EPA Reg. No. 11678-57
Volume 1

MAKHTESHIM
A G A N
of
North America
Inc.

February 21, 2005

Document Processing Desk (FPL)
Registration Division (7504C)
USEPA
Ariel Rios Building
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Attn: Dr. Oonni Oonnithan
Insecticide-Rodenticide Branch
Phone: 703-305-5404

Re: Final printed labeling
Rimon Technical, EPA Reg. No. 11678-57
Your letter dated 1-25-05

Dear Dr. Oonnithan:

Enclosed is one copy of final printed labeling for the referenced product. The following administrative documents are attached:

- Application Form (EPA Form 8570-1)
- One copy of final printed labeling

Should you have additional questions, please contact me at 901-861-4400.

Sincerely,

Anne Stout

Anne Stout
Registration Specialist
For Makhteshim-Agan

Enclosures

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

Please read instructions on reverse before completing form.

Form Approved. 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 11678-57	2. EPA Product Manager S. Oonnithan	3. Proposed Classification ☑ None ☐ Restricted
4. Company/Product (Name) Rimon Technical	PM# IRB	
5. Name and Address of Applicant *(Include ZIP Code)* Makhteshim-Agan of North America, Inc. 551 Fifth Avenue, Suite 1100 New York, NY 10176 ☐ *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 _____
☑ Notification - Explain below.
☑ Final printed labels in repsonse to Agency letter dated 1-25-05
☐ "Me Too" Application.
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

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	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☐ 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)
Anne Stout	Registration Specialist	901-861-4400

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 Anne Stout	3. Title Registration Specialist
4. Typed Name Anne Stout	5. Date 2-21-05

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

NOT REVIEWED
In Accordance with PR Notice 82-2
Based on Draft Labeling Dated

JAN 25 2005

TECHNICAL

(Novaluron)

For The Manufacture of Insecticides Only

	% BY WT.
ACTIVE INGREDIENT: Novaluron: 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	98.5%
INERT INGREDIENTS:	1.5%
TOTAL	100.0%

KEEP OUT OF REACH OF CHILDREN

CAUTION

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

FIRST AID

IF ON SKIN OR CLOTHING:
- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor 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.

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 eye.
- Call a poison control center or doctor 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 for further treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment.

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION. Harmful if absorbed through skin. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters except in accordance with the requirements of a 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 treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

NET CONTENTS 55 POUNDS

EPA Reg. No. 11678-57
EPA Est. No. 11678-ISR-002

Makhteshim Chemical Works, Ltd.
c/o Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. This pesticide is for the further manufacture of formulated insecticides only. Formulators using this product are responsible for obtaining EPA registration for their formulated products.

Only for formulation into an insecticide for the following uses:

(1) Ornamentals (greenhouses, shadehouses, and outdoor nurseries), cotton, pome fruits, and potatoes
(2) Uses for which USEPA has accepted the required data and/or citations of data that the formulator has submitted in support of registration; and
(3) Uses for experimental purposes that are in compliance with USEPA requirements.

STORAGE AND DISPOSAL

STORAGE: Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited.
PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of at an approved waste disposal facility.
CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If drum is contaminated and cannot be reused, dispose of in the same manner.

WARRANTY STATEMENT

MAKHTESHIM CHEMICAL WORKS, LTD. warrants that this product conforms to the chemical description on the label thereof and is reasonably fit for purposes stated on such label only when used in accordance with directions under normal use conditions. It is impossible to eliminate all risks inherently associated with use of this product. Crop injury, ineffectiveness, or other unintended consequences may result because of such factors as weather conditions, presence of other materials, or the manner of use or application, all of which are beyond the control of MAKHTESHIM CHEMICAL WORKS, LTD.. In no case shall MAKHTESHIM CHEMICAL WORKS, LTD. be liable for consequential, special, or indirect damages resulting from the use or handling of this product. All such risks shall be assumed by the Buyer. In addition to the foregoing, no purchaser of this product (other than an end user) shall be entitled to any reimbursement for any loss suffered as a result of any suspension or cancellation of the registration for this product by the U.S. Environmental Protection Agency. Except as expressly provided herein, MAKHTESHIM CHEMICAL WORKS, LTD. makes no warranties, guarantees, or representations of any kind, either expressed or implied, or by usage of trade, statutory or otherwise, with regard to the product sold, including, but not limited to merchantability, fitness for a particular purpose, use or eligibility of the product for any particular trade usage. The exclusive remedy of any buyer or user of this product for any and all losses, injuries, or damages resulting from or in any way arising from the use, handling, or application of this product, whether in contract, warranty, tort, negligence, strict liability, or otherwise, shall be damages not exceeding the purchase price paid for this product or, at MAKHTESHIM CHEMICAL WORKS, LTD's. election, the replacement of this product.

Rimon Technical (11678-57)(EPA app 1-25-05)

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

D354556/~~B~~775348

MAR - 4 2005

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Dr. Robert C. Everich
Registration Agent
Makhteshim-Agan of North America, Inc.
551 Fifth Ave., Suite: 1100
New York, N.Y. 10176

Dear Dr. Everich

Subject: EPA Reg. No. 11678-57
EPA Reg. No. 66222-~~35~~ 57
Request for EPA Review DERs for Novaluron

Hard copies of the DERs are enclosed, per your request (E-mail copy attached) for the EPA reviews of studies submitted for the registration of the products, referred to above,. Should you have any questions, do not hesitate to contact me at 703-605-0368.

Sincerely,

Suku Oonnithan
Entomologist
Insecticide Rodenticide Branch
Registration Division (7505C)

Encl.

Robert Everich
<rob@manainc.com>
03/02/05 10:47 AM

To Suku Oonnithan/DC/USEPA/US@EPA
cc
bcc
Subject FW: DER Request

#124002

Dear Oonni:

I sent this message to Rachel Holloman yesterday. I have worked with Terri Stowe in the past to get these DER's but she's out on medical leave.

Now I'm thinking that perhaps I should have asked you first...

We have a New York State registration pending for Rimon 7.5 WG (EPA Reg No. 66222-57) based on novaluron technical (EPA Reg No. 11678-57). They are asking for EPA DER's for the acute tox studies and the 90 day dog studies in order to complete this review. If they are not available, they require a letter from EPA stating that fact.

Below is a list of MRID numbers for the studies in question.

Acutes
45638421
45638422
45638423
45638424
45638425

66222-57

Dog Studies
46152301
46152302

11678-57

Would you let me know if you can locate these or if they are unavailable? We need to respond soon or we will have to start the registration process over again.

Thanks,

Rob Everich

Robert C Everich, Ph.D.
Senior Scientist
Makhteshim-Agan of North America Inc.
551 Fifth Ave., Suite 1100
New York, NY 10176
(212) 896-4945
cell (917) 209-4523

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

JAN 25 2005

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Robert C. Everich, Ph.D.
Senior Scientist
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite: 1100
New York, NY. 10176

Subject: EPA Reg. No. 11678-57
Rimon Technical
Label Amendment: Adding uses on cotton, potatoes and pome fruits
Submission dated Sept. 26, 2003

Dear Dr. Everich:

Your application for a label amendment for the product referred to above, submitted in connection with registration under the Federal Insecticide, Fungicide and Rodenticide Act, as amended is acceptable. A stamped copy of the label is enclosed for your records. Submit one (1) copy of your final printed labeling before you release the product for shipment. Should you have any questions, do not hesitate to contact the reviewer of this product, Mr. Suku Oonnithan at 703-605-0368.

Sincerely,

Daniel C. Kenny
Product Manager (01)
Insecticide Rodenticide Branch
Registration Division (7505C)

Encl.

RimOn®

ACCEPTED
JAN 25 2005
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 11678-57

TECHNICAL

(Novaluron)

For The Manufacture of Insecticides Only

	% BY WT.
ACTIVE INGREDIENT: Novaluron: 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	98.5%
INERT INGREDIENTS:	1.5%
TOTAL	100.0%

KEEP OUT OF REACH OF CHILDREN

CAUTION

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

FIRST AID

IF ON SKIN OR CLOTHING:
- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor 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.

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 eye.
- Call a poison control center or doctor 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 for further treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment.

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION. Harmful if absorbed through skin. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters except in accordance with the requirements of a 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 treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

NET CONTENTS 55 POUNDS

MAKHTESHIM AGAN NORTH AMERICA

Makhteshim Chemical Works, Ltd.
c/o Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

EPA Reg. No. 11678-57
EPA Est. No. 11678-ISR-002

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. This pesticide is for the further manufacture of formulated insecticides only. Formulators using this product are responsible for obtaining EPA registration for their formulated products.

Only for formulation into an insecticide for the following uses:

(1) Ornamentals (greenhouses, shadehouses, and outdoor nurseries), cotton, pome fruits, and potatoes.
(2) Uses for which USEPA has accepted the required data and/or citations of data that the formulator has submitted in support of registration; and
(3) Uses for experimental purposes that are in compliance with USEPA requirements.

STORAGE AND DISPOSAL

STORAGE: Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited.
PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of at an approved waste disposal facility.
CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If drum is contaminated and cannot be reused, dispose of in the same manner.

WARRANTY STATEMENT

MAKHTESHIM-AGAN OF NORTH AMERICA INC. warrants that this product conforms to the chemical description on the label thereof and is reasonably fit for purposes stated on such label only when used in accordance with directions under normal use conditions. It is impossible to eliminate all risks inherently associated with use of this product. Crop injury, ineffectiveness, or other unintended consequences may result because of such factors as weather conditions, presence of other materials, or the manner of use or application, all of which are beyond the control of MAKHTESHIM-AGAN OF NORTH AMERICA INC. In no case shall MAKHTESHIM-AGAN OF NORTH AMERICA INC. be liable for consequential, special, or indirect damages resulting from the use or handling of this product. All such risks shall be assumed by the Buyer. In addition to the foregoing, no purchaser of this product (other than an end user) shall be entitled to any reimbursement for any loss suffered as a result of any suspension or cancellation of the registration for this product by the U.S. Environmental Protection Agency. Except as expressly provided herein, MAKHTESHIM-AGAN OF NORTH AMERICA INC. makes no warranties, guarantees, or representations of any kind, either expressed or implied, or by usage of trade, statutory or otherwise, with regard to the product sold, including, but not limited to merchantability, fitness for a particular purpose, use or eligibility of the product for any particular trade usage. The exclusive remedy of any buyer or user of this product for any and all losses, injuries, or damages resulting from or in any way arising from the use, handling, or application of this product, whether in contract, warranty, tort, negligence, strict liability, or otherwise, shall be damages not exceeding the purchase price paid for this product or, at MAKHTESHIM-AGAN OF NORTH AMERICA INC's election, the replacement of this product.

Rimon Technical (11678-57; EPA app 6-18-02)
Proposed 09-25-03

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

October 16, 2003

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

ROB EVERICH
MAKHTESHIM CHEMICAL WORKS LTD
C/O MAKHTESHIM-AGAN OF N. AMERICA INC
551 FIFTH AVE SUITE 1100
NEW YORK, NY 10176

PRODUCT NAME: RIMON TECHNICAL
COMPANY NAME: MAKHTESHIM CHEMICAL WORKS LTD
OPP IDENTIFICATION NUMBER: 259577
EPA FILE SYMBOL: 11678-57
EPA RECEIPT DATE: 09/30/03

SUBJECT: RECEIPT OF AMENDMENT

DEAR REGISTRANT:

The Office of Pesticide Programs has received your application for an amendment and it has passed an administrative screen for completeness.

During the initial screen we determined that the application appears to qualify for fast track review. The package will now be forwarded to the Product Manager for review to determine its acceptability for fast track status.

If you have any questions, please contact Registration Division, Risk Management Team 1, at (703) 305-7546.

Sincerely,

Front End Processing Staff
Information Services Branch
Information Resources and Services Division

Please read instructions on reverse before completing form

Form Approved. OMB No. 2070-0060 Approval expires 05-31-98

EPA

United States
Environmental Protection Agency
Washington, DC 20460

☐ **Registration**
☒ **Amendment**
☐ **Other**

OPP Identifier Number
259577

Application for Pesticide - Section I

1. Company/Product Number
11678-57

2. EPA Product Manager
Dan Kenny

3. Proposed Classification
☐ None ☐ Restricted

4. Company/Product (Name)
Rimon™ Technical

PM#
4A

5. Name and Address of Application *(Include ZIP Code)*
Makhteshim-Agan North America Inc.
551 Fifth Ave., Suite 1100
New York, NY 10176
☐ *Check if this is a new address*

6. Expedited Review. 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 _____
☐ Notification - Explain below.
☐ Final printed labels in response to Agency letter dated _____
☐ "Me Too" Application.
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For Section I and Section II.)
Add new uses: cotton, pome fruits and potatoes

Section - III

1. **Material This Product Will Be Packaged In:**

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
☐ Yes	☐ Yes	☐ Yes	☐ Metal
☐ No	☐ No	☐ No	☐ Plastic
* *Certification must be submitted*	If "Yes", Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	☐ Glass ☐ Paper ☐ Other (Specify) _____

3. Location of Net Contents Information
☑ Label ☐ Container

4. Size(s) Retail Container

5. Location of Label Directions
☐ On Label
☐ On Labeling accompanying product

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)
Rob Everich, Ph.D.	Senior Scientist	Phone: (212) 896-4945

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 knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received
(Stamped)

2. Signature

3. Title
Senior Scientist

4. Typed Name
Rob Everich

5. Date
09-26-03

EPA Form 8570-1 (Rev. 8-94) Previous editions are obsolete.

White - EPA File Copy (original) Yellow - Applicant Copy

MAKHTESHIM
A G A N
of
North America
Inc.

September 26, 2003

US Environmental Protection Agency
c/o Document Processing Desk
Room 266A, Crystal Mall 2
1921 Jefferson Davis Highway
Arlington, VA 22202

Delivered by Courier

Attn: Mr. Dan Kenny - PM Team 4A

Dear Mr. Kenny,

Subject: RIMON™ TECHNICAL (EPA Reg. No. 11678-57),
RIMON™ 10EC (EPA Reg. No. 66222-35),
Application for Amended Registration,
Add Cotton, Pome Fruits and Potatoes

Makhteshim-Agan of North America Inc. (MANA) is herewith submitting an application to amend the subject registrations by allowing the use of Novaluron, the active ingredient of RIMON™10EC on cotton, pome fruits (see PP#2F6430) and potatoes (PP# not assigned yet).

RIMON™ TECHNICAL and its end-use product, Rimon™ 10EC, were first registered for its use on ornamentals in greenhouses, shade houses and nurseries on September 25, 2001, following the Agency's decision for "Reduced-Risk Status" dated February 1, 2000. On March 21, 2002, the Agency granted "OP Alternative Status" for RIMON's first food uses, cotton and pome fruits. Since then, MANA has submitted all required information in support of the cotton and pome fruit petition (February 28, 2002) and potatoes (Petition for Tuberous and Corm Vegetables, September 26, 2003). Based on the product's "OP Replacement" designation, the Agency is planning to expedite the review process for this chemical and its proposed new uses (presently part of the 2004 work plan).

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

To facilitate this registration action, enclosed are the following Administrative Materials:

1. EPA Form 8570 -1:
   An executed "Application for Pesticide Registration" for each product (OPP Identifier # 259576 and 259577) has been enclosed.

2. Proposed Label
   Five copies of each product and its proposed label amendment, adding the use on cotton, pome fruits and potatoes are enclosed.

3. Data Matrix
   Data matrix (EPA form 8570-35; one copy for Agency Internal Use and one Public File copy) of all previously submitted data in support of its existing and proposed registrations (RIMON™ 10EC, RIMON™ Technical) is enclosed.

4. Certification with Respect to Citation of Data
   EPA form 8570-34 with respect to citation of data has been enclosed.

In view of the designated "OP Alternative" status, we appreciate your expeditious processing of this application for amending the subject registrations and a receipt of the stamped, approved product labels for our records.

If you have any questions or need further information regarding this application, please fee free to contact me at 212-896-4945 or Bert Volger at 610-793-3222.

Very truly yours,

Robert C. Everich, Ph.D.
Senior Scientist
Makhteshim-Agan of North America Inc.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

November 8, 2004

Robert C. Everich, Ph.D.
Senior Scientist
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

SUBJECT: Request for EPA Reviews Associated with MRIDs for Novaluron

Novaluron Technical	EPA Registration No.11678-57
Rimon 7.5 WDG	EPA Registration No. 66222-57
Rimon 10 EC	EPA Registration No. 66222-35

Dear Dr. Everich:

Per your request for EPA reviews associated with 142 MRIDs and a waiver request for an acute inhalation study for Rimon 7.5WDG for Novaluron, please see the attached reviews associated with MRID studies 45638218, 45638219, 45638408 and 46086203.

If you have any questions, please contact me by phone at (703) 305-6117 or by e-mail at stowe.terri@epa.gov.

Sincerely yours,

Terri Stowe

Terri Stowe
Senior Regulatory Specialist
Office of Pesticide Programs
Registration Division (Mail Code 7505C)
Registration Support Branch

Attachments

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

November 5, 2004

Robert C. Everich, Ph.D.
Senior Scientist
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

SUBJECT: Request for EPA Reviews Associated with MRIDs for Novaluron

Novaluron Technical	EPA Registration No.11678-57
Rimon 7.5 WDG	EPA Registration No. 66222-57
Rimon 10 EC	EPA Registration No. 66222-35

Dear Dr. Everich:

Per your request for EPA reviews associated with 142 MRIDs and a waiver request for an acute inhalation study for Rimon 7.5WDG for Novaluron, I have found an additional 79 MRIDs which will be delivered to you along with this letter by a representative of Exponent, Inc. (Kevin Tucker). The following MRID studies have been requested from the Environmental Fate and Effects Division and will be sent to you via e-mail in an electronic (.tif) format: 45638218, 45638219, 45638408, and 46086203. The following MRID studies do not usually get reviews/DERs: 45703201, 45638410, and 45638402. Please see the tables below for a listing of the MRIDs that are associated with this letter/found and those that are still outstanding and are unavailable at this time.

MRIDs attached to this letter/found						
MRID #	**MRID #**	**MRID #**	**MRID #**	**MRID #**	**MRID #**	**MRID #**
44961010	45499007	45638227	45499001	45638211	45638314	45638301
44961008	45476802	45771803	45638219	45638221	45638413	45771802
44961011	45638305	45638302	45638216	45638223	45785801	45771801
44961012	45638420	45638303	45638213	45638220	45638206	46082701
44961009	45638412	45638413	45638214	45638226	45638411	46086207
46141001	45082601	45638312	45638215	45638407	45785802	46086208
45499004	45638203	45638205	45638405	45638224	45785805	46086206
45499006	45638222	45638204	45638209	45638225	45789203	46086201
45499005	45638304	45638202	45638212	45638217	45638201	46086205
45499003	45638307	45789204	45638210	45638403	45638306	46185801

MRIDs attached to this letter/found						
MRID #	**MRID #**	**MRID #**	**MRID #**	**MRID #**	**MRID #**	**MRID #**
45785804	45638311	45638404	45638208	45638409	45638207	45476801
45499002	45638308					

MRIDs not found and/or are unavailable at this time						
MRID #	**MRID #**	**MRID #**	**MRID #**	**MRID #**	**MRID #**	**MRID #**
45651506	45638416	45638321	45638421	45638424	45638406	46152301
44964508	45638426	45638322	45638422	45638425	45785803	46152302
44964509	45651501	45638315	45638423	45638414	45789201	

If you have any questions, please contact me by phone at (703) 305-6117 or by e-mail at stowe.terri@epa.gov.

Sincerely yours,

Terri Stowe

Terri Stowe
Senior Regulatory Specialist
Office of Pesticide Programs
Registration Division (Mail Code 7505C)
Registration Support Branch

Attachments

Robert Everich
<rob@manainc.com>
11/02/2004 11:12 AM

To Terri Stowe/DC/USEPA/US@EPA
cc Selina Donaldson <sdonaldson@exponent.com>, Kevin Tucker <ktucker@exponent.com>
bcc
Subject RE: DER's

Hi Terri:

This e-mail authorizes a representative from our consulting firm, Exponent to receive a set of DER's regarding the active ingredient novaluron on our behalf.

Sincerely,

Robert C. Everich, Ph.D.
Senior Scientist
Makhteshim-Agan of North America Inc.

-----Original Message-----
From: Kevin Tucker [mailto:ktucker@exponent.com]
Sent: Tuesday, November 02, 2004 9:16 AM
To: Robert Everich
Cc: Selina Donaldson
Subject: DER's

Hi Rob:

I spoke with Terri and she would like you to send an e-mail to her authorizing Exponent to pick-up the DER's on your behalf. As it looks now, Terri will probably want us to come and pick them on Thursday or Friday.

Regards,

Kevin

Schedule: 11/1/04 to 11/5/04
11/1/04 -- In All Day
11/2/04 -- In All Day
11/3/04 -- In All Day
11/4/04 -- May be out in PM
11/5/04 -- In All Day

Phone/FAX Numbers:
Direct Number: (202) 772-4910 -- Please use!
Main Number: (202) 772-4900
Fax Number: (202) 772-4979

Kevin Tucker
Senior Scientist
Exponent, Inc.
(formerly Novigen Sciences, Inc.)
ktucker@exponent.com

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

October 6, 2004

I, Dan Kenny, Insecticide/Rodenticide Branch, Registration Division, Office of Pesticide Programs, Office of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency ("EPA"), certify that the pesticide product (s) listed below is, as of the date of this letter, a registered product under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, and that as such, the product(s) may be sold and marketed in the United States of America as authorized and limited by FIFRA. A true and correct copy of the product label approved by EPA is attached to accompany this letter.

Registration of this product(s) with EPA also denotes that the registrant listed below is responsible for ensuring full compliance with all the laws of the United States of America, or governing jurisdiction, regarding the sale, storage and/or disposal of the product(s). Further, the recipient of this letter is on notice that the referenced registration and/or the accompanying label may change subsequent to the date of this letter. EPA assumes no responsibility to notify the recipient of this letter of any change in the status of the registration(s) and/or the product label for the product(s) listed below.

EPA has issued registration numbers for the product(s) listed below to:

Makhteshim-Agan Of North America Inc
551 Fifth Avenue - Ste 1100
New York, NY 10176

EPA Registration Number:	66222-57
Name of Product:	Rimon (Novaluron) 7.5 Wdg

Daniel C. Kenny
Product Manager
Insecticide/Rodenticide Branch
Registration Division (7505C)

MAKHTESHIM
A G A N
of
North America
Inc.

September 22, 2004

Mr. Oonni Oonnithan
Product Manager
Registration Division (7505C)
USEPA, OPP
1801 South Bell Street
CM#2, Room 269
Arlington, VA 22202-4501

Re: Gold Certificates

Dear Mr. Oonnithan,

I would like to request the Gold Certificates for the following registrations:

1. Rimon Technical, EPA Reg. No. 11678-57
2. Rimon 10EC, EPA Reg. No. 66222-35
3. Rimon 10SC, EPA Reg. No. 66222-40
4. Rimon 7.5WG, EPA Reg. No. 66222-57

Should you have any questions, please contact me at (212) 896-4932.

Sincerely,

Natalya Bazilevsky

Natalya Bazilevsky
Makhteshim-Agan of North America, Inc.
Regulatory Secretary

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

June 16, 2004

Robert C. Everich, Ph.D.
Senior Scientist
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

SUBJECT: Request for EPA Reviews Associated with MRIDs for Novaluron
Novaluron Technical EPA Registration No.11678-57
Rimon 7.5 WDG EPA Registration No. 66222-57

Dear Dr. Everich:

Per your request for EPA reviews associated with142 MRIDs and a waiver request for an acute inhalation study for Rimon 7.5WDG for Novaluron, I have found 34 MRIDs and the review of the waiver request on your list. I have requested clarification for 3 MRIDs (45638309, 45638310, and 45789202) from our Environmental Fate and Effects Division (EFED). I will keep you informed on the status of these MRIDs.

In addition, I found that the 105 MRIDs/studies listed below are not usually cited in the final DERs risk assessments:

MRID	Study Type	MRID	Study Type	MRID	Study Type
45651506	primary report	45499002	primary report	45638304	primary report
44961010	summary	45476801	primary report	45638307	primary report
44961008	primary report	45499001	primary report	45638311	primary report
44961011	primary report	45499007	primary report	45638308	primary report
44961012	primary report	45476802	primary report	45638306	primary report
44961009	primary report	45638305	primary report	45638321	primary report/assessment
44964508	primary report	45638420	primary report	45638322	primary report
44964509	primary report	45638412	primary report	45638315	preliminary report
46141001	primary report	45638416	primary report	45638226	primary report
45499004	primary report	45638426	primary report	45638227	primary report
45499006	primary report	45703201	response to EPA	45771803	primary report
45499005	primary report	45651501	primary report	45638302	primary report
45499003	primary report	45638203	primary report	45638303	primary report

MRID	Study Type	MRID	Study Type	MRID	Study Type
45785804	primary report	45638222	primary report	45638413	primary report
45638312	primary report	45638223	primary report	45638406	primary report
45638205	primary report	45638220	primary report	45785801	primary report
45638204	primary report	45638407	primary report	45638206	primary report
45638202	primary report	45638410	primary report	45785803	primary report
45789204	summary	45638224	primary report	45785802	primary report
45638404	primary report	45638225	primary report	45789201	primary report
45638207	primary report	45638217	primary report	45785805	primary report
45638201	primary report	45638418	primary report	45789203	primary report
45638218	primary report	45638419	primary report	45638301	primary report
45638219	primary report	45638421	primary report	45771802	primary report
45638216	primary report	45638422	primary report	45771801	primary report
45638213	primary report	45638423	primary report	46082701	primary report
45638214	primary report	45638424	primary report	46086207	primary report
45638215	primary report	45638425	primary report	46086208	primary report
45638405	primary report	45638414	primary report	46086206	primary report
45638209	primary report	45638403	primary report	46086201	primary report
45638212	primary report	45638402	primary report	46086205	primary report
45638210	primary report	45638409	primary report	46086203	primary report
45638208	primary report	45638408	primary report	46152301	primary report
45638211	primary report	45638314	primary report	46152302	primary report
45638221	primary report	45638411	primary report	46185801	primary report

If you have any questions, please contact me by phone at (703) 305-6117 or by e-mail at stowe.terri@epa.gov.

Sincerely yours,

Terri Stowe

Terri Stowe
Senior Regulatory Specialist
Office of Pesticide Programs
Registration Division (Mail Code 7505C)
Registration Support Branch

United States
Environmental Protection Agency
Washington, DC 20460

FEDERAL REGISTER TYPESETTING REQUEST

Requestor: Complete Items 1, 2, 7, 8, 9, 10, 11, 12 and 13. Retain copy number 7 and submit the balance with manuscript copt to the Hq. Federal Register Office.
HQ Federal Register Office: Complete Items 3, 4, 5 and 6. Retain copy number 6 and submit balance to Hq. Printing Management.

