips
Phone #: 202-298-1785
Email: sphillips@gsblaw.com

First Call/Initials:
Date: 12/10/09
Time: 3:45 Pm

Second Call/Initials:
Date:
Time:

This is Jennifer Drolish **, EPA contractor.**

I'm calling regarding your submission in support of
Application to Register Resultix (86865-R).

We have found the following deficiencies regarding:
PR Notice 86.5: Yes or No

Volume/Study Title: Volumes 6, 16, 17: GLP must specify 40 CFR part 160

Volume/Study Title: Volume 20: missing study director's signature ~~and~~ on GLP and must specify 40 CFR Part 160

Volume/Study Title:

Additional volumes continued on back of page: Yes or No

Application Package: Yes or No
Missing Certification (selective method)
Status on Data Matrix not listed

These deficiencies have been approved by EPA.
The corrections can be faxed to 703-305-5060/Attn: _____.

Second Call/Email:
If we do not receive the corrections by _____, we will process your submission, accordingly. Please direct all future calls and correspondence to the appropriate EPA Risk Manager.

Application to Register Resultix - Requested forms and GLP signature pages

Susan Phillips to: Jennifer Drobish 12/15/2009 01:00 PM
Cc: "'Kathy Palma'", "'Matt Schneider'"

As per your request last week I have attached signed and dated EPA Forms 8570-34 (new) and 8570-35 (revised). In addition, the second document contains the GLP page 3 for 4 volumes (6, 16, 17, and 20).

I hope these are satisfactory.

Regards,
Susan Phillips

P.S. This is my home email address; I often work at home. 8570-34 & 35 Revised.pdf 4 GLP pages.PDF

RE: Application to Register Resultix
Jennifer Drobish to: Susan Phillips 12/14/2009 09:51 AM

Just to inform you, the deadline for this application package is this Friday, 12/18/09. I will be out of the office from Wednesday (12/16) until next Monday (12/21). If the paperwork is not ready for me tomorrow I will forward you the contact information of a coworker that will be taking over for me.

"Susan Phillips" Thanks. I hope to get all of the paperwork to yo... 12/14/2009 09:45:57 AM

From: "Susan Phillips" <SPhillips@gsblaw.com>
To: Jennifer Drobish/DC/USEPA/US@EPA
Date: 12/14/2009 09:45 AM
Subject: RE: Application to Register Resultix

Thanks. I hope to get all of the paperwork to you within a few days.

-----Original Message-----
From: Drobish.Jennifer@epamail.epa.gov
[mailto:Drobish.Jennifer@epamail.epa.gov]
Sent: Monday, December 14, 2009 9:44 AM
To: Susan Phillips
Subject: RE: Application to Register Resultix

The wording is acceptable.

Thank you
Jennifer Drobish
EPA Contractor
703-305-1671

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Jennifer Drobish/DC/USEPA/US@EPA

Date: 12/14/2009 09:38 AM

Subject: RE: Application to Register Resultix

The conduct of each study differs from the requirements of EPA GLP because each was done for a FDA submission. Consequently, unless you want the lab to go through the EPA GLP requirements point by point and compare them with the specific FDA requirements under which they were conducted(which could take days), a generalized statement would be appropriate, such as what is already stated on these pages. For example, this would be the wording for the Flammability study:

This study does NOT meet EPA GLP requirements of 40CFR Part 160 and differs in the following way:

This study was conducted in compliance with United States FDA GLP regulations under 21CFR Part 58, with exception of Sections 58.31(d) and 58.105(a) and (b); characterization and stability information was not provided to the testing facility.

For the PK study, which was not a laboratory study, the following would be the wording:

This study does NOT meet EPA GLP requirements of 40CFR Part 160 and differs in the following way:

This clinical study was conducted in accordance with United States FDA regulations pertaining to Good Clinical Practice and Clinical Trials, including the requirements of 21CFR Part 312.21, Investigational New Drug Application (IND): Phases of an Investigation.

If this wording is unacceptable, then I request the exact wording that would be acceptable.

-----Original Message-----
From: Drobish.Jennifer@epamail.epa.gov
[mailto:Drobish.Jennifer@epamail.epa.gov]
Sent: Friday, December 11, 2009 1:16 PM
To: Susan Phillips
Subject: RE: Application to Register Resultix

Ms Phillips

Regarding the GLP statement

If you can cut the original statement and replace it with the statement "This study does not meet the requirements of 40 CFR Part 160 and differs in the following way:" that would be fine. You can write it in, but the FDA information should be removed.

Regarding the study director's signature, you can write in "Study Director" under "Principle Investigator"

Thank you
Jennifer Drobish
EPA Contractor
703-305-1671

From: "Susan Phillips" <SPhillips@gsblaw.com>

To: Jennifer Drobish/DC/USEPA/US@EPA

Cc: <kpalma@piedmontpharma.com>

Date: 12/10/2009 05:52 PM

Subject: RE: Application to Register Resultix

Response:
1. I will send you the Respect to Citation of Data appropriately filled out and signed and dated; and resubmit the Data Matrix with "own" in the "Status" column, also resigned and dated.

2. None of the documents you listed below were conducted for submission to the EPA and consequently were not conducted under 40CFR Part 160, as so stated on page 3 of each volume. These were conducted for submission to the FDA in support of a NDA under the FDA; which does not have a specific GLP/GCP part in 21CFR. Thus do you want the pages with the statement "This study does not meet the requirements of 40 CFR Part 160 and differs in the following way:" above the statements already present?