1. TITLE
NAVALURON; PESTICIDE TOLERANCE

2. SUBMITTING ACTIVITY	3. ASSIGNED FRL NUMBER *(Include alpha & numeric characters for identification.)* 7359-2
4. OPEN REQUISITION NUMBER	5. BILLING CODE 6160-50-S
6. FORWARDED TO GSA, NARS - SIGNATURE	DATE

7. NUMBER OF MANUSCRIPT PAGES	8. ESTIMATED NUMBER OF COLUMNS	9. ESTIMATED COST

10. SIGNATURE: (a) REQUESTING OFFICER		11. SIGNATURE: (a) FEDERAL REGISTER DESIGNEE Priscilla Alberta	
(b) DATE	(c) TELEPHONE NUMBER	(b) DATE 05/19/04	(c) TELEPHONE NUMBER 703-305-6921

12. FUNDS ARE AVAILABLE

Priscilla Alberta	Priscilla Alberta	703-305-6921
NAME OF FUNDS CERTIFYING OFFICER	SIGNATURE OF FUNDS CERTIFYING OFFICER	PHONE NUMBER OF FUNDS CERTIFYING OFFICER

0619-04P H. Green

THIS DOCUMENT WAS SUBMITTED WITH ELECTRONIC TYPESETTING CODES AND IS ELIGIBLE FOR THE 35% TYPESETTING DISCOUNT.

13. Financial and Accounting Data

Line	DCN (Max 6)	Budget/FYs (Max 4)	Appropriation Code (Max 6)	Budget Org/Code (Max 7)	Program Element (Max 9)	Object Class (Max 4)
1	350202	04/05	B	3200AD	701C93B	2413
2						
3						

SFO: 27 (Max 2)

Line	Amount (Dollars)	(Cents)	Site/Project (Max 8)	Cost Org/Code (Max 7)
1	2289	00		
2				
3				

EPA Form 2340-15 (Rev. 8-94) Electronic and paper versions acceptable.

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

OPP–2004–0125; FRL–7359–2]

Novaluron; Pesticide Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes tolerances for residues of novaluron in or on fruit, pome (group 11), apple, wet pomace; cotton, undelinted seed; cotton, gin byproducts; vegetables, tuberous and corm, subgroup 1C; meat, fat, and meat byproducts of sheep, horse, cattle, goat, hog, and poultry; milk; milk, fat; and eggs. Makhteshim-Agan of North America, Inc. requested this tolerance under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act of 1996 (FQPA).

DATES: This regulation is effective [*insert date of publication in the* **Federal Register**]. Objections and requests for hearings must be received on or before [*insert date 60 days after date of publication in the* **Federal Register**].

ADDRESSES: To submit a written objection or hearing request follow the detailed instructions as provided in Unit VI. of the **SUPPLEMENTARY INFORMATION.** EPA has established a docket for this action under Docket ID number OPP–2004–0125. All documents in the docket are listed in the EDOCKET index at *http://www.epa.gov/edocket.* Although listed in the index, some information is not publicly available, i.e., 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 electronically in EDOCKET or in hard copy at the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA. This docket facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The docket telephone number is (703) 305–5805.

0619.04P

CONCURRENCES

SYMBOL	7104T	7104T	7505C	7505C				
SURNAME	H Greene	O.P. Rodia	D Kenna	Davis				
DATE	5-11-04	5/11/2004	5/18/04	5/19/04				

EPA Form 1320-1 (12-70) OFFICIAL FILE

Corrections, p. 12

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: 5/20/04

Director, Office of Pesticide Programs.

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DECISION MEMORANDUM

SUBJECT: Registration of Novaluron for First Food Use

FROM: Lois Rossi, Director
Registration Division (7505C)
Lois Rossi 5/20/04

TO: James J. Jones, Director
Office of Pesticide Programs (7501C)

I. CHEMICAL AND APPLICATION INFORMATION

REGISTRANT: Makhteshim Agan of North America, Inc.

CHEMICAL: Novaluron (N-[[{3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy}phenyl]amino]carbonyl]-2,6-difluorobenzamide

CHEMICAL CLASS: Benzoylphenyl urea

PRODUCTS: Rimon Technical
Rimon 7.5WG Insecticide
Rimon 0.83EC Insecticide

USE: To control chewing and sucking insects on pome fruits, cotton and potatoes.

REGISTRATION TYPE: Conditional Registration

II. HIGHLIGHTS OF SCIENCE REVIEWS

A. ACUTE TOXICITY

Technical Novaluron has low acute toxicity via the oral (Toxicity Category IV), dermal (Toxicity Category III) and inhalation routes (Toxicity Category IV). No ocular (Toxicity Category IV) or dermal irritation (Toxicity Category IV) was noted. Novaluron is not a dermal sensitizer.

B. SUBCHRONIC AND CHRONIC TOXICITY

In subchronic and chronic toxicity studies, novaluron primarily produced hematotoxic effects such as methemoglobinemia, decreased hemoglobin, decreased hematocrit, and decreased red blood corpuscles associated with increased erythropoiesis.

C. NEUROTOXICITY

No signs of neurotoxicity or neuropathology were observed in the subchronic neurotoxicity study in rats at doses up to 1752 mg/kg/day in males and 2000 mg/kg/day in females. Therefore, the Agency concluded that there is not a concern for neurotoxicity resulting from exposure to novaluron.

D. DEVELOPMENTAL/REPRODUCTIVE TOXICITY

The rat and rabbit developmental toxicity studies conducted up to the limit doses produced no maternal and/or developmental toxicity. In the two-generation reproductive toxicity study, both maternal and offspring toxicity were evidenced by spleenomegaly, whereas reproductive toxicity was observed only in males as evidenced by decreases in epididymal sperm counts and increased age at preputial separation in the F_1 generation.

E. MUTAGENICITY

There was no concern for mutagenic activity as indicated by several mutagenicity studies such as a bacterial reverse mutation assay, an *in vitro* mammalian chromosomal aberration assay, an *in vivo* mouse bone-marrow micronucleus assay, and bacterial DNA damage or repair assay.

F. CARCINOGENICITY

There was no evidence of carcinogenic potential in either the rat or mouse carcinogenicity studies. Therefore, novaluron was classified as "not likely to be carcinogenic to humans."

G. TOXICOLOGICAL ENDPOINTS

The human health risk assessment was performed using the exposure scenarios summarized in Table 1. An acute dietary end point was not identified. A chronic dietary endpoint selected for

risk assessment purposes is based on erythrocyte damage and turnover resulting in a regenerative anemia at a LOAEL of 0.36 mg/kg/day. A 10% dermal absorption factor was selected from a rat dermal-absorption study.

The FQPA SF was reduced to 1X, based upon the following: As mentioned above, there is no quantitative or qualitative evidence of increased susceptibility of rat and rabbit fetuses to *in utero* exposure to novaluron in developmental toxicity studies. There is no quantitative or qualitative evidence of increased susceptibility to novaluron following pre-/post-natal exposure in a 2-generation reproduction study. In addition, there is no concern for developmental neurotoxicity resulting from exposure to novaluron, and a developmental neurotoxicity study (DNT) study is not required. Furthermore, the chronic dietary food exposure assessment assumes 100% crops treated for all commodities. The dietary drinking water assessment utilizes water concentration values generated by model and associated modeling parameters which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded. Finally, there are no proposed or existing uses for novaluron which result in residential exposure.

The toxicological endpoints used for assessing dietary and occupational risks of novaluron are summarized in Table 1.

Table 1. Summary of Toxicological Endpoints Used for Assessing Dietary and Occupational Risks of Novaluron.

Exposure Scenario	Doses Used and Level of Concern (LOC)
Acute dietary	None identified
Chronic dietary (general population)	NOAEL = 1.1 mg/kg/day; UF = 100; FQPA SF = 1x cRfD = 0.011 mg/kg/day
Short-term Incidental Oral	NOAEL = 4.38 mg/kg/day Occupational LOC for MOE = 100
Short-term Dermal	None identified
Long-term Dermal	Oral NOAEL = 1.1 mg/kg/day, Dermal Absorption Rate = 10% Occupational LOC for MOE = 100
Short-term Inhalation	Oral NOAEL = 4.38 mg/kg/day, Inhalation Absorption Rate = 10% Occupational LOC for MOE = 100
Long term-term Inhalation	Oral NOAEL = 1.1 mg/kg/day, Inhalation Absorption Rate = 10% Occupational LOC for MOE = 100
Cancer	Not likely to be a carcinogen

III. HUMAN HEALTH RISK ASSESSMENT

A. DIETARY RISK ASSESSMENT

For dietary risk assessment, the residues of the parent compound are the only residues of concern in plant and livestock matrices and in rotational crops. The chronic dietary risk assessment was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™) and Lifeline™ models.

In drinking water, the residues of concern were the parent novaluron and two of the degradates, chlorophenyl urea, and chloroaniline. To estimate concentrations of residues of concern in drinking water, Tier 2 Pesticide Root Zone Model/Exposure Analysis Modeling System (PRZM/EXAMS), FQPA Index Reservoir Screening Tool (FIRST) and Screening Concentration in Ground Water (SCI-GROW) models were used with the most conservative application scenarios. The highest estimated environmental concentration (EEC) of novaluron in ground water (0.009 ug/L) and that in surface water (2.61 ug/L) were used in risk calculations; the EECs of other residues were lower than that of the parent compound. These EEC values are meant to represent the upper-bound estimates of the concentrations that might be found in groundwater and surface water based upon existing and proposed uses of novaluron.

1. Acute Dietary: The acute RfD for the general population, including infants and children, was not estimated since an endpoint of concern attributable to a single oral dose was not identified.

2. Chronic Dietary: The chronic dietary risk analysis assumed 100% crop treated for all commodities; incorporated average field trial residues; empirical processing factors for apple juice (translated to pear juice); and DEEM™ default processing factors for the remaining processed commodities. Anticipated residues were calculated for meat and milk commodities and recommended tolerances were used for poultry commodities. The chronic dietary risks to the four most sensitive population subgroups are summarized in Table 2.

Table 2. Chronic Dietary Exposure and Risk for Novaluron.

Population Subgroup	cPAD mg/kg/day	DEEM		Lifeline	
		Exposure mg/kg/day	% cPAD (Food)	Exposure mg/kg/day	% cPAD (Food)
U.S. Population	0.011	0.001997	18	0.001903	17
Infants < 1 year	0.011	0.003438	31	0.003565	32
Children 1-2 years	0.011	0.007519	68	0.007396	67
Females 13-49 years	0.011	0.001276	12	0.001671	15

For dietary risk, % of cPAD higher than 100 exceeds the Agency's level of concern. The estimated chronic food exposures for novaluron were less than the Agency's level of concern for all population subgroups. The most highly exposed population was Children 1-2 years old (≤68% cPAD). In this analysis, DEEM and Lifeline yielded similar results (Table 2).

B. AGGREGATE RISK ASSESSMENT Aggregate acute, short and intermediate term and chronic exposures to novaluron were estimated using the drinking water level of concern (DWLOC) with contributions from food, drinking water and residential uses. An acute aggregate risk assessment was not performed because an endpoint of concern attributable to a single oral dose was not identified. The short- and intermediate-term aggregate risk assessments also were not conducted due to the lack of residential exposure to novaluron, as no residential uses exist or are proposed. Therefore, the chronic aggregate risk assessment considered only exposures from food and drinking water. The results are summarized in Table 3.

Table 3. Chronic Aggregate Exposure and Risks for Novaluron.

Population Subgroup	Chronic Food Exposure mg/kg/day	Chronic Water Exposure mg/kg/day	Ground Water EEC (ppb)	Surface Water EEC (ppb)	Chronic DWLOC (ppb)
U.S. Population	0.001997	0.00903	0.009	2.61	320
Infants < 1 year	0.003438	0.007562			76
Children 1-2 years	0.007519	0.003481			35
Females 13-49 years	0.001276	0.009724			290

The results of the chronic aggregate risk analysis indicated that drinking water EECs were less than the respective DWLOCs for all the population sub-groups studied. Therefore, the chronic aggregate risk associated with the proposed use of novaluron does not exceed the Agency's level of concern. A cancer aggregate risk assessment was not performed because novaluron has not been shown to be carcinogenic.

C. CUMULATIVE RISK A cumulative risk assessment was not done for novaluron, as the Agency has not made a common mechanism of toxicity finding with any other chemical substances. Also, none of the novaluron degradates appear to have any common toxicity to the metabolites produced by other substances.

D. OCCUPATIONAL RISK ASSESSMENT

1. Exposure to Farm Workers: The primary source of occupational exposure to farm workers occurs during the mixing, loading and applying of the EC and water soluble granule formulations (WSG). Acute and short-term post-application exposure is not a concern as no acute or short-term dermal risks were identified. While dermal post-application over the intermediate-term

duration is a possibility, it is not expected to occur based on the existing and proposed use patterns. Due to the low vapor pressure of novaluron, the post-application inhalation exposure to workers is also considered to be negligible. A 24 hour REI provides further protection from exposure to workers from all exposure routes.

2. Exposure to Commercial Handler/Applicator: Based upon the proposed use patterns, commercial pesticide handlers are expected to be exposed over the short- and intermediate-term durations (1-30 days and 1-6 months, respectively) when handlers treating cotton, moving from farm to farm, use the same pesticide consecutively for more than 30 days. Such a scenario was assessed using PHED Surrogate Exposure Guide and personal protective equipment consistent with the acute toxicity of the novaluron technical and its formulations. The exposure to mixers/loaders and applicators applying EC and WSG formulations ranged for short term inhalation (2,400 to 31,000) and intermediate term dermal and inhalation (10 to 8,000), while the MOE was 100. The MOE of 10 was found when the workers did not wear gloves while mixing/loading/pouring the liquid formulations for aerial applications on cotton and potatoes; but, the MOE raised to 80 fold when the workers wore protective gloves in addition to a single layer of work clothes. So that all estimated commercial handler MOE's are greater than 100, the label will require the use of protective gloves in addition to a single layer of work clothes.

3. Post-Application Exposure: The potential for agricultural workers to have post-application exposure to novaluron was estimated using surrogate data from the Agricultural Re-entry Task Force (ARTF). Using the maximum application rate, the highest transfer coefficient for irrigation in potatoes or cotton, and the assumption that 20% of the application rate is available as foliar dislodgeable residue on day zero after application, an MOE of 760 was estimated for post-application exposures, while an MOE of 100 is adequate to protect agricultural workers from post-application exposures to novaluron.

C. RESIDENTIAL EXPOSURE AND RISK

There are no residential uses for novaluron.

D. INCIDENTS

Novaluron was first registered in September, 2001 for insect control on commercially grown ornamentals. There have been no reported incidents from this use.

IV. ENVIRONMENTAL RISK ASSESSMENT

A. ENVIRONMENTAL FATE

The environmental fate data indicate that novaluron is immobile and moderately persistent in the field. Laboratory studies suggest that novaluron's major route of dissipation is microbially-mediated degradation (half-life 14.5 days). The chemical tends to strongly adsorb to soil and

sediment, and it is stable to abiotic processes. Novaluron has a very low potential to reach ground water. During surface runoff conditions, novaluron may reach water bodies as bound to soil particles and will likely partition into sediments once in surface water. Additionally, contribution to surface water contamination may occur from spray drift. To address risks associated with runoff and drift, labeling will be required to advise the users of the potential for off-site movement and to recommend application methods to minimize it.

The major novaluron degradate of novaluron in soil is chlorophenyl urea formed by aerobic soil microbes (26.6% of the parent converted in 7 days). Another metabolite in soil is chloroaniline formed under aerobic conditions (8.5% of the applied at 120 days). Based on laboratory studies, novaluron degradates appear to have a very low potential for leaching into ground water; but, have the potential to reach surface water through runoff.

B. ECOLOGICAL EFFECTS AND RISK

1. Toxicity and Risks to Aquatic Organisms: Available data on rainbow trout and bluegill sunfish demonstrate that novaluron is of low acute toxicity to fresh water fish ($LC_{50} \geq 0.96$ mg/L for both). A chronic (early life) toxicity study in rainbow trout yielded a no observed adverse effect concentration (NOAEC) of 0.00616 mg/L based on terminal growth and mortality, and demonstrates low chronic risk to freshwater fish. However, available data on the sheepshead minnow demonstrates that novaluron is highly toxic to estuarine fish ($LC_{50} > 0.002$ mg/L). Marine aquatic toxicity data on mysid shrimp and Eastern oyster indicate that novaluron is highly toxic to both species (0.00013 and 0.0015 mg/L, respectively). Chronic data submitted also indicate that daphnia and mysid shrimp are very sensitive to novaluron. The NOAEC for daphnia was 0.000029 mg/L based on survival of the parents and offspring and that for mysid shrimp was 0.000026 mg/L based on reductions in terminal body length. A Tier 1 and Tier II aquatic plant testing conducted on marine diatom was found to have an EC_{50} >9.68 mg ai/L for cell density.

To estimate the risk to aquatic life from the use of novaluron on pome fruits, cotton, and potatoes, risk quotients (RQs) were calculated using the worst case application scenarios. The highest risks are associated with use on pome fruits and are summarized in Table 4.

Table 4. Risk Quotients to Aquatic Organisms from the Use of Novaluron on Pome Fruits.

Aquatic Organism	Acute RQ[1]	Chronic RQ[2]
Fish,[3] fresh water	- -[4]	0.81
Invertebrate, freshwater	34.0	169
Invertebrate, estuarine (Shrimp)	38.8	194
Invertebrate, estuarine (Oyster)	3.4	16.8

Notes:
1. The acute, acute restricted use and acute endangered species Levels of Concern (LOC) for aquatic species are 0.5, 0.1, and 0.05 respectively.
2. The chronic LOC for aquatic species is 1.0.
3. No acute RQs could be calculated on estuarine fish due to lack of an adequate acute LC_{50}. No chronic toxicity data was submitted.
4. No acute RQs could be calculated due to lack of an adequate acute LC_{50}.

To address risks to aquatic organisms, specific buffers between crop fields and aquatic environments will be required and is discussed below under Risk Management Decision.

2. Toxicity and Risks to Birds: Acute toxicity of novaluron to the bobwhite quail and the mallard duck indicates an LD_{50} > 2000 mg/kg. The dietary LC_{50} for both species was > 5200 mg/kg. Chronic testing of novaluron indicates a NOEAC of 301 mg/kg to the bobwhite quail and a NOEAC of 9.8 mg/kg to the mallard duck.

Avian acute RQs for all proposed crops were below the LOC (= 0.5). The highest RQ of <0.04 was observed for birds foraging in short grass at the highest application rate on pome fruits. The chronic RQs exceeded the LOC (= 1.0) for all food categories on all proposed crops, except for fruit, pod, seeds and large insect food categories of birds. To further investigate the chronic avian risk for birds, the impact of foliar dissipation half-lives of 1, 5 and 35 days (default) on novaluron residues concentrations and its impact on reducing risk as well as predicted maximum and mean residues for single applications was evaluated. Although risk quotients were reduced, in most cases the risk quotients were still above the chronic levels of concern.

Proposed banded applications to cotton only exceeded levels of concern for endangered species for 15 gram birds when the application rates were not adjusted for band width. If the rates were adjusted for band width, the acute risk resulting from banded applications could be effectively mitigated.

3. Toxicity and Risks to Mammals: Acute risks to mammals were evaluated using the rat LD50 of > 5000 mg/kg-bw. There were no acute exceedances of the LOCs (highest RQ for the maximum residue level = 0.04). The 2-generation rat study with a NOAEC of 1000 mg/kg-bw was used to evaluate mammalian chronic risk. No LOCs were exceeded for any of the use sites (highest RQ for the maximum residue level = 0.19).

IV. RISK MANAGEMENT DECISION

Novaluron belongs to a relatively new class of pesticides called benzoylphenyl ureas. Some compounds of this group are broad spectrum insecticides with insect growth regulating (IGR) mode of action. These IGRs affect chitin synthesis of immature insects disrupting their normal growth and development. Novaluron has a wide spectrum of activity; it is efficacious against whiteflies, thrips, leafminers, stink bugs, leaf rollers and a number of other pests.

Novaluron has low acute mammalian toxicity. It's chronic, developmental, neurotoxicity and mutagenic activity also are well understood. Novaluron was classified as "not likely to be a carcinogen". Acute dietary risk from use of novaluron on proposed crops was not a concern. Chronic dietary analyses resulted in only 68% of allowed chronic exposure to the population subgroup. The chronic aggregate risk also was below the Agency's level of concern. The occupational exposure did not exceed the level of concern for handlers and applicators.

Environmental toxicity of novaluron is of concern to aquatic organisms. As is expected with an insect growth regulator, it is highly toxic to invertebrates. Although guideline data is not available, supplemental data demonstrates that novaluron also exhibits acute toxicity to fish. To mitigate against risk to aquatic organisms, label language will be added to help reduce exposure to aquatic ecosystems by minimizing runoff and drift from targeted sites. The following measures are expected to significantly lower risk quotients:

- No aerial application will be allowed for use on pome fruits. Ground applications will be restricted from within 75 feet of aquatic areas.

- Aerial applications to cotton will be restricted from within 250 feet of aquatic areas. Ground applications result in risk quotients below the Agency's level of concern; therefore, no buffers will be imposed for applications using ground equipment.

- Aerial applications to potatoes will be restricted from within 150 feet of aquatic areas. Ground applications result in risk quotients below the Agency's level of concern; therefore, no buffers will be imposed for applications using ground equipment.

- Extensive spray drift reduction language (including recommendations for droplet size, swath length, wind speed, etc.) will be incorporated into the labeling.

Novaluron is expected to reduce the reliance on organophosphates (acephate, diazinon, chlorpyrifos, and dimethoate) carbamates (carbaryl and bendiocarb) and pyrethroids (bifenthrin and cyfluthrin). In addition, novaluron has low acute toxicity to honey bees; therefore, it may become a useful component in integrated pest management systems.

V. DATA GAPS

Human Health Effects

- Storage stability data for residues of novaluron in/on cotton meal, hulls, and refined oil
- Additional information regarding the dairy cattle feeding study
- Poultry feeding study

Environmental Fate and Effects

- Freshwater invertebrate studies for both the technical and the formulated products
- Buffer strip effectiveness runoff study
- Sediment toxicity test

RECOMMENDATION

Available data provide adequate information to support the registration of novaluron on the food crops pome fruits, cotton, and potatoes to control insect pests.

I recommend that you concur with the conditional registration of this new chemical insecticide under Section 3(c)(7)(C) of the Act.

CONCUR	5/20/04 DATE
DO NOT CONCUR	DATE

Dan Kenny

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

D15

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 25-MAR-2004

SUBJECT: Novaluron (PC Code 124002) - Human Health Risk Assessment for Proposed Uses on Cotton, Pome Fruit and Potato. PP# 2F6430. DP # 295824.

FROM: Mary Clock-Rust, Biologist
Mark I. Dow, Ph.D., Biologist
George F. Kramer, Ph.D., Chemist
Pramod Terse, Ph.D., Toxicologist
Registration Action Branch 1 (RAB1)
Health Effects Division (HED) (7509C)

TO: Dan Kenny
Risk Management Team 1
Registration Division (RD)

THRU: P.V. Shah, Ph.D., Acting Branch Senior Scientist
RAB1/HED (7509C)

The HED of the Office of Pesticide Programs (OPP) is charged with estimating the risk to human health from exposure to pesticides. The RD of OPP has requested that HED evaluate hazard and exposure data and conduct dietary, occupational, residential and aggregate exposure assessments, as needed, to estimate the risk to human health that will result from proposed/registered uses.

A summary of the findings and an assessment of human risk resulting from the registered and proposed tolerances for novaluron is provided in this document. The risk assessment was provided by Mary Clock-Rust (RAB1), the residue chemistry data review and the dietary risk assessment were provided by George Kramer (RAB1), the hazard characterization by Pramod Terse (RAB1), the occupational/residential exposure assessment by Mark Dow (RAB1), and the drinking water assessment by Iwona Maher of the Environmental Fate and Effects Division (EFED).

Recommendation for Tolerances and Registration

Provided that revised Sections B and F are submitted and successful petition method validations (PMVs) for the proposed plant enforcement methods for crops and livestock are conducted; the residue chemistry, occupational and residential and toxicological databases support the conditional registration and the establishment of the following permanent tolerances for residues of novaluron *per se*:

Fruit, pome, group 11	2.0
Apple, wet pomace	8.0
Cotton, undelinted seed	0.60
Cotton, gin byproducts	30
Vegetables, tuberous and corm, group 1C	0.05
Sheep, meat; Horse, meat; Cattle, meat; Goat, meat	0.60
Sheep, meat byproducts, except liver and kidney; Horse, meat byproducts, except liver and kidney; Cattle, meat byproducts, except liver and kidney; Goat, meat byproducts except liver and kidney	0.60
Sheep, fat; Horse, fat; Cattle, fat; Goat, fat	11
Sheep, liver; Horse, liver; Cattle, liver; Goat, liver	1.0
Sheep, kidney; Horse, kidney; Cattle, kidney; Goat, kidney	1.0
Milk	1.0
Milk, fat	20
Hog, meat	0.01
Hog, meat byproducts	0.01
Hog, fat	0.05
Poultry, meat	0.03
Poultry, meat byproducts	0.04
Poultry, fat	0.40
Eggs	0.05

Registration may be made permanent upon submission of the following:

- Additional validation data for the proposed plant enforcement methods (radiovalidation and an interference study).

- Additional storage stability data for cotton meal, hulls, and refined oil.

- Information pertaining to the storage conditions and intervals of samples from the dairy cattle feeding study (if samples were stored for more than 30 days, then data are required depicting the frozen storage stability of novaluron residues in milk and livestock tissues).

- Recalculation and resubmission of the dosing levels used in the dairy cattle feeding study.

- A poultry feeding study.

Table of Contents

1.0 EXECUTIVE SUMMARY 4

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION 9
- 2.1 Identification of Active Ingredient 9
- 2.2 Structural Formula 9
- 2.3 Physical and Chemical Properties 9

3.0 HAZARD CHARACTERIZATION 10
- 3.1 Hazard Profile 10
- 3.2 FQPA Considerations 19
- 3.3 Dose-Response Assessment 19
- 3.4 Endocrine Disruption 22

4.0 EXPOSURE ASSESSMENT 23
- 4.1 Summary of Proposed Uses 23
- 4.2 Dietary Exposure/Risk Pathway 24
  - 4.2.1 Residue Profile 25
  - 4.2.2 Acute Dietary 32
  - 4.2.3 Chronic Dietary 32
  - 4.2.4 Cancer Dietary 34
- 4.3 Water Exposure/Risk Pathway 34
- 4.4 Residential Exposure/Risk Pathway 36

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION 36
- 5.1 Chronic Risk 37

6.0 CUMULATIVE RISK 38

7.0 OCCUPATIONAL EXPOSURE 38
- 7.1 Occupational Handler 39
- 7.2 Occupational Postapplication 42
- 7.3 Incident Data 43

8.0 DATA NEEDS/LABEL REQUIREMENTS 43
- 8.1 Toxicology 43
- 8.2 Residue Chemistry 43

1.0 EXECUTIVE SUMMARY

Under Section 3 of the Federal Insecticide, Fungicide and Rodenticide Act, as amended, Makhteshim-Agan of North America, Inc. has applied for registration of the active insecticidal ingredient novaluron for use on cotton, pome fruit and potato. Novaluron is currently registered for use on greenhouse/shadehouse grown ornamental plants.

Novaluron, a benzoylphenyl urea compound, is a new pesticide chemical belonging to the class of insecticides called insect growth regulators. Novaluron slowly kills the insects over a period of a few days by disrupting cuticle formation and deposition causing insect mortality during molting. This memorandum serves as HED's estimate of exposure and risk resulting from the proposed uses.

There are presently no registered uses of novaluron on food and feed crops; the current petition represents the first food/feed uses proposed for novaluron. A novaluron end-use product (Rimon™ 10 EC (emulsifiable concentrate); EPA Reg. No. 66222-35) containing 10% novaluron (0.83 lb/gal) was conditionally registered on 9/24/2001 for the control of whiteflies, thrips, leafminers, and armyworms in container-grown ornamental plants in greenhouses, shade houses, and outdoor nurseries. There are no residential uses.

In conjunction with this tolerance petition, the registrant has submitted an application for a Section 3 registration of a 7.5% water-dispersible granular (WDG) formulation (Rimon™ 7.5 WDG Novaluron Insecticide, EPA File Symbol 66222-LT) which is proposed for dormant, delayed dormant, and foliar applications on apples and pears for the control of foliage-feeding insects at a maximum seasonal rate of 0.96 lb ai/A. The petitioner also wishes to amend the 0.83 lb/gal EC formulation (Rimon™ 10 EC) to incorporate broadcast foliar uses on cotton and potato for the control of foliage-feeding insects at a maximum seasonal rate of 0.27 lb ai/A for cotton and 0.23 lb ai/A for potato.

Hazard Characterization

Novaluron has low acute toxicity via the oral (Toxicity Category IV), dermal (Toxicity Category III) and inhalation routes (Toxicity Category IV). No ocular (Toxicity Category IV) or dermal irritation (Toxicity Category IV) was noted. Novaluron is not a dermal sensitizer.

In subchronic and chronic toxicity studies, novaluron primarily produced hematotoxic effects such as methemoglobinemia, decreased hemoglobin, decreased hematocrit, decreased red blood corpuscles (RBCs or erythrocytes) associated with increased erythropoiesis.

The rat and rabbit developmental toxicity studies were tested up to the limit doses that produced no maternal and/or developmental toxicity. In the two-generation reproductive toxicity study, both maternal and offspring toxicity were evidenced by spleenomegaly, whereas reproductive toxicity was observed only in males as evidenced by decreases in epididymal sperm counts and increased age at preputial separation in the F_1 generation.

Acute/subchronic neurotoxicity screening batteries were performed using novaluron in rats. Neurotoxic effects of novaluron were evidenced by clinical signs (piloerection, fast/irregular breathing), functional observation battery (FOB) parameters (head swaying, abnormal gait) and neuropathology (sciatic and tibial nerve degeneration only at limit dose (2000 mg/kg/day). No signs of neurotoxicity or neuropathology were observed in the subchronic neurotoxicity study in rats at doses up to 1752 mg/kg/day in males and 2000 mg/kg/day in females. Therefore, HIARC concluded that there is not a concern for neurotoxicity resulting from exposure to novaluron.

There was no concern for mutagenic activity as indicated by several mutagenicity studies such as a bacterial (*Salmonella, E. coli*) reverse mutation assay, an *in vitro* mammalian chromosomal aberration assay, an *in vivo* mouse bone-marrow micronucleus assay and bacterial DNA damage or repair assay. There was no evidence of carcinogenic potential in either the rat or mouse carcinogenicity studies. Therefore, novaluron was classified as "not likely to be carcinogenic to humans."

Dose Response and Endpoint Selection

The acute oral reference dose (aRfD) for the general population, including infants and children, was not established since an endpoint of concern attributable to a single dose was not identified. The chronic reference dose (cRfD) of 0.011 mg/kg/day was determined on the basis of the chronic carcinogenicity study in rat. An uncertainty factor (UF) of 100 (10-fold for interspecies extrapolation and 10-fold for intra species variability) was applied to the no-observed adverse-effect level (NOAEL) of 1.1 mg/kg/day to derive the cRfD. The lowest-observed adverse-effect level (LOAEL) of 30.6 mg/kg/day was based on evidence of RBC damage and turnover resulting in a regenerative anemia. The FQPA SF of 1X is applicable for chronic dietary risk assessment. Therefore, the cPAD is 0.011 mg/kg/day.

In accordance with the EPA Draft Guidelines for Carcinogen Risk Assessment (July 1999), novaluron is classified as "not likely to be carcinogenic to humans" based on the lack of evidence for carcinogenicity in mice and rats.

The Hazard Identification Assessment Review Committee (HIARC) concluded that no special Food Quality Protection Act (FQPA) safety factor (SF) is needed (i.e. 1X) since there are no residual uncertainties for pre- and/or post-natal toxicity. The decision was based on a lack of increased susceptibility in the rat and/or rabbit developmental toxicity studies at levels up to the limit dose. Also, no increased qualitative and/or quantitative evidence of increased susceptibility was found following pre/post-natal exposure in a 2-generation reproduction study in rats.

HIARC met on December 16, 2003 to select endpoints for risk assessment and to evaluate the potential for increased susceptibility of infants and children from exposure to novaluron according to the February 2002 OPP 10X guidance document. This was a re-evaluation of the toxicology database subsequent to the initial evaluation by the HIARC on June 7, 2001 (TXR# 014682). The special FQPA SF was reduced to 1X based on toxicological considerations by the HIARC (12/16/03; TXR # 0052361), the conservative residue assumptions used in the dietary

and residential exposure risk assessments, and the completeness of the residue chemistry and conservative drinking water assessment evaluated by the risk assessment team.

A 10% dermal-absorption factor was based on an acceptable dermal-absorption study in rats in which the maximum total absorbed dose (expressed as percent of administered dose) ranged from about 0.5% to 10% of the applied dose. The level of concern for residential dermal exposures and occupational dermal and inhalation exposures are for margins of exposure (MOEs) <100. Endpoints applicable to risk assessments performed for novaluron in this diocument are summarized in the table below.

Exposure Scenario	Dose	Endpoint	Study/Effect
Chronic dietary	NOAEL = 1.1 mg/kg/day	cRfD and cPAD = 0.011 mg/kg/day	Combined chronic toxicity/carcinogenicity feeding study-rat-Erythrocyte damage and turnover resulting in a regenerative anemia at the LOAEL of 30.6 mg/kg/day.
Intermediate-term dermal (10% absorption rate) Short-term inhalation Intermediate-term inhalation	NOAEL = 4.38 mg/kg/day	Target MOE = 100 (residential and occupational)	90-day feeding study-rat-clinical chemistry and histopathology at the LOAEL of 8.64 mg/kg/day

Residues of Concern

The Metabolism Assessment and Review Committee (MARC) decided that for tolerance and risk assessment, residues of the parent compound, novaluron are the only residues of concern in plant and livestock matrices, and rotational crops. In drinking water, MARC concluded that parent, chlorophenyl urea, and chloroaniline are the residues of concern to be included in the drinking water assessment.

Chronic Dietary Exposure Estimates

A chronic dietary risk assessment was conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.30) and Lifeline™ (ver. 2.00) models . The analysis incorporated empirical processing factors, average field trial residues, and anticipated residues (ARs) for meat, milk, poultry commodities. The resulting food exposure estimates were less than HED's level of concern (≤68% cPAD); children 1-2 years old were the most highly exposed population; Lifeline™ yielded similar results. The use of percent of crop treated information would further refine HED's estimates.

Drinking Water Estimates

Concentrations of novaluron and its chlorophenyl urea and chloroaniline degradates in surface water and ground water were estimated by EFED using modeling. Tier 2 Pesticide Root Zone Model/Exposure Analysis Modeling System (PRZM/EXAMS) modeling was performed to estimate drinking water concentrations for novaluron (parent) in surface water. Tier 1 modeling was used to estimate concentrations of the degradates in surface water.

Drinking water estimates from EFED are meant to represent upper-bound estimates of the concentrations that might be found in surface water and groundwater based upon existing and proposed uses. Chronic estimates for the terminal degradate, chloroaniline, are the highest (2.61 ppb). This is consistent with the expected degradation pattern for novaluron. Therefore, the estimated drinking water concentration (EDWCs) values for chloroaniline will be used to assess chronic aggregate risk.

Aggregate Exposure Scenarios and Risk Conclusions
An aggregate risk assessment was performed for chronic aggregate exposure (food + drinking water) only. Acute aggregate risk was not estimated because HIARC did not identify an endpoint of concern attributable to a single dose in toxicity studies. Short- and intermediate-term aggregate risk assessments were not performed because no residential exposure is expected based on existing and proposed uses. A cancer aggregate risk assessment was not performed because novaluron has not been shown to be carcinogenic. The EDWCs generated by EFED are less than HED's calculated chronic DWLOCs for chronic exposure to novaluron. Therefore, the chronic aggregate risk associated with the proposed use of novaluron does not exceed HED's level of concern for the general U.S. population or any population subgroups.

Occupational Exposure Estimates
Based upon the proposed use patterns, HED expects that occupational pesticide handlers (i.e., mixers, loaders and applicators) will be exposed over the short- and intermediate-term durations (1-30 days and 1-6 months, respectively). The Scientific Advisory Council for Exposure (ExpoSAC) asserts that it is possible for commercial applicators to experience intermediate-term exposures when commercial applicators move from farm to farm, using the same pesticide consecutively for more than 30 days. The primary source of occupational exposure to novaluron is expected to occur during handling activities (mixing, loading and applying). Short-term postapplication exposure is not a concern since an endpoint for assessment of short-term dermal risk was not identified. As recommended by the HED Risk Assessment Review Committee (RARC), intermediate-term postapplication dermal risk was assessed and resulted in an MOE of 760.

For handlers, HED calculated estimates of risk for both short-term and intermediate-term inhalation exposures and intermediate-term dermal exposure. No chemical-specific data are available with which to assess potential exposure to pesticide handlers (i.e., mixer/loaders and applicators). Therefore, estimates of exposure are based on study data available in the Pesticide Handler Exposure Database Version 1.1 (PHED, Surrogate Exposure Guide, 8/98). **Provided that mixer/loaders supporting aerial operations wear protective gloves** in addition to a single layer of work clothes, all MOEs are greater than 100 and therefore, do not exceed HED's level of concern.

Recommendation for Tolerances and Registration
The HED Hazard Identification Assessment Review Committee (HIARC) requested a 28-day inhalation toxicity study as a condition of registration. However, based on the low volatility and low inhalation toxicity (Category IV) of novaluron and inhalation margins of exposure (MOEs)

>1000 for the proposed uses in this risk assessment, novaluron qualifies for a waiver of the 28-day inhalation toxicity study for the proposed uses [HED Standard Operating Procedure (SOP) 2002.01: *Guidance: Waiver Criteria for Multiple-Exposure Inhalation Toxicity Studies*, 08/15/02]. **The requirement for the 28-day inhalation toxicity study is waived for this action only.** If in the future, requests for new uses or formulations are submitted that may result in a significant change in either the toxicity profile or exposure scenarios, HED will reconsider this data requirement.

Provided that revised Sections B and F are submitted and successful petition method validations (PMVs) for the proposed plant enforcement methods for crops and livestock are conducted; the residue chemistry and toxicological databases support the conditional registration and the establishment of the following permanent tolerances for residues of novaluron *per se*:

Fruit, pome, group 11	2.0
Apple, wet pomace	8.0
Cotton, undelinted seed	0.60
Cotton, gin byproducts	30
Vegetables, tuberous and corm, group 1C	0.05
Sheep, meat; Horse, meat; Cattle, meat; Goat, meat	0.60
Sheep, meat byproducts, except liver and kidney; Horse, meat byproducts, except liver and kidney; Cattle, meat byproducts, except liver and kidney; Goat, meat byproducts except liver and kidney	0.60
Sheep, fat; Horse, fat; Cattle, fat; Goat, fat	11
Sheep, liver; Horse, liver; Cattle, liver; Goat, liver	1.0
Sheep, kidney; Horse, kidney; Cattle, kidney; Goat, kidney	1.0
Milk	1.0
Milk, fat	20
Hog, meat	0.01
Hog, meat byproducts	0.01
Hog, fat	0.05
Poultry, meat	0.03
Poultry, meat byproducts	0.04
Poultry, fat	0.40
Eggs	0.05

Registration may be made permanent upon submission of the following:

- Additional validation for the proposed plant enforcement methods (radiovalidation and an interference study).

- Additional storage stability data for cotton meal, hulls, and refined oil.

- Information pertaining to the storage conditions and intervals of samples from the dairy cattle feeding study (if samples were stored for more than 30 days, then data are required

depicting the frozen storage stability of novaluron residues in milk and livestock tissues).

▸Recalculation and resubmission of the dosing levels used in the dairy cattle feeding study.

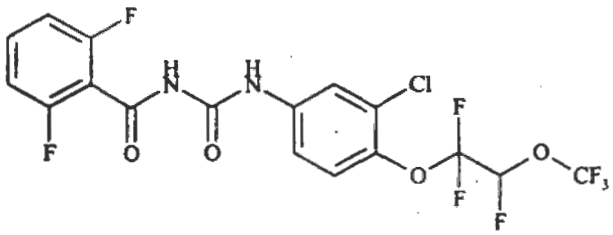
▸A poultry feeding study.

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

2.1 Identification of Active Ingredient

Registrant:	Makhteshim-Agan of North America, Inc.
Common name:	Novaluron
Pesticide Type:	Insecticide
Chemical Class:	Benzoylphenyl urea
Target Pests:	Foliar-feeding insects
Formulation:	Rimon™
% a.i.:	10, 7.5
Trade Names:	Rimon™ 10 EC Insecticide, Rimon™ 7.5 WDG Insecticide
EPA Reg Nos.:	66222-35, 66222-LT
CAS Number:	116714-46-6
PC Code:	124002
Chemical name:	*N*-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]amino]carbonyl]-2,6-difluorobenzamide
Empirical Formula:	$C_{17}H_9F_8ClN_2O_4$
Molecular Weight:	492.4

2.2 Structural Formula



2.3 Physical and Chemical Properties

The review of product chemistry data associated with this petition is under the purview of RD. Product chemistry data in support of this petition have been submitted by the petitioner and were forwarded by RD to their Product Chemistry Review Section on 11/3/00 (Memo B. Kitchens, D263780). All applicable product chemistry data requirements must be met for a Section 3 registration of the proposed use of novaluron on pome fruit, cotton, and potato.

Appearance:	white
Vapor Pressure:	1.6×10^{-5} Pa at 25°C
Water Solubility:	3 ug/L
Partition Coefficient (Octanol/Water):	log P_{ow} = 4.3 at 25°C
Melting Point:	176.5 - 178.0 °C

Novaluron is a solid at room temperature with a low vapor pressure; thus, any losses due to volatilization/sublimation are expected to be minimal.

3.0 HAZARD CHARACTERIZATION

Reference: *Novaluron - 3rd Report of the Hazard Identification Assessment Review Committee.* Pramod S. Terse. 02/03/2004. TXR # 0052361.

3.1 Hazard Profile

The existing toxicology database for novaluron supports the establishment of permanent tolerances for residues of novaluron in the commodities resulting from the proposed uses.

On December 16, 2003, the HED HIARC reviewed the recommendations of the toxicology reviewer for novaluron with regard to the acute and chronic RfDs and the toxicological endpoint selection for use as appropriate in occupational/residential exposure risk assessments. Since this is the first food use registration, the potential for increased susceptibility of infants and children from exposure to novaluron was also evaluated as required by the FQPA of 1996 under the November, 2002 OPP 10X Guidance. Novaluron was previously evaluated by the HIARC for non-food use (TXR# 014682).

Table 1. Acute Toxicity of Novaluron

Guideline No.	Study Type	MRID #(s)	Results	Toxicity Category
870.1100 (81-1)	Acute Oral (rat)	44961001	LD_{50} > 5000 mg/kg	IV
870.1200 (81-2)	Acute Dermal (rat)	45003201	LD_{50} > 2000 mg/kg	III
870.1300 (81-3)	Acute Inhalation (rat)	45003202	LC_{50} > 5.15 mg/L	IV
870.2400 (81-4)	Primary Eye Irritation (rabbit)	45003203	Not an eye irritant	IV
870.2500 (81-5)	Primary Skin Irritation (rabbit)	45003204	Not a dermal irritant	IV
87.2600 (81-6)	Dermal Sensitization (guinea pig)	45084001	Not a dermal sensitizer	N/A

Novaluron has low acute toxicity via the oral (Toxicity Category IV), dermal (Toxicity Category III) and inhalation routes (Toxicity Category IV). No ocular (Toxicity Category IV) or dermal irritation (Toxicity Category IV) was noted. Novaluron is not a dermal sensitizer. Novaluron exhibits marginal oral absorption (16-18%), relatively rapid and complete excretion within 48 hours primarily via the feces and to a lesser extent via urine in rats. Biliary contribution for fecal excretion appears to be insignificant. Absorption appeared to be approaching saturation at high doses. Peak plasma concentration occurred at 2-5 hours. Excretion via expired air was biologically insignificant. There was no evidence for selective tissue accumulation or sequestration.

In subchronic and chronic toxicity studies, novaluron primarily produced hematotoxic effects such as methemoglobinemia, decreased hemoglobin, decreased hematocrit, decreased Erythrocyte counts associated with increased erythropoiesis. However, the mechanism of action for this toxicity is not completely understood. Novaluron is metabolized into two groups of metabolites in rats, mainly, 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy) aniline and 2,6-difluorobenzoic acid. The aniline-related metabolites of novaluron appear to cause hematotoxicity. Anilines are known to cause hematotoxic effects (methemoglobinemia, decreased hemoglobin, decreased hematocrit and decreased RBC counts) by forming aniline-hemoglobin adducts. Aniline exposure also produces selective toxicity to the spleen of rats.

In the rat subchronic oral toxicity study, the primary effects included mild anemia (decreased hemoglobin, decreased hematocrit, decreased RBC counts), increased erythropoiesis and hemosiderosis in spleen. Subchronic oral toxicity in the mouse is characterized by mild anemia, inclusion bodies in the Erythrocytes and the spleenomegaly. Although rats treated topically with novaluron did not show signs of systemic toxicity, at the limit dose a small treatment related increase in methemoglobin was seen which was not considered biologically relevant.

In the chronic oral rat study, toxic effects included anemia, methemoglobinemia, hemosiderosis in the spleen and spleenomegaly. In the mouse chronic oral toxicity study, hematotoxicity was indicated by anemia, Heinz body inclusions in erythrocytes, increased erythropoisis, hemosiderosis in the spleen and spleenomegaly. The dog chronic toxicity is characterized by anemia (decreased hematocrit, decreased hemoglobin, decreased RBC counts), methemoglobinemia, increased hematopoiesis, hemosiderosis in liver and spleen, and spleenomegaly.

The rat and rabbit developmental toxicity studies were tested at doses up to 1000 mg/kg/day that produced no maternal and/or developmental toxicity. In the two-generation reproductive toxicity study, both the maternal and offspring toxicity were evidenced by spleenomegaly whereas the reproductive toxicity was observed only in males as evidenced by decreases in epididymal sperm counts and increased age at preputial separation in the F_1 generation.

Acute/subchronic neurotoxicity screening batteries were performed using novaluron in rats. Neurotoxic effects of novaluron were evidenced by clinical signs (piloerection, fast/irregular breathing), FOB parameters (head swaying, abnormal gait) and neuropathology (sciatic and tibial nerve degeneration) only at the limit dose (2000 mg/kg/day). No signs of neurotoxicity or neuropathology were observed in the subchronic neurotoxicity study in rats at doses up to 1752 mg/kg/day in males and 2000 mg/kg/day in females. Therefore, HIARC concluded that there is not a concern for neurotoxicity resulting from exposure to novaluron.

There was no concern for mutagenic activity as indicated by several mutagenicity studies such as a bacterial (*Salmonella, E. coli*) reverse mutation assay, an *in vitro* mammalian chromosomal aberration assay, an *in vivo* mouse bone marrow micronucleus assay and bacterial DNA damage or repair assay.

There was no evidence of carcinogenic potential in either the rat or mouse carcinogenicity studies and therefore novaluron was classified as "not likely to be carcinogenic to humans."

Table 2: Toxicity Profile of Novaluron.

Guideline No/ Study type	MRID No.(year)/ classification/Doses	Results
870.4300 Chronic/Carcinogenicity-rat	45651506 (1995); 0, 25, 700, or 20,000 ppm test material; M: 0, 1.1, 30.6, and 884.2 mg/kg/day F: 0, 1.4, 39.5, and 1113.5 mg/kg/day **Acceptable/Guideline**	NOAEL (M/F) =1.1/1.4 mg/kg/day LOAEL (M/F)=30.6/39.5 mg/kg/day based on Erythrocyte damage and turnover resulting in a regenerative mild anemia
870.4300 Chronic/Carcinogenicity-mouse	45651507/45877901 (2000/2003); 0, 30, 450, or 7000 ppm test material; M: 0, 3.6, 53.4, or 800.0 mg/kg/day F: 0, 4.3, 63.3, or 913.4 mg/kg/day **Acceptable/Guideline**	NOAEL (M/F)=3.6/4.3 mg/kg/day LOAEL (M/F)=53.4/63.3 mg/kg/day based on increased erythrocyte turnover due to hemoglobin oxidation and resulting in a mild anemia
870.4100b Chronic toxicity - dog	45638320 (1999); 0, 10, 100, 1000 mg/kg/day **Acceptable/Guideline**	NOAEL= 10 mg/kg/day LOAEL=100 mg/kg/day based on hematologic changes associated with histopathological changes in liver and spleen
870.3800 Reproduction and fertility- rat	45651505 (Main Study, 1999), 45638319 (Preliminary Study, 1998) 0, 1000, 4000 or 12,000 ppm ; M: 0, 74.2, 297.5 or 894.9 mg/kg/day F: 0, 84.0, 336.7 or 1009.8 mg/kg/day **Acceptable/Guideline**	Parental NOAEL= Not established; LOAEL (M/F)= 74.2/84.0 mg/kg/day based on increased absolute and relative spleen weights. Offspring NOAEL= Not established; LOAEL (M/F)= 74.2/84.0 mg/kg/day based on increased absolute and relative spleen weights. Reproductive NOAEL (M/F)= 74.2/≥ 1009.8 mg/kg/day; LOAEL= 297.5 mg/kg/day based on decreased epididymal sperm counts and increased age of preputial separation in the F_1 generation, reproductive LOAEL for females was not established.

Guideline No/ Study type	MRID No.(year)/ classification/Doses	Results
870.3200 28-day Dermal Toxicity - rat	45288501 (1998); 0, 75, 400, 1000 mg/kg/day **Acceptable/Guideline**	Systemic NOAEL= 1000 mg/kg/day; LOAEL= not established Dermal NOAEL= 1000 mg/kg/day; LOAEL= not established
870.6200 Acute Neurotoxicity screening battery- rat	45082601 (1999); 0, 200, 650, 2000 mg novaluron/kg **Acceptable/Guideline**	NOAEL= 650 mg/kg/day; LOAEL=2000 mg/kg/day based on clinical signs (piloerection, irregular breathing), FOB parameters (increased head swaying, abnormal gait) and neuropathology (sciatic and tibial nerve degeneration).
870.6200b Subchronic Neurotoxicity screening battery- rat	46086204 (2002); 0, 17.5, 174, 1752 mg/kg/day **Acceptable/Guideline**	NOAEL (M/F)=≥ 1752/≥ 2000 mg/kg/day; LOAEL= not established

Guideline No/ Study type	MRID No.(year)/ classification/Doses	Results
870.7485 Metabolism-rat	45638401(2000), 45638323(1998); single dose of 2 mg/kg or 1000 mg/kg, or 14 multiple 2 mg/kg/day doses of unlabeled RIMON (Lot no. 970211/4, 99.3% chemical purity) followed by a single dose of radiolabeled RIMON. **Acceptable/Guideline**	Novaluron exhibited marginal absorption (16-18%), relatively rapid and complete excretion within 48 hours primarily via the feces and to a lesser extent via urine in rat. Biliary contribution for fecal excretion appears to be insignificant. Absorption appeared to be approaching saturation at high doses. Peak plasma concentration occurred at 2-5 hours. Urinary metabolite profiles revealed 15 components and 8 components following administration of [chlorophenyl-^{14}C]RIMON or [difluorophenyl-^{14}C]RIMON, respectively. The most prevalent urinary metabolite was 2,6-difluorobenzoic acid represented the majority of the urinary radioactivity. Other components individually represented no more than 5.9% of the dose and most represented considerably less than 1%. Parent compound was the most prevalent contributor in the feces. The fecal metabolite profile revealed two metabolites; 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline, and 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea. Quantitatively, these were minor components accounting for <2% of the dose. In the repeated dose group some tissues such as fat contained measurable radioactivity at 168 hours post dose but did not appear to suggest significant potential for bioaccumulation or sequestration at the doses tested.
870.7600 Rat Dermal Penetration	45638415 (2000); 1.0, 0.067, 0.0048, or 0.0003 mg/cm^2 **Acceptable/Guideline**	Recovery of administered radioactivity was an acceptable 90.19-105.26%. The maximum total absorbed dose (expressed as per cent of administered dose and determined as the sum of radioactivity in excreta, cage wash, untreated skin, fat, blood, and residual carcass) ranged from about 0.5% to 10% of that administered.
870.3700a Prenatal Developmental in rodents-Rat	45082602 (1997); 0, 250, 500, 1000 mg/kg/day **Acceptable/Guideline**	Maternal NOAEL: ≥ 1000; LOAEL: not established Developmental NOAEL: ≥ 1000; LOAEL: not established

Guideline No/ Study type	MRID No.(year)/ classification/Doses	Results
870.3700b Prenatal Developmental in nonrodents-Rabbit	45638316, 45638318, 45638317 (1997,1998); 0, 100, 300, 1000 mg/kg/day **Acceptable/Guideline**	Maternal NOAEL: ≥ 1000; LOAEL: not established Developmental NOAEL: ≥ 1000; LOAEL: not established
870.5100 *Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay	44961013 (1997) 0, 312.5, 625, 1250, 2500 or 5000 µg/plate in the presence and absence of metabolic activation (±S9) **Acceptable/Guideline**	Novaluron, tested up to the limit of solubility (2500 µg/plate) and the limit dose (5000 µg/plate), was not cytotoxic with or without S9 activation in four *S. typhimurium* strains and one strain of *E. coli*, and did not induce a genotoxic response in any strain
870.5100 *Salmonella typhimurium*- bacterial reverse gene mutation assay	45030003 (1986) 0, 10, 33, 100, 333, 1000, or 3333 µg/plate in the presence and absence of mammalian metabolic activation (±S9) **Acceptable/Guideline**	Novaluron, tested up to the limit of solubility (3333 µg/plate), was not cytotoxic with or without S9 activation in five *S. typhimurium* strains, and did not induce a genotoxic response in any strain.
870.5300 Gene Mutation	45638321(1989); 0, 50, 100, 125, 150, 175 or 200 µg/mL with and without metabolic activation (S9-mix) in two independent assays. **Acceptable/Guideline**	There was no evidence of biologically significant induction of mutant colonies over background

Guideline No/ Study type	MRID No.(year)/ classification/Doses	Results
870.5395 Mammalian erythrocyte micronucleus test in mice	45638322(1989); 0, 1250, 2500 or 5000 mg/kg body weight **Acceptable/Guideline**	There was no statistically significant increase in the frequency of micronucleated polychromatic erythrocytes in mouse bone marrow at any dose or harvest time
870.5375 *In vitro* mammalian chromosome aberration test	44961015 (1992) 40, 200, and 1000 µg/mL, with and without metabolic activation (±S9) **Acceptable/Guideline**	Novaluron produced no evidence of clastogenic activity in primary human lymphocytes, in the presence or absence of S9 activation
870.5550 Unscheduled DNA Synthesis in HeLa S3 Human Epithelioid cells	45030002 (1988) 0.125, 0.25, 0.5, 1, 2, 4, 8, 16, 32, 64, 128, or 256 µg/mL (±S9) **Acceptable/Guideline**	Novaluron was considered not to show any evidence of causing DNA damage to HeLa S3 epithelioid cells in this unscheduled DNA synthesis test for mutagenic potential
870.5500 Mutagenicity-Rec assay with *Bacillus subtilis*	44961014 (1998) 50, 150, 500, 1,500, or 5,000 µg/plate, with and without mammalian metabolic activation (±S9) **Acceptable/Guideline**	Novaluron was equivocal for bacterial DNA damage in the absence of S9 activation, and negative for bacterial DNA damage in the presence of S9 activation

M - Male; F - Female

3.2 FQPA Considerations

On December 16, 2003, the HED HIARC evaluated the potential for increased susceptibility of infants and children from exposure to novaluron according to the February 2002 OPP 10X guidance document. The HIARC concluded that the toxicology database was complete for FQPA purposes and that there are no residual uncertainties for pre-/post-natal toxicity (Memo, P. Terse, 02/02/04; TXR NO. 0052361). Based on the hazard data, the HIARC recommended the special FQPA SF be reduced to 1X. Although the 2-generation study has no NOAEL established, the HIARC did not apply database UF because the LOAEL in this study is 74.2 mg/kg bw/day and it is widely accepted that there is a 10 fold difference in LOAEL and NOAEL. Thus, in this case the NOAEL would be 7.42 mg/kg bw/day, which is well above the dose selected for cRfD (1.1 mg/kg/day). The novaluron risk assessment team evaluated the quality of the exposure data; and, based on these data, recommended that the special FQPA safety factor be reduced to 1X. The recommendation is based upon the following:

- There is no quantitative or qualitative evidence of increased susceptibility of rat and rabbit fetuses to *in utero* exposure to novaluron in developmental toxicity studies. There is no quantitative or qualitative evidence of increased susceptibility to novaluron following pre-/post-natal exposure in a 2-generation reproduction study.
- There is no concern for developmental neurotoxicity resulting from exposure to novaluron. A developmental neurotoxicity study (DNT) study is not required.
- The toxicological database is complete for FQPA assessment.
- The chronic dietary food exposure assessment assumes 100% crops treated for all commodities.
- The dietary drinking water assessment utilizes water concentration values generated by model and associated modeling parameters which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded.
- There are no proposed or existing uses for novaluron which result in residential exposure.