Because none of these studies were conducted for submission to the EPA as already stated on these pages, can I just hand write in the statement above and just resubmit the pages to you or do I have to retype the pages, and go back to the study director or principal investigator to get their signatures again? They have already acknowledged on these pages that the studies were not conducted for the EPA and consequently, could not have been done under 40CFR part 160.

3. The "study director" for the PK study is D. Garg because he is the principal investigator as described in the page containing the Synopsis (#2) and throughout this study report; usually for human clinical studies the term principal investigator rather than study director is used. Thus, for our purposes, "principal investigator" should be considered synonymous to "study director". Shall I handwrite below the phrase "Principal Investigator" "(Study Director)" to help clarify the nomenclature?

-----Original Message-----
From: Drobish.Jennifer@epamail.epa.gov
[mailto:Drobish.Jennifer@epamail.epa.gov]
Sent: Thursday, December 10, 2009 3:45 PM
To: Susan Phillips
Subject: Application to Register Resultix

Ms Phillips

This is Jennifer Drobish, EPA Contractor. I'm writing in regards to your submission in support of the application to register Resultix. We have found several deficiencies regarding the application package and PR Notice 86.5.

Application package:

-the Certification with Respect to Citation of Data (EPA Form 8570-34) is missing
-the status of the studies listed on the Data Matrix (EPA Form 8570-35) is not listed. If the status for any of the studies is "own," please be sure to check the "selective method" on the Certification

PR Notice 86.5:

The GLP statements for the following studies must state 40 CFR 160 compliance
-Volume 6 - Flammability / Flash Point
-Volume 16 - 28-Day Oral Toxicity Study in Rats with a 14-Day Recovery
-Volume 17 - 28-Day Dermal Toxicity Study in Pigs with a 14-Day Recovery

Volume 20 - Pharmacokinetic, Safety and Tolerance Study of RESULTZ Pediculicide Rinse in Pediatric Subjects with Pediculosis Capitis must state 40 CFR 160 compliance and is missing the study director's signature

The corrections can be faxed to 703-305-5060/Attn: Jennifer Drobish or emailed to me at drobish.jennifer@epa.gov

Thank you
Jennifer Drobish
EPA Contractor
703-305-1671

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

December 7, 2009

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

OPP Decision Number: D-424225
EPA File Symbol or Registration Number: 86865-R
Product Name: RESULTIX TM
EPA Receipt Date: 03-Dec-2009
EPA Company Number: 86865
Company Name: PIEDMONT ANIMAL HEALTH

KATHLEEN G. PALMA, PH.D.
PIEDMONT ANIMAL HEALTH
204 MUIRS CHAPEL ROAD, SUITE 200
GREENSBORO, NC 27410-

SUBJECT: Receipt of Application and 75% Small Business Waiver Request

Dear Registrant:

The Office of Pesticide Programs has received your application, 75% small business waiver request, and certification of payment. If you submitted data with this application, the results of the PRN-86-5 screen will be communicated separately. During the administrative screen, the Office of Pesticide Programs has determined that this Action is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act.

The Action has been identified as Action Code: B600
NEW AI;NON-FOOD USE;MICROBIAL/BIOCHEMICAL;

Your request for waiver has been forwarded for review. You will be notified in writing when a determination is made regarding your request. If your waiver request is approved, the decision review time period will start on the date of approval. If your waiver request is denied, you will receive an invoice for the outstanding balance.

If you have any questions, please contact the Pesticide Registration Service Fee Ombudsman at (703) 308-8260.

Sincerely,

Teresa Downs

Front End Processing Staff
Information Technology & Resources Management Division

Receipt for Section 3

S: 863571 Resubmission: Yes No

Regulatory Type: Product Registration - Section 3 Fee For Service: Yes No

Application Type: New Registration Billable: Yes No

Company: 86865 PIEDMONT ANIMAL HEALTH

Print Letter

Enter More Information

Tracking

Risk Manager: Biologicals & Pollution Prevention Division, PM Team 91

Product #: 86865-R Product Name: RESULTIX TM

Overridek

Me Too Section3: Me Too Product Name:

Application Date: 03-Dec-2009 OPP Rec'vd Date: 03-Dec-2009

Front End Date: 04-Dec-2009 Risk Manager Send Date:

FFS Due Date: Negotiated Due Date:

OPP Target Date:

Receipt Content

Study

CSF

View/Edit

Fast Track: New Ingredient:

Receipt Description:

Pesticide registration submission

New Ingredient Request Date:

New Ingredient Received Date:

Form A: Signature Date: Form B: Signature Date:

Fee for Service

{863571.~

This package includes the following

- ◉ New Registration
- ○ Amendment

☑ Studies? ☑ Fee Waiver?

☐ volpay % Reduction: ____

for Division

- ○ AD
- ◉ BPPD
- ○ RD

Risk Mgr. 91

Receipt No.	S- 863571
EPA File Symbol/Reg. No.	86865-R
Pin-Punch Date:	12/3/2009

☐ This item is NOT subject to FFS action.

Action Code:

Requested:

Granted: B600

Amount Due: $ _____

Parent/Child Decisions:

☐ Inert Cleared for Intended Use ☐ Uncleared Inert in Product

Reviewer: Andrew Bycelonis Date: 12/4/09

Remarks:

FEE FOR SERVICE

Pages 404-411 *Confidential Statement of Formula may be entitled to confidential treatment*