3.3 Dose-Response Assessment

Table 3. Summary of Toxicological Dose and Endpoints for Novaluron

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
(1) Acute Dietary	Not applicable	None	An endpoint of concern attributable to a single dose was not identified. An acute RfD was not established.
(2) Chronic Dietary (All populations)	NOAEL= **1.1** mg/kg/day UF = **100** **Chronic RfD = 0.011** mg/kg/day	FQPA SF = **1X** **cPAD =** chronic RfD / FQPA SF **= 0.011** mg/kg/day	**Combined chronic toxicity/carcinogenicity feeding in rat** 45651506 LOAEL = **30.6** mg/kg/day based on **erythrocyte damage and turnover resulting in a regenerative anemia.** 870.4300
(3) Short-Term Incidental Oral (1-30 days)	NOAEL= **4.38** mg/kg/day	**Residential** LOC for MOE = **100** **Occupational** LOC for MOE = 100	**90-day feeding study in rat** LOAEL = **8.64** mg/kg/day based on **clinical chemistry** (decreased hemoglobin, hematocrit and RBC counts) and histopathology (increased hematopoiesis and hemosiderosis in spleen and liver).
(4) Intermediate-Term Incidental Oral (1- 6 months)	NOAEL= **4.38** mg/kg/day	**Residential** LOC for MOE = **100** **Occupational** LOC for MOE = 100	**90-day feeding study in rat** LOAEL = **8.64** mg/kg/day based on **clinical chemistry** (decreased hemoglobin, hematocrit and RBC counts) and histopathology (increased hematopoiesis and hemosiderosis in spleen and liver).
(5) Short-Term Dermal (1 to 30 days)	Not applicable	None	No toxicity observed at the limit dose in dermal study and there were no developmental toxicity concerns at the limit-dose; therefore, quantification of short-term dermal risk is not necessary.
(6) Intermediate-Term Dermal (1 to 6 months)	Oral NOAEL = **4.38** mg/kg/day (dermal-absorption rate = **10%**)	**Residential** LOC for MOE = **100** **Occupational** LOC for MOE = **100**	**90-day feeding study in rat** LOAEL = **8.64** mg/kg/day based on **clinical chemistry** (decreased hemoglobin, hematocrit and RBC counts) and histopathology (increased hematopoiesis and hemosiderosis in spleen and liver).
(7) Long-Term Dermal (>6 months)	Oral NOAEL= **1.1** mg/kg/day (dermal-absorption rate = **10 %**)	**Residential** LOC for MOE = **100** **Occupational** LOC for MOE = **100**	**Combined chronic toxicity/carcinogenicity feeding in rat** = #1 LOAEL = **30.6** mg/kg/day based on **erythrocyte damage and turnover resulting in a regenerative anemia.**

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Short-Term Inhalation (1 to 30 days)	Oral NOAEL = **4.38** mg/kg/day (inhalation absorption rate = 100%)	**Residential** LOC for MOE = **100** **Occupational** LOC for MOE = **100**	**90-day feeding study in rat** LOAEL = **8.64** mg/kg/day based on **clinical chemistry** (decreased hemoglobin, hematocrit and RBC counts) and histopathology (increased hematopoiesis and hemosiderosis in spleen and liver).
Intermediate-Term Inhalation (1 to 6 months)	Oral NOAEL = **4.38** mg/kg/day (inhalation absorption rate = 100%)	**Residential** LOC for MOE = **100** **Occupational** LOC for MOE = **100**	**90-day feeding study in rat** LOAEL = **8.64** mg/kg/day based on **clinical chemistry** (decreased hemoglobin, hematocrit and RBC counts) and histopathology (increased hematopoiesis and hemosiderosis in spleen and liver).
Long-Term Inhalation (>6 months)	Oral NOAEL= **1.1** mg/kg/day (inhalation absorption rate = 100%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	**Combined chronic toxicity/carcinogenicity feeding in rat** (# 1) LOAEL = **30.6** mg/kg/day based on **erythrocyte damage and turnover resulting in a regenerative anemia.**
Cancer	Not likely to be carcinogenic to humans		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no-observed adverse-effect level, LOAEL = lowest-observed adverse-effect level, PAD = population-adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

Endpoint Selection Rationale and Discussion

Acute Dietary Endpoint: The aRfD for the general population, including infants and children, was not established since an endpoint of concern attributable to a single dose was not identified. In the acute neurotoxicity study, neurotoxic signs and neuropathology was seen only at 2000 mg/kg (limit dose) with a relatively high NOAEL (650 mg/kg) and no developmental toxicity was seen at the limit-dose either in rat or rabbit pre-natal studies.

Chronic Dietary Endpoint: The cRfD of 0.011 mg/kg/day was determined on the basis of the chronic carcinogenicity study in rat. An UF of 100 (10-fold for interspecies extrapolation and 10-fold for intra species variability) was applied to the NOAEL of 1.1 mg/kg/day to derive the cRfD. The LOAEL of 30.6 mg/kg/day based on evidence of erythrocyte damage and turnover resulting in a regenerative anemia . The FQPA SF of 1X is applicable for chronic dietary risk assessment. Therefore, the cPAD is 0.011 mg/kg/day.

Carcinogenicity: In accordance with the EPA Draft Guidelines for Carcinogen Risk Assessment (July 1999), novaluron is classified as "not likely to be carcinogenic to humans" based on the lack of evidence for carcinogenicity in mice and rats.

Short- and Intermediate-Term Incidental Oral, Dermal, and Inhalation Endpoints: Incidental oral (short and intermediate), dermal (intermediate), and inhalation (short and intermediate) endpoints are based on clinical chemistry (decreased hemoglobin, hematocrit and RBC counts) and histopathology (increased hematopoiesis and hemosiderosis in spleen and liver) seen in a 90-day feeding study in rat (NOAEL = 4.38 mg/kg/day). A short term dermal endpoint was not selected since there were no dermal, systemic or developmental toxicity concerns at the limit-dose. Since oral studies were selected for intermediate-term dermal exposure assessment, a dermal penetration factor is required. The HIARC selected a dermal penetration factor of 10% based on a dermal penetration study in rats. Since the HIARC selected oral NOAELs for long-term inhalation exposure assessment, an inhalation absorption factor of 100% should be used. The level of concern for residential exposure is for MOEs <100 and for occupational exposure is for MOEs <100.

Long-Term Dermal and Inhalation Endpoints: Long term dermal and inhalation endpoints are based on erythrocyte damage and turnover resulting in a regenerative anemia seen in the combined chronic toxicity/carcinogenicity feeding study in rat (NOAEL 1.1 mg/kg/day). Since oral studies were selected for dermal exposure assessment, a dermal penetration factor is required. The HIARC selected a dermal penetration factor of 10% based on a dermal penetration study in rats. Since the HIARC selected oral NOAELs for long-term inhalation exposure assessment an inhalation absorption factor of 100% should be used. The level of concern for residential exposure is for MOEs <100 and for occupational exposure is for MOEs <100.

3.4 Endocrine Disruption

EPA is required under the Federal Food Drug and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA has authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, novaluron may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

4.0 EXPOSURE ASSESSMENT

References: *PP#2F06430. Novaluron. Petition for the Establishment of Permanent Tolerances for Use on Cotton, Pome Fruits, and Potato. Summary of Analytical Chemistry and Residue Data.* G. Kramer. 03/22/2004. DP# 285474.

Novaluron. Chronic Dietary Exposure Assessment for the Section 3 Registration on Cotton, Pome Fruits, and Potato (PP#2F06430). G. Kramer. 03/22/2004 DP# 298783

4.1 Summary of Proposed Uses

Registered Uses

There are presently no registered uses of novaluron on food and feed crops; the current petition represents the first food/feed uses proposed for novaluron. A novaluron end-use product (Rimon™ 10 EC (emulsifiable concentrate); EPA Reg. No. 66222-35) containing 10% novaluron (0.83 lb a.i./gal) was conditionally registered on 9/24/2001 for the control of whiteflies, thrips, leafminers, and armyworms in container-grown ornamental plants in greenhouses, shade houses, and outdoor nurseries.

Proposed Uses

In conjunction with this tolerance petition, Makhteshim-Agan has submitted an application for a Section 3 registration of a 7.5% WDG formulation (Rimon™ 7.5 WDG Insecticide, EPA File Symbol 66222-LT) which is proposed for dormant, delayed dormant, and foliar applications on apples and pears for the control of foliage-feeding insects at a maximum seasonal rate of 0.96 lb ai/A (Table 4). The petitioner also wishes to amend the 0.83 lb/gal EC formulation (Rimon™ 10 EC) to incorporate broadcast foliar uses on cotton and potato for the control of foliage-feeding insects at a maximum seasonal rate of 0.27 lb ai/A.

Diamond

max rate

Diamond 0.83 EC 66222-35

max rate

Table 4. Summary of Directions for Use of Novaluron.

Trade Name	Applic. Timing, Type, and Equip.	Applic. Rate	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Apple and Pear						
Rimon™ 7.5 WDG Novaluron Insecticide	Dormant, delayed dormant, and foliar; Dilute or concentrated spray; Ground equipment	Dilute: 0.04-0.08 lb ai/100 gal Concentrate: 0.04-0.32 lb ai/A	3	0.96	14	Applications may be made in a minimum of 50 gal/A to trellised trees or trees ≤10 feet tall. For trees >10 feet tall use a minimum of 100 gal/A. Do not exceed 400 gal/A. Depending on the target pest, the product should be applied at 10-14 day intervals to maintain control.
Cotton						
Rimon™ 10 EC Novaluron Insecticide	Foliar; Broadcast or banded application; Ground or aerial equipment	0.013-0.09 lb ai/A	3	0.27	30	Applications may be made in a minimum of 5 gal/A using ground equipment and 2-5 gal/A using aerial equipment. Depending on the target pest, the product should be applied at 7-14 day intervals to maintain control.
Potato						
Rimon™ 10 EC Novaluron Insecticide	Foliar; Broadcast application; Ground or aerial equipment	0.02-0.078 lb ai/A	3	0.23	~~30~~ 14	Applications may be made using ground equipment (minimum of 5 gal/A) or aerial (2-10 gal/A) with a 10- to 14-day retreatment interval.

Both labels recommend the use of novaluron in sequence with other classes of insecticides with a different mode of action in order to reduce selection pressure from resistant pests. The labels also specify that applications of novaluron through irrigation systems are prohibited. No rotational crop restrictions have been proposed. The petitioner should submit a revised Section B indicating that only registered crops may be rotated to a treated field within 30 days of the final application.

4.2 Dietary Exposure/Risk Pathway

The residue chemistry data submitted in support of proposed petition were reviewed in the HED memorandum dated 02/22/04 (G. Kramer; DP# 285474). The drinking water assessment was completed by EFED on February 11, 2004 (I. Maher DP# 285477). The chronic dietary exposure assessment was completed in a HED memorandum dated 2/??/04 (G. Kramer; DP# 298783).

4.2.1 Residue Profile

Background

Makhteshim-Agan has proposed the establishment of permanent tolerances for residues of the insecticide novaluron in/on the following commodities:

Pome Fruits	2.0 ppm
Apple Pomace	3.0 ppm
Cottonseed	0.6 ppm
Cotton Gin By-Products	30 ppm
Tuberous and Corm Vegetables	0.05 ppm
Cattle, meat	0.4 ppm
Cattle, mbyp	7.0 ppm
Cattle, fat	7.0 ppm
Cattle, liver	0.5 ppm
Cattle, kidney	0.5 ppm
Milk	0.5 ppm

Novaluron, a benzoylphenyl urea compound, is a new pesticide chemical belonging to the IGR class of insecticides. IGRs slowly kill the insects over a period of a few days by disrupting the normal growth and development of immature insects. Novaluron acts as an insecticide mainly by ingestion, but has some contact activity.

Nature of the Residue in Plants and Livestock

Plants: HED concludes that the nature of the residue in plants is adequately understood based on acceptable metabolism studies conducted on apples, cabbage, cotton, and potatoes. These studies indicate that novaluron is not metabolized in these crops. The parent compound, novaluron, was either the only residue component identified or was the predominant residue component in all analyzed plant matrices. The reviewed studies also indicate novaluron, when foliarly applied during the vegetative growth stage, is not readily translocated to mature apple fruit, potato tubers or cottonseed. The HED Metabolism Assessment Review Committee (MARC) reviewed these studies and determined that the residue of concern in crops for purposes of tolerance enforcement and risk assessment is novaluron *per se* (DP # 297646, G. Kramer *et al.*, 2/3/04).

Livestock: The nature of the residue in livestock is adequately understood based on acceptable studies on dairy cattle and laying hens. Novaluron is primarily excreted and not extensively metabolized in livestock matrices. A small amount of novaluron was metabolized in goats producing low levels of 2,6-difluorobenzoic acid in urine and kidney, and 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea in feces and liver. The HED MARC determined that the residue of concern in livestock for purposes of tolerance enforcement and risk assessment is novaluron *per se* (DP # 297646, G. Kramer *et al.*, 2/3/04).

Residue Analytical Methods

Plants: The petitioner has submitted two residue analytical methods for the analysis of novaluron residues in/on crop commodities. The first is a gas chromatography/electron-capture detection (GC/ECD) method for determination of novaluron in/on pome fruit, cabbage, and potatoes. The second is an high-performance liquid chromatography/ultraviolet (HPLC/UV) method for determination of novaluron in/on cotton commodities. The submitted GC/ECD and HPLC/UV methods are adequate for gathering data on novaluron, the terminal residue of concern in plants (apple, cabbage, cotton, and potato). The methods were adequately validated by the petitioner and by an independent laboratory. The methods may be used for tolerance enforcement pending completion of a successful PMV by Analytical Chemistry Laboratory/Biological and Economics Analysis Division (ACL/BEAD) and provided radiovalidation and interference studies are submitted by the petitioner. Radiovalidation of the GC/ECD and HPLC/UV methods are required, using radiolabeled samples from the metabolism studies, in order to determine whether the methods adequately extract aged (weathered) residues of novaluron. An interference study is required to determine whether other pesticides registered on the same commodities interfere with the determination of novaluron; an interference study may be waived if a specific single analyte confirmatory method is submitted.

Livestock: A GC/ECD method, which is similar in principles to the GC/ECD method submitted for plant commodities, was the data-collection method used in the analysis of samples collected from a dairy cattle feeding study. Based on acceptable method recoveries, the GC/ECD method is adequate for data collection. A high-performance liquid chromatography (HPLC)/mass spectrometry (MS)/MS method (MAK/670-01R) was also submitted. Method MAK/670-01R was successfully validated by an independent laboratory using milk, muscle, and liver as matrices. Method MAK/670-01R may be used for tolerance enforcement pending completion of a successful PMV by ACL/BEAD. The GC/ECD method is available as a confirmatory method.

Multiresidue Method (MRM)

Novaluron was analyzed according to the Food and Drug Administration (FDA) MRM Test guidelines in PAM Vol. I, Appendix II (1/94). The results indicate that novaluron is not adequately recovered by any of the MRMs.

Storage Stability

The submitted storage stability data indicate that novaluron is stable under frozen storage conditions in pear fruit for 5.2 months; in apples and potatoes for 12 months; in broccoli, cabbage, tomatoes for 6 months; and in apple juice for 3.3 months. These data are adequate to support the storage conditions and intervals of samples that were collected from the pome fruit, cotton and potato field trials and apple processing study only. Additional storage stability data are required to demonstrate the stability of residues of novaluron in/on cotton meal, hulls, and refined oil for up to 3.5 months. Information pertaining to the storage conditions and intervals of milk and tissue samples that were collected during the conduct of a dairy cattle feeding study (MRID 45638311) was not provided and is required for this registration request. If samples were stored frozen for less than 30 days prior to analysis, then no storage stability data are required. However, if samples were stored for more than 30 days, then data are required depicting the frozen storage stability of novaluron residues in milk and livestock tissues.

Magnitude of Residues in Plants

In support of the proposed uses, residue data were submitted on potatoes, cotton, apples and pears. A summary table of the results of the crop field trial studies can be found below in Table 5.

Pome Fruit: The petitioner has submitted data depicting the magnitude of the residue of novaluron in/on apples and pears, which are the representative commodities of the Pome Fruit Group (Crop Group 11). In these trials, the test formulation was applied at an exaggerated rate of 2.0 lb ai/A (2.1x the maximum proposed seasonal rate). However, the rate per application was ~0.34 lb ai/A (~1x) and the exaggerated total rate was the result of 3 early-season applications. As the majority of the residues at harvest would result from the late-season applications, HED concludes that these data support the proposed use. The number and geographical location of the field trials were adequate and support the proposed tolerance level of 2.0 ppm for pome fruit.

Cotton: The petitioner has submitted data depicting the magnitude of the residue of novaluron in/on undelinted cottonseed and cotton gin byproducts. In these trials, the test formulation was applied at an exaggerated rate of 0.377 lb ai/A (1.4x the maximum proposed seasonal rate). However, the rate per application was ~0.09 lb ai/A (~1x) and the exaggerated total rate was the result of 2 early-season applications. As the majority of the residues at harvest would result from the late-season applications, HED concludes that these data support the proposed use. The number and geographical location of the field trials were adequate and support the proposed tolerance levels of 0.6 and 30.0 ppm for cottonseed and cotton gin byproducts, respectively.

Potato: The petitioner has submitted a total of 20 field trials depicting the magnitude of the residue of novaluron in/on potatoes. However, 18 of these trials were conducted in Europe using a total rate of ~0.046 lb ai/A (0.2x the maximum proposed seasonal rate). In the U.S. trials conducted at ~0.50 lb ai/A (~2X), apparent novaluron residues of ~0.01 ppm were observed in both control and treated samples. HED concludes that the available data are adequate to conclude that novaluron residues will not exceed 0.05 ppm in potatoes for the following reasons:

1) plant metabolism studies indicate novaluron, when foliarly applied, is not readily translocated to potato tubers (TRR <0.001 ppm); 2) in the European trials, residues were <0.01 ppm, indicating that residues would have been <0.05 ppm at a 1X treatment rate; and 3) the PHI in the U.S. exaggerated-rate trials was 7 days compared to 30 days on the novaluron label. As potatoes are the representative crop of Tuberous and Corm Vegetables (Crop Group 1C), a tolerance of 0.05 ppm is appropriate for "Vegetables, tuberous and corm, subgroup 1C."

Table 5. Summary of Residue Data from Field Trials with Novaluron.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Type of spray	Analyte	Residue Levels (ppm)					
					n	Min.	Max.	HAFT [1]	Mean	Std. Dev.
[illegible]										
U.S. trials										
Apple	1.998-2.048	13/14	concentrate	novaluron	24	0.195	1.15	1.06	0.594	0.235
	2.007-2.010; (2.709) [2]	14	dilute	novaluron	8	0.242	0.557	0.522	0.408	0.100
Pear	1.983-2.020	14	concentrate	novaluron	12	0.177	1.66	1.34	0.578	0.406
	2.007-2.011	14	dilute	novaluron	4	0.424	0.807	0.785	0.606	0.208
Canadian trials										
Apple	1.995-2.077	14/15	concentrate	novaluron	12	0.260	0.960	0.955	0.660	0.240
Pear	1.996-2.039	14	concentrate	novaluron	8	0.726	1.95	1.79	1.33	0.438
[illegible]										
Cottonseed	0.372-0.384	29-32		novaluron	24	<0.05	0.484	0.401	0.115	0.129
Cotton gin byproducts (picker varieties)	0.372-0.380	29-30		novaluron	8	3.46	28.3	26.7	15.3	9.56
Cotton gin byproducts (stripper varieties)	0.375-0.382	30-32		novaluron	6	2.83	12.1	11.4	7.29	3.62
[illegible]										
European trials										
Potato tuber	0.044-0.048	21/22		novaluron	14	<0.01	<0.01	<0.01	0.005	-
Potato tuber	0.046-0.051	0, 3, 7, 14, & 21		novaluron	20	<0.01	<0.01	<0.01	0.005	-
U.S. trials										
Potato tuber	0.509-0.516	7		novaluron	4	<0.05	<0.05	<0.05	<0.05	-

[1] HAFT = Highest Average Field Trial

[2] One trial received a higher rate for one application because of a mixing error; residues from this trial were within the residue range of the other (nominal rate) trials

Magnitude of Residues in Processed Commodities

Apple: The apple processing data are adequate. They indicate that residues of novaluron concentrate in wet apple pomace (7.2x processing factor) but not in apple juice (0.1x processing

factor) processed from apples bearing detectable residues of novaluron. These data suggest that a tolerance is needed for wet apple pomace but not for apple juice. The maximum expected residue in wet apple pomace, resulting from the above use pattern is: 1.06 ppm (HAFT) x 7.2 (processing factor) = 7.65 ppm. Based on this calculation, the proposed tolerance of 3.0 ppm for apple pomace is inadequate and that a tolerance value of 8.0 ppm is appropriate.

Cotton: Pending submission of supporting storage stability data, the submitted cotton processing study is deemed acceptable. The processing data indicate that residues of novaluron do not appear to concentrate in cotton meal, hulls, and refined oil. Based on the results of the reviewed processing study, tolerances for cotton meal, hulls, and refined oil are not needed.

Potato: A potato processing study was not submitted as part of this petition request. In the U.S. trials conducted at ~0.50 lb ai/A (~2X), apparent novaluron residues of ~0.01 ppm were observed in both control and treated samples. As the theoretical maximum concentration factor is 5X for potatoes (OPPTS 860.1520, Table 1), residues in potato processed commodities are not expected to exceed 0.05 ppm. A potato processing study is thus not required for this petition.

Magnitude of Residues in Meat, Milk, Poultry and Eggs (MMPE)

Ruminants: The dairy cattle feeding study will be classified as scientifically acceptable pending recalculation and resubmission by the petitioner of the dosing levels used in the study. The residue intake level should be based on feed consumption and not in terms of mg ai/day. According to OPPTS 860.1480(f)(5), the level of the test materials in the total diet should be expressed in parts per million (mg/kg feed) (dry weight basis for ruminants). In addition, the petitioner is required to submit information pertaining to sample storage conditions and intervals. If sample integrity was maintained by appropriate storage and if samples were stored for less than 30 days, then no storage stability data are required. However, if samples were stored for more than 30 days, then data are required depicting the frozen storage stability of novaluron residues in livestock milk and tissues. The secondary residues in meat and milk are summarized below.

Table 6. Expected Secondary Residues in Meat and Milk

Tissue	Residue (ppm)*	Recommended Tolerance
Cattle# Muscle	0.55	0.60
Cattle# Liver	0.88	1.0
Cattle# Kidney	0.79	1.0
Cattle# Fat	10.5	11
Milk	0.78	1.0
Milk Fat	19.5**	20
Hog Muscle	0.0029	0.01
Hog Liver	0.0047	0.01
Hog Kidney	0.0042	0.01
Hog Fat	0.040	0.05

* Maximum Theoretical Dietary Burdens x Transfer Factor
** Milk residue x 25 (maximum concentration factor for milk fat)
# Cattle, goat, horse, sheep

Poultry: The petitioner has requested a waiver for the conduct of a poultry feeding study. Based on the maximum residues observed in the poultry metabolism study conducted at a feeding level of 12 ppm (100X), quantifiable residues would be expected in a feeding study. HED thus requests that the petitioner submits a poultry feeding study. Until these data are available, HED recommends that the results of the poultry metabolism study be used to determine the appropriate tolerances for poultry commodities. The following tolerances are based on the levels of novaluron in the poultry metabolism study normalized to 1x and then multiplied by a factor of 10x to account for the longer duration of a feeding study:

Poultry, meat ..... 0.03 ppm
Poultry, mbyp ..... 0.04 ppm
Poultry, fat ..... 0.40 ppm
Eggs ..... 0.05 ppm

Confined and Field Accumulation in Rotational Crops

In the submitted confined rotational crop study, the test substance was applied at only 0.3x the maximum proposed seasonal rate for rotatable crops (cotton and potato). HED generally requires that the confined rotational crop study be conducted at 1.0x the proposed maximum seasonal rate for annual crops (or crops which can be rotated). However, as the TRR was <0.005 ppm in all of the rotated crop commodities, it is unlikely that significant residues would be present at 1x. HED thus concludes that the results of this study are applicable to the current petition.

The submitted confined rotational crop study is adequate to satisfy the confined rotational crop

data requirements. MARC concluded that for tolerance assessment and risk assessment, parent only is the residues of concern. A confined rotational crop study conducted with [difluorophenyl-^{14}C(U)]novaluron will not be required as the difluorophenyl-derived metabolites are expected to be significantly less toxic than the chlorophenyl metabolites. However, future uses that have significantly higher application rates will require confined rotational crop studies at higher rates using chlorophenyl-labeled novaluron.

As the TRR may exceed 0.01 ppm at a 1X rate, the appropriate PBI for all non-labeled crops is 30 days. The petitioner should thus submit a revised Section B indicating that only registered crops may be rotated to a treated field within 30 days of the final application.

Tolerance Recommendation

The HED MARC has determined that the proposed tolerance expression, which is in terms of novaluron *per se*, is appropriate. A list of the tolerance summary for novaluron is presented below in Table 7.

Table 7. Tolerance Summary for Novaluron

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments (correct commodity definition)
Pome Fruit	2.0	2.0	Fruit, pome, group 11
Apple Pomace	3.0	8.0	Apple, wet pomace
Cottonseed	0.6	0.60	Cotton, undelinted seed
Cotton Gin By-products	30	30	Cotton, gin byproducts
Tuberous and Corm Vegetables	0.05	0.05	Vegetables, tuberous and corm, subgroup 1C
Cattle, meat	0.4	0.60	Sheep, meat; Horse, meat; Cattle, meat; Goat, meat
Cattle, mbyp	7.0	0.60	Sheep, meat byproducts, except liver and kidney; Horse, meat byproducts, except liver and kidney; Cattle, meat byproducts, except liver and kidney; Goat, meat byproducts except liver and kidney
Cattle, fat	7.0	11	Sheep, fat; Horse, fat; Cattle, fat; Goat, fat
Cattle, liver	0.5	1.0	Sheep, liver; Horse, liver; Cattle, liver; Goat, liver
Cattle, kidney	0.5	1.0	Sheep, kidney; Horse, kidney; Cattle, kidney; Goat, kidney
Milk	0.5	1.0	
Milk, fat	-	20	
Hog, meat		0.01	

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments (correct commodity definition)
Hog, meat byproducts		0.01	
Hog, fat		0.05	
Poultry, meat	-	0.03	
Poultry, meat byproducts	-	0.04	
Poultry, fat	-	0.40	
Eggs	-	0.05	

There are currently no established Codex, Canadian, or Mexican maximum residue limits (MRLs) for novaluron.

4.2.2 Acute Dietary

The aRfD for the general population, including infants and children, was not established since an endpoint of concern attributable to a single dose was not identified. See Section 3.0 of this document for details.

4.2.3 Chronic Dietary

The chronic analysis assumed 100% crop treated for all commodities; incorporated average field trial residues; empirical processing factors for apple juice (translated to pear juice); and DEEM™ (ver 7.76) default processing factors for the remaining processed commodities. ARs were calculated for meat and milk commodities and recommended tolerances were used for poultry commodities.

Several reasonable peer-reviewed programs have recently been emerging for modeling dietary exposure to pesticides. For a variety of technical, historical, and availability reasons, DEEM™ was the program generally used by EPA's Office of Pesticide Programs for conducting its dietary risk assessments. With the advent and current availability of a number of other exposure software programs, OPP, registrants, and other interested parties have available to them the option of selecting other peer-reviewed exposure software in conducting risk assessments for pestices. Lifeline™ is one such model and is the sofware being used in this HED review. Dietary exposure assessments may also be performed with other, similar programs, and if submitted, such results will be reviewed by EPA for acceptability and comparability to existing peer-reviewed software being used by OPP.

DEEM-FCID™ Program and Consumption Information

A chronic dietary exposure assessments was conducted for novaluron using DEEM-FCID™, Version 1.30, which incorporates consumption data from USDA's CSFII, 1994-1996 and 1998. Based on analysis of the 1994-96, 98 CSFII consumption data, which took into account dietary patterns and survey respondents, HED concluded that it is most appropriate to report risk for the

following population subgroups: the general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, adults 20-49, females 13-49, and adults 50+ years old.

Lifeline™ Program and Consumption Information

A chronic dietary exposure estimate was also conducted using the Lifeline™ model (Version 2.0). This Lifeline™ assessment was conducted using the same consumption data as the DEEM-FCID™ (CSFII, 1994-1996 and 1998 consumption data with FCID). Lifeline™ uses the recipe file to relate RACs to foods "as-eaten." Lifeline™ converts the RAC residues into food residues by randomly selecting a RAC residue value from the "user-defined" residue distribution (created from the residue, percent crop treated, and processing factors data), and calculating a net residue for that food based on the ingredients' mass contribution to that food item. For example, 'apple pie' will have a residue distribution based on the residues provided for apples (adjusted by the appropriate processing factors and percent crop treated), as well as the residues for each of the other ingredients in the apple pie recipe for which there may be tolerances. Lifeline™ calculates dietary exposure from 'apple pie' based on the amount eaten, and the residue drawn from the 'apple pie' residue distribution for that eating occasion.

Lifeline™ models the individual's dietary exposures over a season by selecting a new CSFII diary each day from a set of similar individuals based on age and season attributes. Lifeline™ groups CSFII diaries based on the respondents' age and the season during which the food diary was recorded. Further information regarding the Lifeline™ model can be found at the following web site: www.theLifelinegroup.org.

As stated above, for a chronic assessment, HED is concerned when dietary risk exceeds 100% of the PAD. The DEEM-FCID™ analysis estimates the dietary exposure of the U.S. population and various population subgroups. The results in Table 8 are reported for the general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50+ years. The resulting food exposure estimates were less than HED's level of concern (≤68% cPAD); children 1-2 years old were the most highly exposed population.

Results of the Lifeline™ analysis are fully consistent with DEEM-FCID™ results. The Lifeline™ chronic dietary exposure estimate for children aged 1-2 years old is 67% of the cPAD.

Table 8: Summary of Chronic Dietary Exposure and Risk for Novaluron.

Population Subgroup	cPAD (mg/kg/day)	Exposure (mg/kg/day)		%cPAD	
		DEEM-FCID	Lifeline	DEEM-FCID	Lifeline
General U.S. Population	0.011	0.001997	0.001903	18	17
All Infants (< 1 year old)		0.003438	0.003565	31	32
Children 1-2 years old		0.007519	0.007396	68	67
Children 3-5 years old		0.005737	0.005627	52	51
Children 6-12 years old		0.003418	0.003195	31	29
Youth 13-19 years old		0.001772	0.001668	16	15
Adults 20-49 years old		0.001368	0.001454	12	13
Adults 50+ years old		0.001165	0.001409	11	12
Females 13-49 years old		0.001276	0.001671	12	15

Characterization of Inputs/Outputs

The chronic analysis was refined through the use of empirical processing factors, average field trial residues, and ARs for meat and milk commodities. Despite this, HED concludes that the chronic estimates are conservative since they assumed average residues based on field trial data (maximum application rate; minimum pre-harvest interval; frozen immediately after harvest) and assumed 100% crop treated. The chronic analysis could be further refined through the use of anticipated market share data and/or preparation/cooking factors.

A chronic dietary risk assessment was conducted using the DEEM-FCID™ (ver. 1.30) and Lifeline™ (ver. 2.00) models . The analysis incorporated empirical processing factors, average field trial residues, and ARs for meat and milk. The resulting food exposure estimates were less than HED's level of concern (≤68% cPAD); children 1-2 years old were the most highly exposed population; Lifeline™ yielded similar results).

4.2.4 Cancer Dietary

In accordance with the EPA Draft Guidelines for Carcinogen Risk Assessment (July 1999), novaluron is classified as "not likely to be carcinogenic to humans" based on the lack of evidence for carcinogenicity in mice and rats. Therefore, an aggregate cancer risk assessment is not necessary.

4.3 Water Exposure/Risk Pathway

Reference: *Novaluron Estimated Drinking Water Concentration for Use in the Human Health Drinking Water Risk Assessment.* I. Maher. 02/11/2004.

The HED MARC concluded that parent, chlorophenyl urea (1 -[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy) phenyl] urea) (also called 275-352I), and chloroaniline (3-chloro-4-

(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline) are residues of potential concern to be included in the drinking water assessment.

Environmental Fate
Environmental fate data indicate that novaluron is immobile and moderately persistent to persistent in the field. Laboratory studies suggest that novaluron's major route of degradation is microbially-mediated. The chemical tends to strongly adsorb to soil and sediment and is stable to abiotic processes. Novaluron has a very low potential to reach ground water. During surface runoff conditions, novaluron may reach water bodies as bound to soil particles and will likely partition into sediments once in surface water. Additionally, contribution to surface water contamination may occur from spray drift.

Chlorophenyl urea is a major degradate of novaluron formed by aerobic soil metabolism and aquatic anaerobic metabolism. The degradate appears to have low to slight mobility (Kds = 16.7 - 61.5), moderately persistent in soil (decline curve estimated $t_{1/2}$ = 46.5 and 45.6 days), and moderately persistent in aquatic environment (decline curve estimated $t_{1/2}$ = 26.6 days). It has the potential to reach surface water through runoff and has low potential to reach ground water resources.

The chloroaniline degradate is formed by aerobic soil metabolism. Formation of chloroaniline in soil did not exceed 10% of the applied dose (i.e., the maximum concentration was 8.5% at 120 days post-treatment). The major degradate chlorophenyl urea is expected to further degrade in the environment to form chloroaniline.

Modeling and Drinking Water Estimates
Monitoring data for novaluron, chlorophenyl urea and chloroaniline in surface water and ground water were not found. Novaluron is not included in the USGS National Water-Quality Assessment (NAWQA) Program, the Pesticides in Ground Water Database (USEPA, 1992), and it was not an analyte in the National Pesticide Survey (USEPA, 1990). Concentrations of novaluron and its degradates, chlorophenyl urea and chloroaniline in surface water and ground water were estimated using modeling.

Tier 2 PRZM/EXAMS modeling was performed to estimate drinking water concentrations for surface water for novaluron *per se*. The scenarios were selected to provide high-end drinking water concentrations for each crop and represent the geographic locations where the specific crops are grown in large quantities.

The most conservative estimates were obtained for airblast applications to Pennsylvania apples at the maximum annual application rate of 0.96 lb a.i./acre, applied three times at 0.32 lb a.i./acre with an interval between applications of ten days.

For surface water, the 1-in-10 year annual mean EDWC for the parent novaluron is 1.8 µg/L (ppb).

A Tier I drinking water analysis was performed for the degradate chlorophenyl urea and chloroaniline. The FQPA Index Reservoir Screening Tool (FIRST) model was used to obtain. surface water estimates. As a conservative assumption, the model assumed chlorophenyl urea was directly applied, i.e. as granular, to the field, assuming no spray drift and no foliar interception. The FIRST model estimates a peak and an annual average value based on the Index Reservoir scenario.

For surface water, the annual average EDWC for chlorophenyl urea is 0.86 µg/L (ppb) and the annual average EDWC for chloroaniline is 2.6 µg/L (ppb). Both of these estimates are based upon the maximum application rate in apples.

For groundwater, the Screening Concentration in Ground Water (SCI-GROW) model was used to predict a groundwater concentration for novaluron at the annual application rate of 0.96 lb a.i./acre (i.e., three applications of 0.32 lb a.i./acre). The estimate for the parent novaluron is 5.5 x 10^{-3} µg/L in drinking water from shallow ground water sources. For chlorophenyl urea, the predicted ground water concentration is 4.5 x 10^{-3} µg/L, and for chloroaniline the concentration is 9.0 x 10^{-3} µg/L. These concentrations were estimated with the same assumptions used for surface water modeling, and may be considered as both the peak and annual average upper bound exposures.

These EDWC values are meant to represent upper-bound estimates of the concentrations that might be found in surface water and groundwater based upon existing and proposed uses. Of the three EDWC values, chronic estimates for the terminal metabolite, chloroaniline are the highest (100% conversion from parent to aniline was assumed). This is consistent with the expected degradation pattern for novaluron. Therefore, the EDWC value for chloroaniline (2.6 ppb) will be used to assess chronic aggregate risk.

4.4 Residential Exposure/Risk Pathway

All uses for novaluron, either proposed or existing, are agricultural (pome fruit, cotton and potatoes) or commercial (greenhouse-grown ornamentals) in nature. No residential uses are proposed, nor are any of the uses expected to result in recreational exposure. Therefore, a residential exposure and risk assessment was not performed for this action.

5.0 AGGREGATE RISK ASSESSMENTS AND RISK CHARACTERIZATION

An aggregate risk assessment was performed for chronic aggregate exposure (food + drinking water) only. An acute aggregate risk assessment was not performed because an endpoint of concern attributable to a single dose was not identified by HIARC. Short- and intermediate-term aggregate risk assessments were not performed because the there are no existing or proposed residential uses for novaluron. A cancer aggregate risk assessment was not performed because novaluron has not been shown to be carcinogenic.

This risk assessment utilizes DWLOCs to evaluate chronic aggregate risk. A DWLOC is a

theoretical upper limit on a pesticide's maximum target concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. A DWLOC will vary depending on the toxicity endpoint, drinking water consumption, body weights, and pesticide uses. Different populations will have different DWLOCs. HED uses DWLOCs in the risk assessment process to assess potential concern for exposure associated with pesticides in drinking water. DWLOC values are not regulatory standards for drinking water.

To calculate DWLOCs, the dietary food estimates (from DEEM-FCID™) were subtracted from the PAD value to obtain the maximum water exposure level. DWLOCs were then calculated using the standard body weights and drinking water consumption figures: 70kg/2L (US Population, adult male, and youth), 60 kg/2L (adult female), and 10kg/1L (infants and children). For chronic dietary exposure, HED is concerned when estimated dietary risk exceeds 100% of the cPAD.

5.1 Chronic Risk

The chronic aggregate risk assessment takes into account average exposure estimates from dietary consumption of novaluron (food and drinking water) and residential uses. However, due to the use patterns, no residential exposures are expected. Therefore, the chronic aggregate risk assessment will consider exposure from food and drinking water only.

The Tier 2 chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (18% of the cPAD) and all population subgroups. The most highly exposed population subgroup is children 1-2 years old, at 68 % of the cPAD. The Tier 2 EDWCs generated by EFED are less than HED's calculated chronic DWLOCs for chronic exposure to novaluron. Therefore, the chronic aggregate risk associated with the proposed use of novaluron does not exceed HED's level of concern for the general U.S. population or any population subgroups. Table 9 summarizes the chronic aggregate exposure estimates to novaluron residues.

Table 9. Chronic DWLOC Calculations for Novaluron

Population	cPAD mg/kg/day	Chronic Food Exp mg/kg/day	Max Chronic Water Exp mg/kg/day[1]	Ground Water EEC (ppb)[2]	Surface Water EEC (ppb)[2]	Chronic DWLOC (ppb)[3]
U.S. Population	0.011	0.001997	0.009003	0.009	2.61	320
Females, 13-49 years		0.001276	0.009724			290
All Infants		0.003438	0.007562			76
Children, 1-2 years		0.007519	0.003481			35
Youth, 13-19 years		0.001772	0.009228			280

1. Maximum water exposure (mg/kg/day) = cPAD (mg/kg/day) - food exposure (mg/kg/day)
2. The crop producing the highest level was used
3. DWLOC calculated as follows:

$$\text{DWLOC} = \frac{(\text{maximium water exposure (mg / kg / day)}) * (\text{body weight (kg)}) * (1000\ \mu g / mg)}{\text{water consumption (liter / day)}}$$

6.0 CUMULATIVE RISK

Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding as to novaluron and any other substances and novaluron does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has not assumed that novaluron has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at http://www.epa.gov/pesticides/cumulative/.

7.0 OCCUPATIONAL EXPOSURE

Reference: *NOVALURON - Exposure and Risk Assessment of Novaluron for Proposed New Uses on Cotton, Pome Fruit and Potato. D298012. M. Dow. 1/20/04.*

The primary source of occupational exposure to novaluron is expected to occur during handling activities (mixing, loading and applying). Short-term postapplication exposure is not a concern since HIARC did not identify an endpoint for the assessment of short-term dermal risk. Therefore short-term dermal postapplication risk was not assessed. While dermal postapplication over the intermediate-term duration (more than 30 consecutive days) is not expected to occur based on the use pattern, intermediate-term dermal postapplication risk was assessed. HED considers

postapplication inhalation exposure to be negligible based on the low vapor pressure (1.6×10^{-5} Pa at 25°C). A 24 hour REI provides further exposure protection.

7.1 Occupational Handler

Based upon the proposed use patterns, HED expects that occupational pesticide handlers (i.e., mixers, loaders and applicators) will be exposed over the short- and intermediate-term durations (1-30 days and 1-6 months, respectively). The ExpoSAC asserts that it is possible for commercial applicators to experience intermediate-term exposures when commercial applicators move from farm to farm, using the same pesticide consecutively for more than 30 days. Although intermediate-term exposures are not typically expected to occur, it is potentially possible for handlers treating crops such as cotton, where up to three applications per year may be made. Therefore, HED calculated estimates of risk for both short- and intermediate-term exposures.

Also based upon the proposed use patterns and upon exposure data available in PHED (v. 1.1, 1998), HED expects the most highly exposed occupational pesticide handlers to be:

1) mixer-loaders using open-pour loading of a liquid;
2) mixer-loaders using open-pour loading of a dry flowable (used as a surrogate for water-dispersible granular);
3) applicators using open-cab ground-boom equipment;
4) applicators using open-cab air-blast equipment.

Pilots (aerial applicators) are not assessed since exposure data indicate they are exposed far less than applicators using open-cab ground equipment.

The available exposure data for combined mixer/loader/applicator scenarios are limited in comparison to the monitoring of these two activities separately. These exposure scenarios are outlined in the PHED Surrogate Exposure Guide (August 1998). HED has adopted a methodology to present the exposure and risk estimates separately for the job functions in some scenarios and to present them as combined in other cases. Most exposure scenarios for hand-held equipment (such as hand wands, backpack sprayers, and push-type granular spreaders) are assessed as a combined job function. With these types of hand held operations, all handling activities are assumed to be conducted by the same individual. The available monitoring data support this and HED presents them in this way. Conversely, for equipment types such as fixed-wing aircraft, groundboom tractors, or air-blast sprayers, the applicator exposures are assessed and presented separately from those of the mixers and loaders. By separating the two job functions, HED determines the most appropriate levels of personal-protective equipment (PPE) for each aspect of the job without requiring an applicator to wear unnecessary PPE that may be required for a mixer/loader (e.g., chemical-resistant gloves may only be necessary during the pouring of a liquid formulation).

No chemical-specific data are available with which to assess potential exposure to pesticide

handlers. The estimates of exposure to pesticide handlers are based upon surrogate study data available in PHED (v. 1.1. 1998). For pesticide handlers, it is HED policy to present estimates of dermal exposure for "baseline;" that is, with a single layer of work clothing consisting of a long-sleeved shirt, long pants, shoes plus socks and no protective gloves and with a single layer of work clothing and **the use of** protective gloves or other PPE as might be necessary. The two proposed product labels involved in this assessment direct pesticide handlers to wear long-sleeved shirt, long pants, chemical-resistant gloves such as barrier laminate, butyl rubber, nitrile rubber, neoprene rubber or Viton®, protective eyewear and shoes plus socks. See Table 10 for a summary of estimated exposures and risks to occupational pesticide handlers.

Table 10. Estimated Handler Exposure and Risk from the Use of Novaluron on Cotton, Potato, Apple and Pear

Unit Exposure[1] mg a.i./lb handled	Application Rate[2]	Units Treated[3] Per Day	Average Daily Dose[4] mg a.i./kg bw/day	MOE[5] ST Inhal.	MOE[5] IT Combined
Mixer/Loader - Liquid - Open Pour - Supporting Aerial Operations for Cotton and Potato					
Dermal: SLNG 2.9 HC SLWG 0.023 HC Inhal 0.0012 HC	0.09 lb a.i./A	1200 A	Dermal: SLNG 0.45 SLWG 0.0035 Inhal 0.0019	2,400	NG 10 WG 820
Mixer/Loader - Dry Flowable - Open Pour - Supporting Ground Airblast Operations for Tree Fruits					
Dermal: SLNG 0.066 LC SLWG 0.066 HC Inhal 0.00077 HC	0.32 lb a.i./A ~ 52 fl.oz/Appl	40	Dermal: SLNG 0.0012 SLWG 0.0012 Inhal 0.00014	31,000	NG 3,300 WG 3,300
Applicator - Ground-boom - Open Cab for Cotton and Potato					
Dermal: SLNG 0.014 HC SLWG 0.014 MC Inhal 0.00074 HC	0.09 lb a.i./A	200 A	Dermal: SLNG 0.00036 SLWG 0.00036 Inhal 0.00019	23,000	NG 8,000 WG 8,000
Applicator - Air-blast - Open Cab for Tree Fruits					
Dermal: SLNG 0.36 HC SLWG 0.24 HC Inhal 0.0045 HC	0.32 lb a.i./A	40 A	Dermal: SLNG 0.0066 SLWG 0.0044 Inhal 0.00082	5,300	NG 590 WG 840

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from PHED Version 1.1, August 1998. Inhalation. Unit Exposures = mg a.i./pound of active ingredient handled. Data Confidence: HC = High Confidence.
2. Applic. Rate. = Taken from proposed RimOn® labels for 10 % EC and 7.5 % WDG.
3. Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; SOP No. 9.1. ExpoSAC; Revised 5 July 2000;
4. Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated * absorption factor ÷ Body Weight (70 kg). (Assumes 10 % dermal absorption and 100 % inhalation absorption.)
5. MOE = Margin of Exposure = No-Observable Adverse-Effect Level (NOAEL) ÷ ADD. No short-term dermal endpoint was identified therefore only short-term inhalation risk is presented (NOAEL = 4.38 mg a.i./kg bw/day). The intermediate-term dermal and inhalation endpoints are the same (NOAEL's 4.38 mg a.i./kg bw/day respectively) and are identified from the same study. Therefore, dermal exposure is summed with inhalation exposure and risk is presented for "baseline" work clothing and NO gloves (NG) as well as "baseline" work clothing WITH the use of protective gloves (WG).

An MOE of 100 is adequate to protect occupational pesticide handlers. Since all estimated MOEs are >100, **provided that mixer/loaders supporting aerial operations wear protective gloves** in addition to a single layer of work clothes, the proposed uses do not exceed HED's level of concern.

7.2 Occupational Postapplication

The HIARC determined that there were no signs of systemic toxicity at the limit dose of 1,000 mg/kg/day in a 4-week dermal toxicity study in rats. As a result, HIARC did not identify an endpoint for the quantification of short-term dermal risk assessment, and a corresponding risk assessment for this duration is not required. Dermal postapplication over the intermediate-term duration (more than 30 consecutive days) is not typically expected to occur based on the use pattern (7-14 day application interval). However, as recommended by the HED Risk Assessment Review Committee (RARC), intermediate-term dermal postapplication risk was assessed below. HED considers postapplication inhalation exposure to be negligible based on the low vapor pressure (1.6×10^{-5} Pa at 25°C).

RimOn® labels indicate a 24-hour restricted-entry interval (REI). The vapor pressure of novaluron is relatively low at 1.2×10^{-7} mm Hg. Therefore, the proposed use is not expected to result in postapplication risks that would exceed HED's level of concern.

Novaluron falls into Category IV for acute dermal toxicity, primary eye irritation and primary skin irritation. Therefore, the interim worker protection standard (WPS) REI of 24 hours is adequate to protect agricultural workers from post-application exposures to novaluron.

There is a potential for agricultural workers to have post-application exposure to pesticides during the course of typical agricultural activities. HED in conjunction with the Agricultural Re-entry Task Force (ARTF) has identified a number of post-application agricultural activities that may occur. HED has also identified Transfer Coefficients (TC) (expressed as cm^2/hr) relative to the various activities.

For most of the proposed crop uses, the activities with the highest TC is irrigation in potatoes or cotton with a TC of 1,500 cm^2/hr. The source study for these data is ARF021 (scouting dry peas). Lacking compound specific data, HED assumes 20% of the application rate is available as foliar dislodgeable residue on day zero after application. This and the transfer coefficient estimate for irrigation are adapted from the Science Advisory Council For Exposure SOP No. 003 (7 May 1998 - Revised 7 August 2000). The following convention may be used to estimate post-application exposure.

Surrogate Dislodgeable Foliar Residue:
DFR =
application rate * 20% available as dislodgeable residue * $(1-D)^t$ * 4.54×10^8 $\mu g/lb$ * 2.47×10^{-8} A/cm^2

and,
Average Daily Dose (ADD) = DFR $\mu g/cm^2$ * TC cm^2/hr * hr/day * 0.001 $mg/\mu g$ * 1/70 kg bw

therefore,
0.09 lb a.i./A * 0.20 * $(1-0)^0$ * 4.54×10^8 $\mu g/lb$ * 2.47×10^{-8} A/cm^2 = 0.20 $\mu g/cm^2$

0.20 $\mu g/cm^2$ * 2,500 cm^2/hr * 8 hr/day * 0.001 mg/μg * 0.10 dermal absorption *1/70 kg bw = 0.0058 mg/kg bw/day

Since **MOE = NOAEL ÷ ADD** then 4.38 mg/kg bw/day ÷ 0.0058 mg/kg bw/day = **760**

A MOE of 100 is adequate to protect agricultural workers from post-application exposures to novaluron. The estimated MOE is based upon conservative assumptions and is > 100, therefore estimated risks from post-application exposures do not exceed HED's level of concern.

7.3 Incident Data

The Office of Pesticide Program's Incident Data System (IDS) (29 DEC 03) indicates "no incident data" are recorded for novaluron.

8.0 DATA NEEDS/LABEL REQUIREMENTS

8.1 Toxicology

The HED Hazard Identification Assessment Review Committee (HIARC) requested a 28-day inhalation toxicity study as a condition of registration. However, based on the low volatility and low inhalation toxicity (Category IV) of novaluron and inhalation margins of exposure (MOEs) >1000 for the proposed uses in this risk assessment, novaluron qualifies for a waiver of the 28-day inhalation toxicity study for the proposed uses [HED Standard Operating Procedure (SOP) 2002.01: *Guidance: Waiver Criteria for Multiple-Exposure Inhalation Toxicity Studies*, 08/15/02]. **The requirement for the 28-day inhalation toxicity study is waived for this action only.** If in the future, requests for new uses or formulations are submitted that may result in a significant change in either the toxicity profile or exposure scenarios, HED will reconsider this data requirement.

8.2 Residue Chemistry

<u>860.1200 Directions for Use</u>

The petitioner should submit a revised Section B indicating that only registered crops may be rotated to a treated field within 30 days of the final application (based on the results of the confined rotational crop study).

<u>OPPTS 860.1340 Residue Analytical Methods - Plants</u>

The proposed plant enforcement methods, GC/ECD and HPLC/UV, need to pass a PMV by ACL/BEAD before the methods can be deemed adequate for tolerance enforcement. In addition, the petitioner is required to submit radiovalidation and interference studies. Radiovalidation of

the GC/ECD and HPLC/UV methods is required, using radiolabeled samples from the plant metabolism studies, in order to determine whether the methods adequately extract aged (weathered) residues of novaluron. An interference study is required to determine whether other pesticides registered on the same commodities interfere with the determination of novaluron; an interference study may be waived if a specific single analyte confirmatory method is submitted.

OPPTS 860.1340 Residue Analytical Methods - Livestock

The proposed livestock enforcement method, HPLC/MS/MS, needs to pass a PMV by ACL/BEAD before the method can be deemed adequate for tolerance enforcement.

860.1380 Storage Stability

Additional storage stability data are required to demonstrate the stability of residues of novaluron in/on cotton meal, hulls, and refined oil for up to 3.5 months.

Information pertaining to the storage conditions and intervals of samples from the dairy cattle feeding study is required. If sample integrity was maintained by appropriate storage and if samples were stored for less than 30 days, then no storage stability data are required. However, if samples were stored for more than 30 days, then data are required depicting the frozen storage stability of novaluron residues in milk and livestock tissues.

860.1480 Meat, Milk, Poultry, and Eggs

The dairy cattle feeding study (MRID 45638311) is inadequate but may be upgraded pending recalculation and resubmission by the petitioner of the dosing levels used in the study. The residue intake level should be based on feed consumption and not in terms of mg ai/day. For additional guidance regarding the resolution of this data gap, the petitioner is referred to OPPTS 860.1480(f)(5) which specifies that the level of the test materials in the total diet should be expressed in parts per million (mg/kg feed) (dry weight basis for ruminants).

The petitioner has requested a waiver for the conduct of a poultry feeding study. Based on the maximum residues observed in the poultry metabolism study, quantifiable residues would be expected in a feeding study. HED thus requests that the petitioner submits a poultry feeding study.

860.1550 Proposed Tolerances

The petitioner is requested to submit a revised Section F as specified above. Also, the appropriate chemical name for novaluron is "N-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]amino]carbonyl]-2,6-difluorobenzamide."

cc: M. Clock-Rust; G. Kramer; P. Terse; M. Dow (RAB1)
M. Clock-Rust:CM#2:806W:(703)308-2718:7509C:RAB1

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

21

MEMORANDUM

Date: 22-MAR-2004

Subject: PP#2F06430. **Novaluron**. Petition for the Establishment of Permanent Tolerances for Use on Cotton, Pome Fruits, and Potato. Summary of Analytical Chemistry and Residue Data.

DP #s:	285474, 287627, 297094, 297228 &298477	Decision #s:	305299 & 305300
PC Code:	124002	MRID #s.:	45638226, 45638227, 45638301-45638308, 45638311, 45638312, 45638412, 45638420, 45771801-45771803, 45785804, 45789202, 46141001, 46082701 & 46185801
40 CFR 180.			

From: George F. Kramer, Ph.D., Chemist
Registration Action Branch 1 (RAB1)
Health Effects Division (HED) (7509C)

Through: P.V. Shah, Ph.D., Acting Branch Senior Scientist
RAB1/HED (7509C)

To: Dan Kenny, PM Team 01
Registration Division (RD) (7505C)

Note: This document was originally prepared under contract by Dynamac Corporation (20440 Century Boulevard, Suite 100; Germantown, MD 20874; submitted 11/07/03) and has been reviewed by the HED and revised to reflect current OPP policies.

Executive Summary

Makhteshim-Agan of North America, Inc. (MANA) has proposed the establishment of permanent tolerances for residues of the insecticide novaluron [*N*-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]amino]carbonyl]-2,6-difluorobenzamide] in/on the following commodities:

Pome Fruits	2.0 ppm
Apple Pomace	3.0 ppm
Cottonseed	0.6 ppm
Cotton Gin By-Products	30 ppm

Tuberous and Corm Vegetables	0.05 ppm
Cattle, meat	0.4 ppm
Cattle, mbyp	7.0 ppm
Cattle, fat	7.0 ppm
Cattle, liver	0.5 ppm
Cattle, kidney	0.5 ppm
Milk	0.5 ppm

There are presently no registered uses of novaluron on food and feed crops; the current petition represents the first food/feed uses proposed for novaluron. A novaluron end-use product (Rimon™ 10 EC (emulsifiable concentrate); EPA Reg. No. 66222-35) containing 10% novaluron (0.83 lb a.i./gal) was conditionally registered on 9/24/2001 for the control of whiteflies, thrips, leafminers, and armyworms in container-grown ornamental plants in greenhouses, shade houses, and outdoor nurseries.

In conjunction with this tolerance petition, MANA has submitted an application for a Section 3 registration of a 7.5% water-dispersible granular (WDG) formulation (Rimon™ 7.5 WDG Novaluron Insecticide, EPA File Symbol 66222-LT) which is proposed for dormant, delayed dormant, and foliar applications on apples and pears for the control of foliage-feeding insects at a maximum seasonal rate of 0.96 lb ai/A. The petitioner also wishes to amend the 0.83 lb/gal EC formulation (Rimon™ 10 EC) to incorporate broadcast foliar uses on cotton and potato for the control of foliage-feeding insects at a maximum seasonal rate of 0.27 lb ai/A.

Based on the reviewed plant (apple, cabbage, cotton, and potato) and ruminant metabolism studies, HED concludes that the nature of the residue in plants and ruminants is adequately understood. The parent compound, novaluron, is the residue of concern in plants and ruminants. The submitted analytical methods for plants (gas chromatography/electron-capture detection (GC/ECD) and high-performance liquid chromatography/ultraviolet (HPLC/UV)) and livestock (HPLC/mass spectrometry (MS)/MS) need to pass a petition method validation (PMV) by the Analytical Chemistry Laboratory/Biological and Economics Analysis Division (ACL/BEAD) before the methods can be deemed adequate for tolerance enforcement. The residue chemistry deficiencies and the impact of those deficiencies on the establishment or assessment of the proposed tolerances are listed in the section below.

Residue Chemistry Deficiencies

860.1200 Directions for Use

The petitioner should submit a revised Section B indicating that only registered crops may be rotated to a treated field within 30 days of the final application (based on the results of the confined rotational crop study).

OPPTS 860.1340 Residue Analytical Methods - Plants

The proposed plant enforcement methods, GC/ECD and HPLC/UV, need to pass a PMV by ACL/BEAD before the methods can be deemed adequate for tolerance enforcement. In addition, the petitioner is required to submit radiovalidation and interference studies. Radiovalidation of the GC/ECD and HPLC/UV methods is required, using radiolabeled samples from the plant metabolism studies, in order to determine whether the methods adequately extract aged (weathered) residues of novaluron. An interference study is required to determine whether other pesticides registered on the same commodities interfere with the determination of novaluron; an interference study may be waived if a specific single analyte confirmatory method is submitted.

OPPTS 860.1340 Residue Analytical Methods - Livestock

The proposed livestock enforcement method, HPLC/MS/MS, needs to pass a PMV by ACL/BEAD before the method can be deemed adequate for tolerance enforcement.

860.1380 Storage Stability

Additional storage stability data are required to demonstrate the stability of residues of novaluron in/on cotton meal, hulls, and refined oil for up to 3.5 months.

Information pertaining to the storage conditions and intervals of samples from the dairy cattle feeding study is required. If sample integrity was maintained by appropriate storage and if samples were stored for less than 30 days, then no storage stability data are required. However, if samples were stored for more than 30 days, then data are required depicting the frozen storage stability of novaluron residues in milk and livestock tissues.

860.1480 Meat, Milk, Poultry, and Eggs

The dairy cattle feeding study (MRID 45638311) is inadequate but may be upgraded pending recalculation and resubmission by the petitioner of the dosing levels used in the study. The residue intake level should be based on feed consumption and not in terms of mg ai/day. For additional guidance regarding the resolution of this data gap, the petitioner is referred to OPPTS 860.1480(f)(5) which specifies that the level of the test materials in the total diet should be expressed in parts per million (mg/kg feed) (dry weight basis for ruminants).

The petitioner has requested a waiver for the conduct of a poultry feeding study. Based on the maximum residues observed in the poultry metabolism study, quantifiable residues would be expected in a feeding study. HED thus requests that the petitioner submits a poultry feeding study.

860.1550 Proposed Tolerances

The petitioner is requested to submit a revised Section F as specified below. Also, the appropriate chemical name for novaluron is "N-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]amino]carbonyl]-2,6-difluorobenzamide."

RECOMMENDATIONS

Provided Sections B and F and additional validation data for the analytical enforcement methods for plants and livestock are submitted and the Agency validations of these analytical enforcement methods are successful, HED concludes there are no residue chemistry data requirements that would preclude the establishment of the following permanent tolerances for residues of novaluron *per se*:

Fruit, pome, group 11	2.0 ppm
Apple, wet pomace	8.0 ppm
Cottonseed	0.6 ppm
Cotton, gin by-products	30 ppm
Vegetables, tuberous and corm, subgroup 1C	0.05 ppm
Cattle#, meat	0.60 ppm
Cattle#, meat byproducts, except liver and kidney	0.60 ppm
Cattle#, fat	11 ppm
Cattle#, liver	1.0 ppm
Cattle#, kidney	1.0 ppm
Hog, meat	0.01 ppm
Hog, meat byproducts	0.01 ppm
Hog, fat	0.05 ppm
Milk	1.0 ppm
Milk, fat	20 ppm
Poultry, meat	0.03 ppm
Poultry, mbyp	0.04 ppm
Poultry, fat	0.40 ppm
Eggs	0.05 ppm

Cattle, goat, horse, sheep

Registration of Rimon™ should be made conditional upon the submission of additional storage stability data, a poultry feeding study and additional information for the dairy cattle feeding study. A human-health risk assessment will be prepared as a separate document.

Background

Novaluron, a benzoylphenyl urea compound, is a new pesticide chemical belonging to the class of insecticides called insect growth regulators (IGR). IGRs slowly kill the insects over a period of a few days by disrupting the normal growth and development of immature insects. Novaluron acts as an insecticide mainly by ingestion, but has some contact activity. The chemical structure and nomenclature of novaluron is listed in Table 1. The physicochemical properties of the technical grade of novaluron are presented in Table 2. The chemical names and structures of novaluron and its transformation products, all of which were identified as minor residue components in the reviewed goat metabolism study, are presented in Table 3.

TABLE 1. Novaluron Nomenclature.

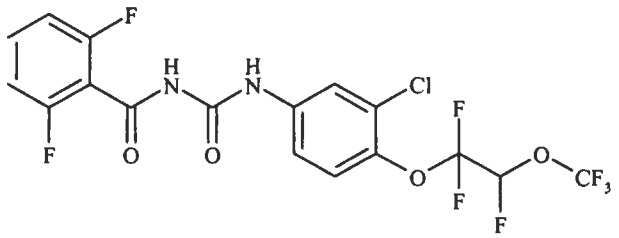
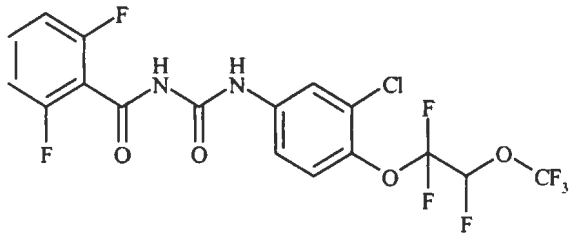
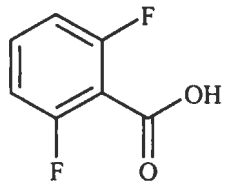
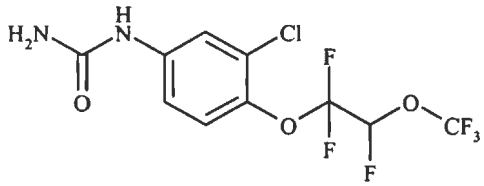
Compound	Chemical Structure
	
Common name	Novaluron
Trade name	Rimon®
IUPAC name	1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-[2,6-difluorobenzoyl]urea
CAS name	*N*-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]amino]carbonyl]-2,6-difluorobenzamide
CAS #	116714-46-6
End-use product/EP	Rimon™ 10 EC Insecticide (EPA Reg. No. 66222-35); Rimon™ 7.5 WDG Insecticide (EPA File Symbol No. 66222-LT)

TABLE 2. Physicochemical Properties of the Technical Grade of Novaluron

Parameter	Value	Reference
Melting point/range	176.5 - 178.0 °C	449610-06
pH	6.5	449610-05
Density	1.56 g/cm^3 at 22 °C	449610-06
Water solubility	3 µg/L at 20 °C	449610-05 449610-06
Solvent solubility (at 25 °C)	8.39 mg/L in n-heptane 1.88 g/L in xylene 14.5 g/L in methanol 198 g/L in acetone 113 g/L in ethyl acetate 0.98 g/L in n-octanol	
Vapor pressure (mm Hg)	1.2×10^{-7}	449610-06
Dissociation constant, pK_a	Not determined due to low water solubility	449610-06
Octanol/water partition coefficient, Log(K_{OW})	4.3 at 25 °C	449610-06

TABLE 2. Physicochemical Properties of the Technical Grade of Novaluron		
Parameter	Value	Reference
UV/visible absorption spectrum	Molar absorption coefficients of at 3 maximum absorbances: 15,400 L/mol • cm at 253 µm (neutral) 9,780 L/mol • cm at 253 µm (acidic) 20,500 L/mol • cm at 263 µm (basic)	449610-06

TABLE 3. Chemical Name and Structure of Novaluron and Its Transformation Products. (All Transformation Products were Identified from the Goat Metabolism Study)		
Common name/code	Chemical name	Chemical structure
Novaluron	N-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]amino] carbonyl]-2,6-difluorobenzamide	
275-158I	2,6-difluorobenzoic acid	
275-352I	1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea	

860.1200 Directions for Use

The petitioner provided copies of the product labels for the 7.5% WDG (Rimon™ 7.5 WDG Novaluron Insecticide, EPA File Symbol 66222-LT) and 0.83 lb/gal EC (Rimon™ 10 EC Novaluron Insecticide; EPA Reg. No. 66222-35) formulations; see Table 4 below. A summary of the proposed uses of novaluron on pome fruit, cotton, and potato is presented in Table 5.

Table 4. Summary of Novaluron End-Use Products.

Trade Name	Reg. No.	ai (% of formulation)	Formulation Type	Target Crops	Target Pests	Label Version
Rimon™ 7.5 WDG Novaluron Insecticide	66222-LT	7.5%	WDG	Apple and Pear	Foliar-feeding insects such as leafminers (spotted tentiform and Western tentiform), pear psylla, codling moth, leafrollers (oblique banded, pandemis, red banded, fruit tree, variegated and eye spotted), tufted apple bud moth, and Oriental fruit moth	Version 7.0, 2/26/02
Rimon™ 10 EC Novaluron Insecticide	66222-35	10% (0.83 lb/gal)	EC	Cotton	Foliar feeding insects such as tobacco budworm, cotton bollworm, armyworm (beet and fall), lygus, whitefly, and thrips	Version 3.0, 2/26/02
				Potato (white and sweet)	Foliar feeding insects such as Colorado potato beetle, European corn borer, beet armyworm, and loopers	Not specified

Table 5. Summary of Directions for Use of Novaluron.

Trade Name	Applic. Timing, Type, and Equip.	Applic. Rate	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Apple and Pear						
Rimon™ 7.5 WDG Novaluron Insecticide	Dormant, delayed dormant, and foliar; Dilute or concentrated spray; Ground equipment	Dilute: 0.04-0.08 lb ai/100 gal Concentrate: 0.04-0.32 lb ai/A	3	0.96	14	Applications may be made in a minimum of 50 gal/A to trellised trees or trees ≤10 feet tall. For trees >10 feet tall use a minimum of 100 gal/A. Do not exceed 400 gal/A. Depending on the target pest, the product should be applied at 10-14 day intervals to maintain control.
Cotton						
Rimon™ 10 EC Novaluron Insecticide	Foliar; Broadcast or banded application; Ground or aerial equipment	0.013-0.09 lb ai/A	3	0.27	30	Applications may be made in a minimum of 5 gal/A using ground equipment and 2-5 gal/A using aerial equipment. Depending on the target pest, the product should be applied at 7-14 day intervals to maintain control.
Potato						
Rimon™ 10 EC Novaluron Insecticide	Foliar; Broadcast application; Ground or aerial equipment	0.02-0.078 lb ai/A	3	0.23	30	Applications may be made using ground equipment (minimum of 5 gal/A) or aerial (2-10 gal/A) with a 10- to 14-day retreatment interval.

Both labels recommend the use of novaluron in sequence with other classes of insecticides with a different mode of action in order to reduce selection pressure from resistant pests. The labels also specify that applications of novaluron through irrigation systems are prohibited. No rotational crop restrictions have been proposed. The petitioner should submit a revised Section B indicating that only registered crops may be rotated to a treated field within 30 days of the final application.

Conclusions: The proposed use directions are adequate to allow HED an assessment of whether the submitted residue data reflect the maximum residues likely to occur in representative commodities of pome fruit (apple and pear), cotton, and potato.

860.1300 Nature of the Residue - Plants

The petitioner submitted metabolism studies conducted on apple, cabbage, cotton, and potato. Summaries from the individual DER reviews of these studies are reproduced below.

Apples

45638226.der.wpd

MANA has submitted an apple metabolism study with novaluron. The test substances, [difluorophenyl-^{14}C(U)]novaluron and [chlorophenyl-^{14}C(U)]novaluron, were separately applied two or three times to mature apple trees at a spray concentration of 0.005% ai per application, which is equivalent to a total rate of 0.045 (0.05x) and 0.071 lb ai/A (0.07x), respectively. The study was designed such that the applications were made 110, 90, and/or 60 days before mature harvest. Samples of apple fruit and leaves were collected following each application, at 1 or 2 intermediate sampling intervals, and at mature harvest.

The total radioactive residues (TRR; expressed as novaluron equivalents) in harvested fruit treated with [difluorophenyl-^{14}C(U)]novaluron were 0.208 ppm after the first application, 0.212 ppm after the second application, 0.079 ppm after the third application, and 0.034 ppm at final harvest (60-day PHI following 3 applications). The TRR in harvested fruit treated with [chlorophenyl-^{14}C(U)]novaluron were 0.174 ppm after the first application, 0.115 ppm after the second application, 0.094 ppm after the third application, and 0.040 ppm at final harvest (60-day PHI following 3 applications). In the translocation portion of the study, no significant level of radioactivity (<0.01 ppm) was detected in protected fruit at harvest following three applications of either difluorophenyl- or chlorophenyl-labeled novaluron which shows that novaluron is not translocated within the plant to the fruit.

All harvested fruit were surface washed with acetonitrile (ACN) within 3-4 hours of sampling. After surface washings, residues in the fruit were extracted with ACN and ACN/water. Surface washings of treated fruit released the majority of radioactivity although the level of released radioactivity gradually declined over time. In fruit treated with [difluorophenyl-^{14}C(U)]novaluron, the surface washes accounted for 98.5% of TRR after the first application, 70.4% of TRR after the second application, 84.6% of TRR after the third application, and 56.6% of TRR at final harvest (following 3 applications). In fruit treated with [chlorophenyl-

^{14}C(U)]novaluron, the surface washes accounted for 98.3% of TRR after the first application, 94.5% of TRR after the second application, 84.6% of TRR after the third application, and 54.2% of TRR at final harvest (following 3 applications).

The remainder of radioactivity in fruit was extracted from the peel and pulp using organic solvents. Higher radioactivity was recovered in the peel than pulp which suggests that novaluron slowly becomes absorbed into the peel of the apple with only low levels present in the flesh. The nonextractable residues after surface washing and extraction with organic solvents were quantitatively insignificant (≤5% TRR).

Chromatographic analysis of surface washes and peel extracts show that the major radioactive component identified in fruit was unmetabolized novaluron. In fruit treated with [difluorophenyl-^{14}C(U)]novaluron, the parent compound accounted for 98.2% of TRR after the first application, 99.8% of TRR after the second application, 96.2% of TRR after the third application, and 92.0% of TRR at final harvest (following 3 applications). In fruit treated with [chlorophenyl-^{14}C(U)]novaluron, the parent compound accounted for 97.5% of TRR after the first application, 99.0% of TRR after the second application, 94.5% of TRR after the third application, and 92.1% of TRR at final harvest (following 3 applications). In addition to the parent, up to five minor metabolites were detected at ≤2.5% TRR each.

Samples of collected apple fruit and leaves were stored frozen (<-15 °C) for an unspecified interval prior to chromatographic analysis. Based on the reported experimental termination date (May 25, 1998), samples may have been stored for up to 347 days (11.4 months). No supporting storage stability data were included in the study submission to validate sample storage conditions and intervals. However, as the parent compound comprised ≥90% of the TRR in all samples, these data will not be required. Under the conditions and parameters used in the study, the apple metabolism data are classified as scientifically acceptable.

Cabbage

45638227.der.wpd

MANA has submitted a cabbage metabolism study with novaluron. The test substances, [difluorophenyl-^{14}C(U)]novaluron and [chlorophenyl-^{14}C(U)]novaluron, were separately applied two times to cabbage plants at 0.027-0.040 lb ai/A/application (30-45 g ai/ha/application). Two separate groups of cabbage plants were treated for each radiolabel, such that the second application coincided with preharvest intervals of 2 or 6 weeks. Samples of cabbages were collected following each application, at 1 or 2 intermediate sampling intervals, and at mature harvest.

In the difluorophenyl label study, the TRR in the 6-week PHI group of cabbage were 0.840 ppm after the first application, 1.029 ppm after the second application, and 0.234 ppm at final harvest. The TRR in the 2-week PHI group of cabbage were 0.530 ppm after the first application, 0.637 ppm after the second application, and 0.448 ppm at final harvest. In the chlorophenyl label study, the TRR in the 6-week PHI group of cabbage were 0.620 ppm after the first application, 1.085 ppm after the second application, and 0.345 ppm at final harvest. The TRR in the 2-week

PHI group of cabbage were 0.496 ppm after the first application, 0.535 ppm after the second application, and 0.323 ppm at final harvest.

At harvest, cabbages were surface washed with ACN. The ACN surface washes accounted for 81.9-96.6% of TRR in cabbage treated with [difluorophenyl-^{14}C(U)]novaluron and 89.3-97.7% of TRR in cabbage treated with [chlorophenyl-^{14}C(U)]novaluron. Surface washed cabbages were separated into outer and inner leaves, and the radioactive residues were sequentially extracted from the outer and inner leaves with ACN and ACN/water. The residues extracted from the outer and inner leaves ranged 2.2-5.1% of TRR after the first application, 3.4-11.7% of TRR after the second application, and 8.0-15.3% of TRR at final harvest. The majority of residues in the extracts was subsequently partitioned into the organosoluble extract, with the remaining aqueous residue accounting for <1% TRR. The nonextractable residues in cabbage were <3% TRR.

Chromatographic analysis of the washes and organosoluble extracts show that the major radioactive component identified in cabbage was unmetabolized novaluron. In cabbage treated with [difluorophenyl-^{14}C(U)]novaluron, the parent compound accounted for 99.2-99.3% of TRR after the first application, 98.3-99.1% of TRR after the second application, and 96.1-99.9% of TRR at final harvest. In cabbage treated with [chlorophenyl-^{14}C(U)]novaluron, the parent compound accounted for 96.9-97.5% of TRR after the first application, 97.2-97.8% of TRR after the second application, and 95.8-96.5% of TRR at final harvest. In addition to the parent, up to two minor unknowns were detected at <2% TRR each.

Under the conditions and parameters used in the study, the cabbage metabolism data are classified as scientifically acceptable.

Cotton

45638302.der.wpd

MANA has submitted a cotton metabolism study with novaluron. The test substances, [difluorophenyl-^{14}C(U)]novaluron and [chlorophenyl-^{14}C(U)]novaluron, were separately applied using two treatment regimes. Regime 1 consisted of two applications, 14 days apart with a 90-day PHI. Regime 2 also consisted of two applications, 14 days apart, but with a 30-day PHI. Each formulated test substance was evenly sprayed to groups of cotton plants at a target rate of 0.045 lb ai/A/application (0.5x) which is equivalent to a total rate of 0.09 lb ai/A (0.3x).

In addition to the treatment regimes described above, the potential for translocation of residues was investigated. At each application, bolls (or immature bolls) on a single plant for each radiolabel and application regime, were protected from direct application using polythene bags. Protected 'bolls' were collected for analysis at final harvest to determine whether translocation of residues occurred from the treated foliage to the protected lint and seed.

Overall, the TRR were higher in cotton matrices that were treated with the difluorophenyl label than those treated with the chlorophenyl label. The TRR in treated gin trash (cotton gin byproducts) were also much higher than treated undelinted seed; consequently, the study focused its residue characterization efforts on gin trash.

Following Treatment Regime 1, the TRR in gin trash treated with difluorophenyl label were 0.629 ppm after the first application, 1.124 ppm after the second application, and 0.267 ppm at final harvest. The TRR in gin trash treated with chlorophenyl label were 0.601 ppm after the first application, 0.877 ppm after the second application, and 0.291 ppm at final harvest. The TRR in undelinted seed treated with both labels were 0.001-0.003 ppm.

Following Treatment Regime 2, the TRR in gin trash treated with difluorophenyl label were 0.369 ppm after the first application, 0.558 ppm after the second application, and 0.851 ppm at final harvest. The TRR in gin trash treated with chlorophenyl label were 0.265 ppm after the first application, 0.474 ppm after the second application, and 0.767 ppm at final harvest. The TRR in undelinted seed treated with both labels were 0.002-0.005 ppm.

The majority of radioactivity in cotton gin trash was adequately extracted with ACN. The proportion of radioactivity extracted from gin trash remained relatively constant and ranged 89.5-98.5% of TRR from all treatment regimes and labels. The nonextractable residues in gin trash after solvent extraction ranged 1.5-10.5% of TRR. Extracts of gin trash were analyzed by chromatographic techniques. The only discrete radioactive component detected in gin trash was unmetabolized novaluron which accounted for 86.1-97.6% of TRR. No other discrete radioactive components were detected during chromatographic analysis of gin trash extracts.

A sample of undelinted seed collected at final harvest after Treatment Regime 2 bore a TRR of 0.005 ppm. Although this sample need not be analyzed according to OPPTS GLN 860.1300, the petitioner performed analytical work on this matrix in order to elucidate the nature of the residue in undelinted seed. Approximately 84.2% of TRR (0.004 ppm) was extractable and 15.8% of TRR (0.001 ppm) was unextractable. Thin-layer chromatography (TLC) analysis of the extract detected novaluron at 78.8% of TRR.

The concentration of radioactivity detected in protected bolls following two applications (0.001 - 0.002 ppm) indicated that slight amounts of translocation occurred within the plant.

Under the conditions and parameters used in the study, the cotton metabolism data are classified as scientifically acceptable.

Potato

45638301.der.wpd (MRID 45771803 is a duplicate submission of 45638301)

MANA has submitted a potato metabolism study with novaluron. The test substances, [difluorophenyl-^{14}C(U)]novaluron and [chlorophenyl-^{14}C(U)]novaluron, were separately applied two times to potato plants at 0.081-0.089 lb ai/A/application. The total applied rate of 0.178 lb ai/A is 0.7x the maximum proposed seasonal rate of 0.24 lb ai/A for potatoes. The study was designed such that the first and second applications were made 43 and 29 days before mature harvest, respectively. Samples of potato tubers and foliage were collected following each application, at two intermediate sampling intervals, and at mature harvest.

No residues were detected in treated potato tubers except for samples collected 10 days before mature harvest (both labels; 2nd intermediate harvest) and at mature harvest (29-day PHI;

chlorophenyl-labeled sample only), each of which bore TRR of 0.001 ppm. No further analytical work was performed on potato tubers.

Detectable residues were observed in potato foliage. Overall, foliage TRR were higher in samples that were treated with the difluorophenyl label than those treated with the chlorophenyl label. In the difluorophenyl label study, the foliage TRR ranged from 0.785 to 9.874 ppm. In the chlorophenyl label study, the foliage TRR ranged from 1.559 to 5.894 ppm.

The majority of radioactivity (~81-96% TRR) was washed off the surface of potato foliage with ACN. After surface washing of foliage with ACN, the remainder of radioactive residues was sequentially extracted with ACN and ACN/water. Nonextractable residues remaining after surface washing and solvent extraction were ≤1.2% TRR in foliage.

The surface washes and organosoluble extracts of potato foliage were analyzed by HPLC. Virtually all radioactive residues were identified as novaluron. In potato foliage treated with [difluorophenyl-^{14}C(U)]novaluron, the parent compound accounted for 99.1% of TRR after the first application, 98.5% of TRR after the second application, and 96.9% of TRR at final harvest. In potato foliage treated with [chlorophenyl-^{14}C(U)]novaluron, the parent compound accounted for 97.6% of TRR after the first application, 96.5% of TRR after the second application, and 96.8% of TRR at final harvest.

The potato metabolism study is classified as scientifically acceptable.

Plant metabolism conclusions. HED concludes that the nature of the residue in plants is adequately understood based on acceptable metabolism studies conducted on apples, cabbage, cotton, and potatoes. These studies indicate that novaluron is not metabolized in these crops. The parent compound, novaluron, was either the only residue component identified or was the predominant residue component in all analyzed plant matrices. The reviewed studies also indicate novaluron, when foliarly applied during the vegetative growth stage, is not readily translocated to mature apple fruit, potato tubers or cottonseed. The HED Metabolism Assessment Review Committee (MARC) reviewed these studies and determined that the residue of concern in crops for purposes of tolerance enforcement and risk assessment is novaluron *per se* (DP # 297646, G. Kramer *et al.*, 2/3/04).

860.1300 Nature of the Residue - Livestock

Goat

45638303.der.wpd

MANA has submitted a study investigating the metabolism of [difluorophenyl-^{14}C(U)]novaluron and [chlorophenyl-^{14}C(U)]novaluron in goats. Radiolabeled novaluron was administered orally to a single lactating goat for each label, at an average of 12.3 ppm (difluorophenyl label) or 10.6 ppm (chlorophenyl label) in the diet. The goats were dosed once per day for five consecutive days. Milk was collected twice daily throughout the study, and tissues (muscle, fat, liver, and kidney) were collected at sacrifice.

In the difluorophenyl label study, TRR were 0.079-0.024 ppm in milk, 0.081-0.087 ppm in muscle, 1.11-1.38 ppm in fat, 0.14 ppm in kidney, and 0.43 ppm in liver. In the chlorophenyl label study, TRR were 0.061-0.23 ppm in milk, 0.081-0.16 ppm in muscle, 1.33-1.93 ppm in fat, 0.16 ppm in kidney, and 0.34 ppm in liver. The majority of the administered dose was excreted; it was reported that urine, feces, and cage wash collectively accounted for ~79-84% of the administered dose.

Radioactive residues in collected goat matrices were adequately extracted with methanol or methanol:water. In the difluorophenyl label study, 92.6-100% of TRR in milk and tissues were extractable. In the chlorophenyl label study, 93.8-99.5% of TRR in milk and tissues were extractable. Nonextractable residues accounted for 0-7% of TRR.

The organosoluble extracts were partitioned with hexane, and the resulting fractions (organic and aqueous) were analyzed by chromatographic techniques. Subcutaneous fat and rump muscle extracts were not further characterized because the petitioner stipulates that analytical data for peritoneal fat are considered representative of subcutaneous fat, and that foreleg muscle data are considered representative of rump muscle.

The parent compound, novaluron, was the only residue component identified in milk (92.6-95.1% TRR), in peritoneal fat (99.5-99.8% TRR), and in foreleg muscle (97.8-98.3% TRR). For other tissues, novaluron remained the predominant residue along with other minor residue components. Novaluron was the major residue identified in kidney (72.8-83.0% TRR) and liver (79.6-84.0% TRR). Minor residues of 2,6-difluorobenzoic acid were identified in difluorophenyl-labeled kidney and liver (≤5.1% TRR), and minor residues of 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea were identified in chlorophenyl-labeled liver (7.3% TRR). In addition, up to six unknowns were characterized in milk, kidney, and liver, each accounting for <8% TRR (≤0.011 ppm). Two unknowns detected by HPLC, one in difluorophenyl-labeled liver at 8.5% TRR (0.036 ppm) and one in chlorophenyl-labeled kidney at 13.2% TRR (0.021 ppm), were re-analyzed by TLC. TLC analysis determined that the difluorophenyl liver unknown consisted of numerous smaller polar components each accounting for <4% TRR. TLC analysis of the chlorophenyl kidney unknown determined smaller components present at <10% TRR; further partitioning of the isolated unknown characterized 6.4% TRR as organosoluble and 4.4% TRR as aqueous soluble.

The submitted metabolism study indicates that novaluron is primarily excreted and not extensively metabolized in goat matrices. A small amount of novaluron was metabolized producing low levels of 2,6-difluorobenzoic acid in urine and kidney, and 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea in feces and liver. The chemical structures of residue components identified from the goat metabolism study are presented in Table 3.

Poultry

46185801.der.wpd

MANA has submitted a study investigating the metabolism of [difluorophenyl-^{14}C(U)]novaluron in hens. Radiolabeled novaluron was administered orally to five laying hens at an average of 12.0 ppm in the diet. The hens were dosed once per day for 14 consecutive days. Eggs were

collected daily throughout the study, and tissues (muscle, fat, liver, and kidney) were collected at sacrifice.

TRR in the pooled tissues and eggs of laying hens sacrificed 23 hours after the last of 14 consecutive daily doses of [difluorophenyl-^{14}C(U)]novaluron in fat (mesenteric/abdominal), skin and subcutaneous fat, liver, kidneys, thigh and breast muscle were 3.62, 1.90, 0.393, 0.390, 0.305 and 0.061 ppm, respectively. The concentration of radioactivity in eggs (final day sample only) was 0.504 ppm. Concentrations of novaluron in fat (mesenteric/abdominal), skin and subcutaneous fat, liver, kidneys, thigh and breast muscle and eggs (final day sample only) were 3.47, 1.84, 0.411, 0.370, 0.313, 0.055 and 0.454 ppm respectively and accounted for between 90.2 - 104.6% of the TRR. The submitted metabolism study indicates that novaluron is not metabolized in hen matrices.

Livestock metabolism conclusions. HED concludes that the nature of the residue in livestock is adequately understood based on the submitted metabolism studies. The HED MARC determined that the residue of concern in livestock for purposes of tolerance enforcement and risk assessment is novaluron *per se* (DP # 297646, G. Kramer *et al.*, 2/3/04).

860.1340 Residue Analytical Methods

Plant commodities

45638304.der.wpd (also includes reviews of MRIDs 45638305 and 45638306)

MANA has submitted two residue analytical methods for the analysis of novaluron residues in/on crop commodities. The first is a GC/ECD method for determination of novaluron in/on pome fruit, cabbage, and potatoes. The second is an HPLC/UV method for determination of novaluron in/on cotton commodities. The methods are briefly described below.

Using the GC/ECD method, residues in/on homogenized samples of cabbage, pome fruit (apple and pear), processed apple commodities (juice and wet pomace), and potato tubers are extracted with methanol/water. The filtered extracts are concentrated to aqueous and repeatedly partitioned with hexane. The resulting hexane fractions are cleaned up by chromatography through a NH_2-SPE (solid-phase extraction) cartridge, the eluate is evaporated to dryness, and residues are redissolved in ethyl acetate or hexane for analysis by GC/ECD. The validated limits of quantitation (LOQs) are 0.01 ppm in potatoes and 0.05 ppm in apples (including juice and wet pomace) and cabbage.

Using the HPLC/UV method, residues in/on undelinted cottonseed and its processed fractions (meal, hulls, and refined oil) are homogenized and extracted with ACN. The extracts are filtered and repeatedly partitioned with hexane. The resulting ACN fraction is cleaned up by gel-permeation chromatography (GPC), silica gel chromatography, and/or NH_2-SPE. For cotton gin byproducts, homogenized samples are extracted with ACN/water. The filtered extracts are repeatedly partitioned with dichloromethane (DCM). The resulting DCM fraction (concentrated and redissolved in ACN) is then repeatedly partitioned with hexane. The resulting ACN fraction

is cleaned up by GPC, silica-gel chromatography, and/or NH_2-SPE. Residues are redissolved in HPLC solvent for analysis by HPLC/UV. The method LOQ is 0.05 ppm for undelinted cottonseed, cotton gin byproducts, and the processed commodities of hulls, meal, and refined oil.

The GC/ECD method was adequately validated by the petitioner using pome fruit, cabbage, and potatoes as matrices. Recovery ranges for novaluron were: (i) 78-101% in apple at fortification levels of 0.05-1.0 ppm; (ii) 80-107% in cabbage at fortification levels of 0.05-1.0 ppm; and (iii) 87-110% in potato at fortification levels of 0.01-0.50 ppm. The same GC/ECD method was the data-collection method used to analyze samples collected from the pome fruit and potato field trials, and apple processing studies (MRIDs 45638420, 45771801-02, and 45785804). Acceptable concurrent method validation recoveries were obtained during sample analysis.

No method validation data were available for the HPLC/UV method; however, acceptable concurrent method validation recoveries were obtained during analysis of samples collected from the cotton field trials and processing study (MRIDs 45638412 and 45638412).

Successful independent laboratory validations (ILVs) of the GC/ECD and HPLC/UV methods have been completed with apples and undelinted cottonseed, respectively. No radiovalidation or interference data are available for the submitted methods, and a confirmatory method was not provided.

Conclusions: The submitted GC/ECD and HPLC/UV methods are adequate for gathering data on novaluron, the terminal residue of concern in plants (apple, cabbage, cotton, and potato). The methods were adequately validated by the petitioner and by an independent laboratory. The methods may be used for tolerance enforcement pending completion of a successful PMV by ACL/BEAD and provided radiovalidation and interference studies are submitted by the petitioner. Radiovalidation of the GC/ECD and HPLC/UV methods are required, using radiolabeled samples from the metabolism studies, in order to determine whether the methods adequately extract aged (weathered) residues of novaluron. An interference study is required to determine whether other pesticides registered on the same commodities interfere with the determination of novaluron; an interference study may be waived if a specific single analyte confirmatory method is submitted.

Livestock commodities

Data-collection method (GC/ECD)

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MANA has submitted validation data for a GC/ECD method for the analysis of novaluron residues in eggs, milk, and ruminant tissues. The subject method is similar in principles to the GC/ECD method submitted for plant commodities (MRIDs 45638304, 45638305 and 45638306). Briefly, homogenized bovine tissue samples (fat, muscle, kidney, and liver) are extracted with methanol and centrifuged to separate the phases. Milk and egg samples are extracted with methanol by ultrasonication and then centrifuged to separate the phases. The extracts are concentrated to aqueous and repeatedly partitioned with hexane. The resulting hexane fractions are cleaned up by chromatography through a NH_2-SPE, the eluate is evaporated

to dryness, and residues are redissolved in hexane for analysis by GC/ECD. The validated LOQ is 0.01 ppm in fat, kidney, liver, muscle, milk, and egg.

The GC/ECD method was adequately validated by the petitioner. Recovery ranges for novaluron were: (i) 81-111% in fat; (ii) 79-105% in kidney; (iii) 72-116% in liver; (iv) 75-109% in muscle; (v) 83-109% in milk; and (vi) 77-100% in egg. The same method was the data-collection method used in the analysis of samples collected from a dairy cattle feeding study (MRID 45638311). Acceptable concurrent method recoveries were obtained during analysis of collected samples.

Enforcement method (HPLC/MS/MS)

45638308.der.wpd

MANA has submitted the results of an ILV study for Method MAK/670-01R, an HPLC/MS/MS method which determines residues of novaluron in milk, muscle, and liver. Based on the title of the method, "Development and Validation of Methodology For The Post-Registration Monitoring of Residues of Novaluron in Tissues (Fat, Kidney, Liver, Muscle) And Milk," it appears that the petitioner wishes to propose the subject method as an livestock enforcement method. The HPLC/MS/MS method uses similar extraction and cleanup procedures described above for the GC/ECD data-gathering method. Method MAK/670-01R is briefly described below.

Residues in tissue samples (fat, kidney, liver, and muscle) are extracted with methanol using a homogenizer and then centrifuged to separate the phases. Milk samples are sequentially extracted with methanol and ACN, and then centrifuged. The combined extracts are concentrated and repeatedly partitioned with hexane. The resulting hexane fractions are cleaned up by chromatography through a NH_2-SPE cartridge; the eluate is evaporated to dryness, and residues are redissolved in methanol and water for analysis by HPLC/MS/MS. The validated LOQs are 0.02 ppm for milk and muscle and 0.05 ppm for liver. No radiovalidation data were submitted in support of the proposed enforcement method. However, the data-gathering method was adequately radiovalidated in poultry tissues and eggs (MRID# 46185801). As the data-gathering method uses the same extraction and cleanup procedures as the proposed HPLC/MS/MS enforcement method, additional radiovalidation data are not required.

The ILV of Method MAK/670-01R was successful. In milk, method recoveries ranged 89-102% at a fortification level of 0.02 ppm and 80-98% at a fortification level of 0.20 ppm. In muscle, method recoveries ranged 87-120% at a fortification level of 0.02 ppm and 75-108% at a fortification level of 0.20 ppm. In liver, method recoveries ranged 74-96% at a fortification level of 0.05 ppm and 87-99% at a fortification level of 0.50 ppm. The ILV study submission, however, did not specify the number of worker-hours or calendar days required to complete extraction and analysis of a set of samples.

Conclusions: A GC/ECD method, which is similar in principles to the GC/ECD method submitted for plant commodities, was the data-collection method used in the analysis of samples collected from a dairy cattle feeding study. Based on acceptable method recoveries, the GC/ECD method is adequate for data collection.

An HPLC/MS/MS method (MAK/670-01R) was also submitted. Method MAK/670-01R was successfully validated by an independent laboratory using milk, muscle, and liver as matrices. Method MAK/670-01R may be used for tolerance enforcement pending completion of a successful PMV by ACL/BEAD. The GC/ECD method is available as a confirmatory method.

860.1360 Multiresidue Methods (MRMs)

45789202.der.wpd

Novaluron was analyzed according to the Food and Drug Administration (FDA) MRM Test guidelines in PAM Vol. I, Appendix II (1/94). The results indicate that novaluron is not adequately recovered by any of the MRMs. This study will be forwarded to FDA for further evaluation. The results are summarized below.

Novaluron did not exhibit natural fluorescence at an excitation wavelength of 253 nm; therefore, Protocol A testing was terminated. Testing using Protocol B was not required because novaluron is not an acid or phenol.

Testing using Protocol C Level II yielded adequate responses using a DB-1 column and electron-capture (ECD) and electrolytic-conductivity (ELCD) detectors; however, significant peak tailing was observed for both detectors.

Novaluron could not be accurately quantitated using the usual Protocol D procedures (peak heights) due to varying peak shapes and relative intensity from injection to injection. Corrected recoveries, obtained by summing the peak areas for standards and samples were 140% and 140% at the 0.1 ppm level, and 81% and 72% at the 2.0 ppm level.

Protocols E and F require the evaluation of Florisil cleanup. Novaluron was recoverable from the 303/304 C1 cleanup in the 15% and 50% diethyl ether/hexane fractions but was not recoverable (<30%) from the 303/304 C2 cleanup in eluant 3. Novaluron was partially recovered with Protocol E testing using extraction 303 E4/C1 with apples at 0.5 ppm (56% and 80%), but high bias recoveries were obtained at 2.0 ppm (118% and 139%). Variable results and inconsistent recoveries were obtained with Protocol F testing using extraction 304 E1/C1 with ground beef; recoveries were 6% and 30% at 0.05 ppm, and 33% and 84% at 2.0 ppm.

860.1380 Storage Stability

Plant commodities

45785804.der.wpd

MANA has included storage stability data in their submission of a study which depicts the magnitude of novaluron residues in pome fruit and the processed commodities of apple. Untreated samples of pear fruit and apple juice were fortified with novaluron at a level of 0.10 and 0.50 ppm, respectively. The fortified samples were then stored frozen (temperature

unspecified) for a duration of 158 days (5.2 months) for pear fruit and 99 days (3.3 months) for apple juice. Under these conditions, novaluron was found to be reasonably stable; residues did not significantly increase or decrease in tested commodities for the study duration. The maximum storage intervals of samples that were collected from the pome fruit field trials and apple processing study were: 5.0 months for apples, 5.1 months for pears, 3.1 months for apple juice, and 3.2 months for apple pomace. The reviewed storage stability data are adequate to support the storage conditions and intervals of samples that were collected from the pome fruit field trials and apple processing study.

46141001.der.wpd

Untreated samples of cottonseed and gin byproducts were fortified with novaluron at 0.10 ppm. The fortified samples were then stored frozen (-20°C) for a duration of 5 months. Analyses were performed at intervals of 1 and 5 months. Under these conditions, residues of novaluron did not significantly increase or decrease in the tested commodities. HED, therefore, concludes that novaluron is stable under frozen storage conditions in/on cottonseed and gin byproducts for up to 5 months. The maximum storage intervals of samples that were collected from the cotton field trials and cotton processing study were: 3.8 months for cottonseed, 5.3 months for cotton gin by product, 3.5 months for cotton meal, 3.3 months for cotton hulls, and 3.1 months for refined cotton oil. The reviewed storage stability data are adequate to support the storage conditions and intervals of cottonseed and gin byproducts samples that were collected from the cotton field trials and processing study only. Additional storage stability data are required to demonstrate the stability of residues of novaluron in/on cotton meal, hulls, and refined oil for up to 3.5 months.

46086207.der.wpd

Samples of untreated apples and potatoes were fortified with novaluron at a level of 0.05, 0.25 and 1.0 ppm (apples) or 0.01, 0.10 and 0.5 ppm (potatoes). The fortified samples were then stored frozen (-18°C) for a duration of 12 months. Under these conditions, residues of novaluron did not significantly increase or decrease in the tested commodities. HED, therefore, concludes that novaluron is reasonably stable under frozen storage conditions in/on potatoes and apples for up to 12 months. The maximum storage interval of samples that were collected from the U.S. and European potato field trials is 6.9 months for potato tubers. The reviewed storage stability data are adequate to support the storage conditions and intervals of samples that were collected from the potato field trials.

46086208.der.wpd

Samples of treated broccoli, cabbage, tomatoes and orange matrices (wet and dry pomace, peel and marmalade) with field-incurred residues of novaluron at levels of 0.02-1.80 ppm were stored frozen (-18°C) for a duration of 6 months. Under these conditions, residues of novaluron did not significantly increase or decrease in broccoli, cabbage, and tomatoes. HED concludes that novaluron is reasonably stable under frozen storage conditions in/on these commodities for at least 6 months. Residues in orange matrices were significantly higher after storage.

Conclusions: The submitted storage stability data indicate that novaluron is stable under frozen storage conditions in pear fruit for 5.2 months; in apples and potatoes for 12 months; in broccoli,

cabbage, tomatoes for 6 months; and in apple juice for 3.3 months. These data are adequate to support the storage conditions and intervals of samples that were collected from the pome fruit, cotton and potato field trials and apple processing study only. Additional storage stability data are required to demonstrate the stability of residues of novaluron in/on cotton meal, hulls, and refined oil for up to 3.5 months.

Livestock commodities

Information pertaining to the storage conditions and intervals of milk and tissue samples that were collected during the conduct of a dairy cattle feeding study (MRID 45638311) was not provided and is required for this registration request. If samples were stored frozen for less than 30 days prior to analysis, then no storage stability data are required. However, if samples were stored for more than 30 days, then data are required depicting the frozen storage stability of novaluron residues in milk and livestock tissues.

860.1480 Meat, Milk, Poultry, and Eggs

There are livestock and poultry feed items associated with the proposed uses of novaluron on pome fruit, potatoes and cotton. The maximum theoretical dietary burdens (MTDBs) of novaluron to beef cattle, dairy cattle, poultry, and hog are presented in Table 6. These burdens were calculated using the HED-recommended tolerances.

Table 6. Calculation of MTDBs of Novaluron to Livestock.

Feed Commodity	% Dry Matter[1]	% Diet[1]	Recommended Tolerance, ppm	Dietary Contribution, ppm[2]
Beef Cattle				
Apple, wet pomace	40	40	10	10.0
Cotton, gin byproducts	90	20	30	6.67
Cotton, undelinted seed	88	25	0.60	0.17
Cotton, meal	89	15	0.60 [3]	0.10
Total Burden		100		**16.9**
Dairy Cattle				
Apple, wet pomace	40	20	10	5.0
Cotton, gin byproducts	90	20	30	6.67
Cotton, undelinted seed	88	25	0.60	0.17
Cotton, meal	89	15	0.60 [3]	0.10
Total Burden		80		**11.9**
Poultry				
Cotton, meal	89	20	0.60 [3]	0.12
Total Burden		20		**0.12**

Table 6. Calculation of MTDBs of Novaluron to Livestock.				
Feed Commodity	% Dry Matter[1]	% Diet[1]	Recommended Tolerance, ppm	Dietary Contribution, ppm[2]
Hog				
Cotton, meal	89	15	0.60 [3]	0.09
Total Burden		15		**0.09**

[1] Table 1 (OPPTS Guideline 860.1000).
[2] Contribution = [tolerance / % DM (cattle)] x % diet). Poultry and hog diets are not corrected for % dry matter.
[3] The HED-recommended tolerance was used in the calculation.

Dairy cattle feeding study

45638311.der.wpd

Four groups of dairy cows were orally dosed with novaluron twice a day at levels equivalent to 7, 53, 159, and 530 mg ai/day for 42-44 consecutive days. The residue intake level based on feed consumption was not reported; therefore, the exact relationship between the dosing levels and dietary burden could not be determined. However, based on a nominal feed intake of 20 kg/animal/day, these doses are equivalent to 0.40, 2.6, 8.0, and 26.5 ppm, respectively. The maximum dose tested thus appears to be 1.6X the MTDB. Cows were milked twice daily, milk samples were composited, and samples collected on Days 14, 28, and 42 were separated into cream and skimmed milk. Cows were sacrificed within 16-24 hours of the final dose administration, and samples of muscle, liver, kidney and fat (subcutaneous and peritoneal) were collected. Samples were analyzed for residues of novaluron *per se* using the previously described GC/ECD method. The maximum residues of novaluron in milk and tissues are listed below in Table 7.

Table 7. Results of a Dairy Cattle Feeding Study with Novaluron.				
Matrix	Maximum Residue Levels (ppm) of Novaluron by Feeding Level*			
	7 mg ai/day	53 mg ai/day	159 mg ai/day	530 mg ai/day
Whole milk	0.06	0.17	0.43	2.07
Cream	1.12	3.06	7.66	20.90
Skimmed milk	<0.01	0.02	0.04	0.14
Muscle	0.05	0.09	0.34	0.56
Kidney	0.06	0.14	0.35	1.20
Liver	0.05	0.14	0.41	1.36
Subcutaneous Fat	0.43	1.24	4.36	8.21
Peritoneal Fat	0.56	2.25	6.83	12.89

*Based on a nominal feed intake of 20 kg/animal/day, these doses are equivalent to 0.40 (0.02X), 2.6 (0.15X), 8.0 (0.47X), and 26.5 ppm (1.6X), respectively.

Table 8. Tissue-To-Feed Ratios*	
Tissue	Ratio
Cattle muscle	0.0327
Cattle fat (Peritoneal)	0.621
Cattle liver	0.0521
Cattle kidney	0.0468
Whole Milk	0.0657

*Based on maximum residues of parent observed at the 3 highest dose levels.

The secondary residues in meat and milk are summarized below.

Table 9. Expected Secondary Residues in Meat and Milk		
Tissue	Residue (ppm)*	Recommended Tolerance
Cattle# Muscle	0.55	0.60
Cattle# Liver	0.88	1.0
Cattle# Kidney	0.79	1.0
Cattle# Fat	10.5	11
Milk	0.78	1.0
Milk Fat	19.5**	20
Hog Muscle	0.0029	0.01
Hog Liver	0.0047	0.01
Hog Kidney	0.0042	0.01
Hog Fat	0.040	0.05

* MTDB x Transfer Factor
** Milk residue x 25 (maximum concentration factor for milk fat)
# Cattle, goat, horse, sheep

The depuration portion of the study indicates that residues of novaluron generally decreased with cessation of dosing; however, quantifiable residues remained in milk and tissues collected up to 36 days following the last dose from the 53 and 530 mg ai/day dose levels.

Conclusions: The dairy cattle feeding study will be classified as scientifically acceptable pending recalculation and resubmission by the petitioner of the dosing levels used in the study. The residue intake level should be based on feed consumption and not in terms of mg ai/day. According to OPPTS 860.1480(f)(5), the level of the test materials in the total diet should be expressed in parts per million (mg/kg feed) (dry weight basis for ruminants). In addition, the petitioner is required to submit information pertaining to sample storage conditions and intervals. If sample integrity was maintained by appropriate storage and if samples were stored for less than

30 days, then no storage stability data are required. However, if samples were stored for more than 30 days, then data are required depicting the frozen storage stability of novaluron residues in livestock milk and tissues.

When the requested data and information has been submitted, HED will reassess the adequacy of the recommended livestock commodity tolerances.

Poultry feeding study waiver

The petitioner has requested a waiver for the conduct of a poultry feeding study. Based on the maximum residues observed in the poultry metabolism study conducted at a feeding level of 12 ppm (100X), quantifiable residues would be expected in a feeding study. HED thus requests that the petitioner submits a poultry feeding study. Until these data are available, HED recommends that the results of the poultry metabolism study be used to determine the appropriate tolerances for poultry commodities. The following tolerances are based on the levels of novaluron in the poultry metabolism study normalized to 1x and then multiplied by a factor of 10x to account for the longer duration of a feeding study:

Poultry, meat . . . . . 0.03 ppm
Poultry, mbyp . . . . . 0.04 ppm
Poultry, fat . . . . . 0.40 ppm
Eggs . . . . . 0.05 ppm

860.1500 Crop Field Trials

Pome Fruit

45638420.der.wpd (also includes review of MRID 45785804)

Table 10. Summary of Residue Data from Pome Fruit Field Trials with Novaluron.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Type of spray	Analyte	Residue Levels (ppm)					
					n	Min.	Max.	HAFT[1]	Mean	Std. Dev.
Proposed use: Maximum seasonal rate = 0.96 lb ai/A; 14-day PHI										
U.S. trials										
Apple	1.998-2.048	13/14	concentrate	novaluron	24	0.195	1.15	1.06	0.594	0.235
	2.007-2.010; (2.709)[2]	14	dilute	novaluron	8	0.242	0.557	0.522	0.408	0.100
Pear	1.983-2.020	14	concentrate	novaluron	12	0.177	1.66	1.34	0.578	0.406
	2.007-2.011	14	dilute	novaluron	4	0.424	0.807	0.785	0.606	0.208
Canadian trials										
Apple	1.995-2.077	14/15	concentrate	novaluron	12	0.260	0.960	0.955	0.660	0.240
Pear	1.996-2.039	14	concentrate	novaluron	8	0.726	1.95	1.79	1.33	0.438

[1] HAFT = Highest Average Field Trial.
[2] One trial received a higher rate for one application because of a mixing error; residues from this trial were within the residue range of the other (nominal rate) trials.

MANA has submitted data depicting the magnitude of the residue of novaluron in/on apples and pears, which are the representative commodities of the Pome Fruit Group (Crop Group 11). A total of 28 trials (18 apple and 10 pear) were conducted in the U.S. and Canada during the 2001 growing season. The U.S. apple trials were conducted in Regions 1 (NY and PA; 3 trials), 2 (VA; 1 trial), 5 (IL; 1 trial), 5A (MI; 1 trial), 9 (UT; 1 trial), 10 (CA; 1 trial), and 11 (OR and WA; 4 trials). The Canadian apple trials were conducted in Regions 1A (NS; 1 trial), 5A (ON; 2 trials), and 5B (QC; 3 trials). The U.S. pear trials were conducted in Regions 1 (PA; 1 trial), 10 (CA; 2 trials), and 11 (OR and WA; 3 trials) and the Canadian pear trials were conducted in Regions 1A (NS; 1 trial) and 5A (ON; 3 trials).

Samples of apples and pears were harvested 13-15 days following the last of six broadcast foliar spray applications of a 6.7% and/or 7.5% WDG formulation of novaluron at ~0.34 lb ai/A/application, for a total rate of ~2 lb ai/A (2.1x the maximum proposed seasonal rate). Applications were made as concentrate sprays (44.6-55.3 gal/A of water); however, separate plots in 4 apple trials and 2 pear trials received dilute spray volumes (362.8-410.9 gal/A of water). In two trials (WA2, apple and OR3, pear), samples of apples and pears were collected at 0, 3, 7, 14, and 28 days following the last application to evaluate residue decline.

The collected samples were analyzed by an adequate GC/ECD data-collection method described in the 860.1340 Residue Analytical Methods section of this document. The storage conditions and intervals of samples are supported by adequate storage stability data. The results of the residue trials are presented in Table 10. It is noted that novaluron residues are higher in pome fruit that received concentrate spray volumes than those treated with dilute spray volumes. Based on the results of the decline study, it appears that novaluron generally decreased slightly with increased sampling intervals. Average novaluron residues declined in/on apples from 0.9395 ppm at Day-0 to 0.594 ppm at Day-14, and increased to 0.746 ppm at Day-28. Average novaluron residues declined in/on pears with each sampling interval, from 0.743 ppm at Day-0 to 0.278 ppm at Day-28.

Conclusions: In these trials, the test formulation was applied at an exaggerated rate of 2.0 lb ai/A (2.1x the maximum proposed seasonal rate). However, the rate per application was ~0.34 lb ai/A (~1x) and the exaggerated total rate was the result of 3 early-season applications. As the majority of the residues at harvest would result from the late-season applications, HED concludes that these data support the proposed use. The number and geographical location of the field trials were adequate and support the proposed tolerance level of 2.0 ppm for pome fruit.

Cotton

45638412.der.wpd

Table 11. Summary of Residue Data from Cotton Field Trials with Novaluron.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	Min.	Max.	HAFT [1]	Mean	Std. Dev.
Proposed use: Maximum seasonal rate = 0.27 lb ai/A; 30-day PHI									
Cottonseed	0.372-0.384	29-32	novaluron	24	<0.05	0.484	0.401	0.115 [2]	0.129 [2]
Cotton gin byproducts (picker varieties)	0.372-0.380	29-30	novaluron	8	3.46	28.3	26.7	15.3	9.56
Cotton gin byproducts (stripper varieties)	0.375-0.382	30-32	novaluron	6	2.83	12.1	11.4	7.29	3.62

[1] HAFT = Highest Average Field Trial.
[2] The study reviewer calculated the mean and standard deviation using ½ the LOQ (<0.025 ppm) for all residues reported below the LOQ.

MANA has submitted data depicting the magnitude of the residue of novaluron in/on undelinted cottonseed and cotton gin byproducts. In 12 cotton field trials conducted in Regions 2 (GA; 1 trial), 4 (AR, LA, and MS; 3 trials), 6 (OK and TX; 2 trials), 8 (TX; 3 trials), and 10 (AZ and CA; 3 trials), mature cotton was harvested 29-32 days following the last of five broadcast foliar applications of the 0.83 lb/gal EC formulation for a total rate of ~0.377 lb ai/A (1.4x the maximum proposed seasonal rate). The first two applications were made early season (3-4 weeks after crop emergence and 14 days later) at ~0.052 lb ai/A/application, and the last three applications were made late season at ~0.091 lb ai/A/application.

Samples of undelinted cottonseed were collected from all 12 field sites. Samples of cotton gin byproducts were collected from 7 trial sites including 4 sites of picker cotton harvested by hand or using picker equipment, and 3 sites of stripper cotton harvested by hand or using stripper equipment. In one cotton field trial, additional samples of cottonseed and gin byproducts were collected at 0, 7, 14, and 45 days following the last application to evaluate residue decline.

Residues of novaluron in cottonseed and cotton gin byproducts were quantitated using an acceptable HPLC/UV method described in the 860.1340 Residue Analytical Methods section of this document. The maximum storage intervals of crop samples from harvest to analysis were 114 days (3.8 months) for undelinted cottonseed and 161 days (5.3 months) for cotton gin byproducts. The stability of novaluron residues in/on frozen cottonseed and gin byproducts has been demonstrated for up to 5 months (46141001.der).

The maximum residues of novaluron were 0.484 ppm in/on treated undelinted cottonseed samples and 28.3 ppm in/on treated cotton gin byproducts; see Table 11. Residues of novaluron were 3.46-28.3 ppm in/on treated gin byproducts from picker varieties of cotton and 2.83-12.1 ppm in/on treated gin byproducts from stripper varieties of cotton, indicating that residues were generally higher (>2x) from picker varieties of cotton.

Although residues decreased from the 0-day PHI to the 45-day PHI in cottonseed and gin byproduct samples from the residue decline study, a trend could not be determined because

residues were variable in/on treated samples at various sampling intervals. For undelinted cottonseed, the maximum average novaluron residue (0.287 ppm) was observed at the 14-day posttreatment interval and declined to 0.094 ppm at the 45-day PHI. For cotton gin byproducts, the maximum average novaluron residue (9.02 ppm) was observed at the 0-day posttreatment interval and declined to 1.39 ppm at the 45-day PHI.

Conclusions: In these trials, the test formulation was applied at an exaggerated rate of 0.377 lb ai/A (1.4x the maximum proposed seasonal rate). However, the rate per application was ~0.09 lb ai/A (~1x) and the exaggerated total rate was the result of 2 early-season applications. As the majority of the residues at harvest would result from the late-season applications, HED concludes that these data support the proposed use. The number and geographical location of the field trials were adequate and support the proposed tolerance levels of 0.6 and 30.0 ppm for cottonseed and cotton gin byproducts, respectively.

Potato

45771802.der.wpd

Table 12. Summary of Residue Data from European Potato Field Trials with Novaluron.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm) [1]					
				n	Min.	Max.	HAFT [2]	Mean	Std. Dev.
Proposed use: Maximum seasonal rate = 0.27 lb ai/A; 30-day PHI									
Potato tuber	0.044-0.048	21/22	novaluron	14	<0.01	<0.01	<0.01	0.005	0.0

[1] For the calculation of minimum, maximum, and HAFT values, the LOQ value (<0.01 ppm) was used for residues reported between the LOQ and LOD and as nondetectable (ND). For calculation of the mean and standard deviation, ½ the LOQ (0.005 ppm) was used for residues reported as ND or below half the LOQ. For the decline trials, residue data from the normal harvest interval only were included in the summary calculations.
[2] HAFT = Highest Average Field Trial.

MANA has submitted data depicting the magnitude of the residue of novaluron in/on potatoes grown in Europe. A total of 14 potato field trials was conducted during the 2000 growing season in Germany (4 trials), Northern France (3 trials), Southern France (2 trials), Spain (3 trials), and Italy (2 trials). Potato tubers were harvested 21 or 22 days following the last of two foliar broadcast spray applications of a 0.83 lb/gal EC formulation at ~0.023 lb ai/A/application, for a total rate of ~0.046 lb ai/A (0.2x the maximum proposed seasonal rate). In four trials, samples of potato tubers were collected at 0 and 21 days following the last application to evaluate residue decline.

Residues of novaluron in/on potato tubers were quantitated using the GC/ECD method described in the 860.1340 Residue Analytical Methods section of this document. The validated method LOQ is 0.01 ppm, and the reported LOD is 0.002 ppm. This method is adequate for data collection based on acceptable concurrent method recovery data. The maximum freezer storage interval of crop samples, from harvest to analysis, was 210 days (6.9 months) for potato tubers. The stability of novaluron residues in/on frozen potatoes has been demonstrated for up to 12 months (46086207.der).

Residues of novaluron were less than the method LOQ (<0.01 ppm) in/on all treated potato tuber samples; see Table 12. All samples collected from the residue decline trials also bore residues below the LOQ.

45771801.der.wpd

Table 13. Summary of Residue Data from European Potato Decline Trials with Novaluron.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm) [1]					
				n	Min.	Max.	HAFT [2]	Mean	Std. Dev.
Proposed use: Maximum seasonal rate = 0.23 lb ai/A; 30-day PHI									
Potato tuber	0.046-0.051	0	novaluron	4	<0.01	<0.01	<0.01	0.0050	0.0
		3		4	<0.01	<0.01	<0.01	0.0051	0.0001
		7		4	<0.01	<0.01	<0.01	0.0056	0.0011
		14		4	<0.01	<0.01	<0.01	0.0050	0.0
		21		4	<0.01	<0.01	<0.01	0.0053	0.0004

[1] For the calculation of minimum, maximum, and HAFT values, the LOQ value (<0.01 ppm) was used for residues reported between the LOQ and LOD and as nondetectable (ND). For calculation of the mean and standard deviation, ½ the LOQ (0.005 ppm) was used for residues reported as ND or below half the LOQ.
[2] HAFT = Highest Average Field Trial.

MANA has submitted residue decline data on potatoes with novaluron. Four decline trials were conducted in Spain (1 trial), Italy (1 trial), and Germany (2 trials). Potato tubers were harvested 0, 3, 7, 14, and 21 days following the last of two foliar broadcast spray applications of the 0.83 lb/gal EC formulation at ~0.023 lb ai/A/application, for a total rate of ~0.046 lb ai/A (0.2x the maximum proposed seasonal rate). Applications were made at BBCH growth stages 69-95 with a retreatment interval of 14 days.

Residues of novaluron in/on potato tubers were quantitated using the GC/ECD method described in the 860.1340 Residue Analytical Methods section of this document. The validated method LOQ is 0.01 ppm, and the reported LOD is 0.002 ppm. This method is adequate for data collection based on acceptable concurrent method recovery data. The maximum freezer storage interval of crop samples, from harvest to analysis, was 130 days (4.3 months) for potato tubers. The stability of novaluron residues in/on frozen potatoes has been demonstrated for up to 12 months (46086207.der).

Residues of novaluron were less than the method LOQ (<0.01 ppm) in/on all treated potato tuber samples harvested at each sampling interval; see Table 13. No conclusions regarding residue decline could be made because residues of novaluron were below the LOQ in all potato tuber samples from the decline study.

46082701.der.wpd

TABLE 14. Summary of Residue Data from U.S. Potato Field Trials with Novaluron.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)					
				n	Min.	Max.	HAFT	Mean	Std. Dev.
Potato tuber	0.509-0.516	7	novaluron	4	<0.05	<0.05	<0.05	<0.05	-

In 2 potato field trials conducted in Regions 1 (PA) and 11 (OR), mature tubers were harvested 7 days following the last of 2 broadcast foliar applications of the 0.83 lb/gal emulsifiable-concentrate (EC) formulation at 0.255-0.261 lb ai/A/application (~3X) for a total rate of ~0.50 lb ai/A (~2X) with a retreatment interval of 14 days.

Residues of novaluron in/on potato tubers were quantitated using a GC/ECD method. The validated LOQ is 0.05 ppm. This method is adequate for data collection based on acceptable concurrent method recovery data. The maximum storage interval of crop samples from harvest to analysis was 189 days (6 months) for potato tubers. The stability of novaluron residues in/on frozen potatoes has been demonstrated for up to 12 months (46086207.der).

Residues of novaluron were less than the method LOQ (<0.05 ppm) in/on all treated potato tuber samples. Examination of the submitted chromatograms showed apparent novaluron residues of ~0.01 ppm in both control and treated samples.

Conclusions: MANA has submitted a total of 20 field trials depicting the magnitude of the residue of novaluron in/on potatoes. However, 18 of these trials were conducted in Europe using a total rate of ~0.046 lb ai/A (0.2x the maximum proposed seasonal rate). In the U.S. trials conducted at ~0.50 lb ai/A (~2X), apparent novaluron residues of ~0.01 ppm were observed in both control and treated samples. HED concludes that the available data are adequate to conclude that novaluron residues will not exceed 0.05 ppm in potatoes for the following reasons: 1) plant metabolism studies indicate novaluron, when foliarly applied, is not readily translocated to potato tubers (TRR <0.001 ppm); 2) in the European trials, residues were <0.01 ppm, indicating that residues would have been <0.05 ppm at a 1X treatment rate; and 3) the PHI in the U.S. exaggerated-rate trials was 7 days compared to 30 days on the novaluron label. As potatoes are the representative crop of Tuberous and Corm Vegetables (Crop Group 1C), a tolerance of 0.05 ppm is appropriate for "Vegetables, tuberous and corm, subgroup 1C."

860.1520 Processed Food and Feed

Apple

45638420.de2.wpd

MANA has submitted an apple processing study. Residues of novaluron were 0.4050 ppm in/on apple fruit (RAC) from one trial conducted in Ephrata, WA and harvested 14 days following the last of six broadcast foliar spray applications of the 6.7% WDG formulation at 0.334-0.337 lb ai/A/application, for a total seasonal rate of 2.011 lb ai/A (2.1x the maximum proposed seasonal rate). The collected apples were processed into juice and wet pomace within 5 days of harvest using simulated commercial processing procedures.

The processing data for apple juice and wet pomace indicate that residues of novaluron concentrate in wet apple pomace (7.2x processing factor) but do not concentrate in apple juice (0.1x processing factor) processed from apples bearing detectable residues of novaluron.

The maximum theoretical concentration factors for apples and apple pomace listed in Tables 1 and 4 of OPPTS 860.1520 are >14x and 14x, respectively, and are experimental factors (based on comparison of proposed/established feed additive tolerances with proposed/established RAC tolerances). The reported concentration factors do not exceed the theoretical concentration factors.

Samples of apple and its processed commodities (juice and wet pomace) were analyzed for residues of novaluron using the GC/ECD method described in the 860.1340 Residue Analytical Methods section of this document. The method LOQ was 0.05 ppm each for apple, juice, and wet pomace. This method is adequate for data collection based on acceptable concurrent method recovery data. The storage conditions and intervals of processed samples are supported by adequate storage stability data.

Conclusions: The apple processing data are acceptable. They indicate that residues of novaluron concentrate in wet apple pomace (7.2x processing factor) but not in apple juice (0.1x processing factor) processed from apples bearing detectable residues of novaluron. These data suggest that a tolerance is needed for wet apple pomace but not for apple juice.

The maximum expected residue in wet apple pomace, resulting from the above use pattern is:

1.06 ppm (HAFT) x 7.2 (processing factor) = 7.65 ppm

Based on this calculation, the proposed tolerance of 3.0 ppm for apple pomace is inadequate and that a tolerance value of 8.0 ppm is appropriate.

Cotton

45638412.de2.wpd

MANA has submitted a cotton processing study. In one trial conducted in LA, mature cottonseed was harvested mechanically (commercial cotton picker) 29 days following the last of five broadcast foliar spray applications of the 0.83 lb/gal EC formulation at either the field trial nominal rate or an exaggerated rate, for a total of 0.376 lb ai/A or 1.893 lb ai/A, respectively (1.4x or 7.0x the maximum proposed seasonal rate, respectively). Residues of novaluron were <0.05 ppm in/on the undelinted cottonseed field RAC samples and 0.081 ppm in/on the undelinted cottonseed (RAC) from the processor treated at the 0.376 lb ai/A rate. Residues of novaluron were <0.05 and 0.061 ppm in/on the undelinted cottonseed RAC field samples and <0.05 ppm in/on the undelinted cottonseed RAC from the processor treated at the exaggerated rate (1.893 lb ai/A). Undelinted cottonseed from both treatment plots was processed into meal, hulls, and oil within 13-15 days of harvest using simulated commercial processing procedures.

Residues of novaluron were below the method LOQ (<0.05 ppm) in all processed cotton commodity samples. The processing data reflecting the nominal application rate of the cotton field trials (0.376 lb ai/A) indicate that residues of novaluron reduced (0.6x) in cotton meal, hulls, and refined oil. The processing data reflecting the exaggerated application rate (1.893 lb ai/A; 5x the nominal field trial rate) indicate that residues of novaluron do not appear to concentrate in cotton meal, hulls, and refined oil. An accurate processing factor could not be

determined because the residue was less than the method LOQ in both the RAC and processed commodities from the exaggerated rate study. The theoretical concentration factors are 3.8x for cotton seed hulls, 2.2x for cotton seed meal, and 6.3x for cotton seed oil (OPPTS 860.1520, Table 3).

Residues of novaluron in/on undelinted cottonseed and cotton processed commodities were quantitated using the HPLC/UV method described in the 860.1340 Residue Analytical Methods section of this document. The method LOQ was 0.05 ppm for undelinted cottonseed, hulls, meal, and refined oil. This method is adequate for data collection based on acceptable concurrent method recovery data. The maximum storage intervals of processing study samples, from collection to analysis, were 110 days (3.6 months) for cottonseed and 95-105 days (3.1-3.5 months) for cotton processed commodities. No storage stability data are available for cotton processed commodities.

Conclusions: Pending submission of supporting storage stability data, the submitted cotton processing study is deemed acceptable. The processing data indicate that residues of novaluron do not appear to concentrate in cotton meal, hulls, and refined oil. Based on the results of the reviewed processing study, tolerances for cotton meal, hulls, and refined oil are not needed.

Potato

A potato processing study was not submitted as part of this petition request. In the U.S. trials conducted at ~0.50 lb ai/A (~2X), apparent novaluron residues of ~0.01 ppm were observed in both control and treated samples. As the theoretical maximum concentration factor is 5X for potatoes (OPPTS 860.1520, Table 1), residues in potato processed commodities are not expected to exceed 0.05 ppm. A potato processing study is thus not required for this petition.

860.1850 Confined Accumulation in Rotational Crops

45638312.der.wpd

MANA has submitted a confined rotational crop study with novaluron. The radiolabeled test substance, [chlorophenyl-^{14}C(U)]novaluron, was applied once directly to sandy loam soil placed in plastic containers at a nominal rate of ~0.089 lb ai/A (100 g ai/ha). The application rate of 0.089 lb ai/A is equivalent to 0.3x the maximum proposed seasonal rate of 0.27 lb ai/A for cotton and potatoes. Rotational crops consisting of spinach, turnip, and spring wheat were planted in the treated soil 30 days after treatment (DAT) and then maintained in an environmentally controlled room until maturity. At appropriate intervals, immature and mature commodity samples were collected from each crop for determination of the TRR. TRR did not accumulate at ≥0.005 ppm in any of the rotated crop commodities planted in treated soil. No further extraction or analysis of any rotated crop samples was performed because of the low TRR levels. The in-life and analytical phases of the study were conducted by Huntingdon Life Sciences (Cambridgeshire, England).

No storage stability data are required to support the storage conditions of the rotated crop samples because the final harvest crop samples were stored for a maximum of <6 months from collection to TRR analysis.

Conclusions: In the submitted confined rotational crop study, the test substance was applied at only 0.3x the maximum proposed seasonal rate for rotatable crops (cotton and potato). HED generally requires that the confined rotational crop study be conducted at 1.0x the proposed maximum seasonal rate for annual crops (or crops which can be rotated). However, as the TRR was <0.005 ppm in all of the rotated crop commodities, it is unlikely that significant residues would be present at 1x. HED thus concludes that the results of this study are applicable to the current petition.

The submitted confined rotational crop study is adequate to satisfy the confined rotational crop data requirements. MARC concluded that for tolerance assessment and risk assessment, parent only is the residues of concern. A confined rotational crop study conducted with [difluorophenyl-^{14}C(U)]novaluron will not be required as the difluorophenyl-derived metabolites are expected to be significantly less toxic than the chlorophenyl metabolites. However, future uses that have significantly higher application rates will require confined rotational crop studies at higher rates using chlorophenyl-labeled novaluron.

As the TRR may exceed 0.01 ppm at a 1X rate, the appropriate PBI for all non-labeled crops is 30 days. The petitioner should thus submit a revised Section B indicating that only registered crops may be rotated to a treated field within 30 days of the final application.

860.1900 Field Accumulation in Rotational Crops

No field accumulation data in rotational crops were submitted as part of this petition request. Provided the petitioner submits a revised Section B indicating that only registered crops may be rotated to a treated field within 30 days of the final application, a field accumulation study will not be required for this petition.

860.1550 Proposed Tolerances

The HED MARC has determined that the proposed tolerance expression, which is in terms of novaluron *per se*, is appropriate. Table 15 lists the tolerance summary for novaluron.

Table 15. Tolerance Summary for Novaluron (*N*-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy) ethoxy]phenyl]amino]carbonyl]-2,6-difluorobenzamide)

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments (correct commodity definition)
Pome Fruit	2.0	2.0	Fruit, pome, group 11
Apple Pomace	3.0	8.0	Apple, wet pomace
Cottonseed	0.6	0.60	Cotton, undelinted seed
Cotton Gin By-products	30	30	Cotton, gin byproducts
Tuberous and Corm Vegetables	0.05	0.05	Vegetables, tuberous and corm, subgroup 1C
Cattle, meat	0.4	0.60	Sheep, meat; Horse, meat; Cattle, meat; Goat, meat
Cattle, mbyp	7.0	0.60	Sheep, meat byproducts, except liver and kidney; Horse, meat byproducts, except liver and kidney; Cattle, meat byproducts, except liver and kidney; Goat, meat byproducts except liver and kidney
Cattle, fat	7.0	11	Sheep, fat; Horse, fat; Cattle, fat; Goat, fat
Cattle, liver	0.5	1.0	Sheep, liver; Horse, liver; Cattle, liver; Goat, liver
Cattle, kidney	0.5	1.0	Sheep, kidney; Horse, kidney; Cattle, kidney; Goat, kidney
Milk	0.5	1.0	
Milk, fat	-	20	
Hog, meat		0.01	
Hog, meat byproducts		0.01	
Hog, fat		0.05	
Poultry, meat	-	0.03	
Poultry, meat byproducts	-	0.04	
Poultry, fat	-	0.40	
Eggs	-	0.05	

There are currently no established Codex, Canadian, or Mexican maximum residue limits (MRLs) for novaluron. An International Residue Limits Status (IRLS) sheet is appended to this document.

860.1650 Submittal of Analytical Reference Standards

An analytical reference standard for novaluron is available at the EPA National Pesticide Standards Repository (Source: 8/28/03 e-mail correspondence between T. Cowen of Dynamac and P. Schermerhorn of EPA).

References

45638226.der.wpd	860.1300 Nature of the Residue (Apples)
45638227.der.wpd	860.1300 Nature of the Residue (Cabbage)
45638302.der.wpd	860.1300 Nature of the Residue (Cotton)
45638301.der.wpd	860.1300 Nature of the Residue (Potato)
45638303.der.wpd	860.1300 Nature of the Residue (Ruminants)
46185801.der.wpd	860.1300 Nature of the Residue (Poultry)
45638304.der.wpd	860.1340 Residue Analytical Methods (Crops)
45638307.der.wpd	860.1340 Residue Analytical Methods (Livestock)
45638308.der.wpd	860.1340 Residue Analytical Methods (Livestock)
45789202.der.wpd	860.1360 Multiresidue Methods
46141001.der.wpd	860.1380 Storage Stability (Crops)
46086207.der.wpd	860.1380 Storage Stability (Crops)
46086208.der.wpd	860.1380 Storage Stability (Crops)
45785804.der.wpd	860.1380 Storage Stability (Crops)
45638311.der.wpd	860.1480 Meat, Milk, Poultry, and Eggs (Ruminants)
45638420.der.wpd	860.1500 Crop Field Trials (Pome Fruit)
46086206.der.wpd	860.1500 Crop Field Trials (Pome Fruit)
45638412.der.wpd	860.1500 Crop Field Trials (Cotton)
46086205.der.wpd	860.1500 Crop Field Trials (Cotton)
45771802.der.wpd	860.1500 Crop Field Trials (Potato)
45771801.der.wpd	860.1500 Crop Field Trials (Potato)
46082701.der.wpd	860.1500 Crop Field Trials (Potato)
45638420.de2.wpd	860.1520 Processed Food and Feed (Apple)
45638412.de2.wpd	860.1520 Processed Food and Feed (Cotton)
45638312.der.wpd	860.1850 Confined Accumulation in Rotational Crops

Attachment: International Residue Limit Status Sheet (IRLS)

DOCUMENT TRACKING

cc: G. Kramer
RDI: P.V. Shah (1/28/04), RAB1 Chemists (1/28/04), ChemSAC (2/4/04)
G.F. Kramer:806T:CM#2:(703)305-5079:7509C:RAB1
Petition Number: PP#2F06430
DP Barcodes: D285474
PC Code: 124002
Template Version April 2003

INTERNATIONAL RESIDUE LIMIT STATUS

Chemical Name:	Common Name:	☒ Proposed tolerance ☐ Reevaluated tolerance ☐ Other	Date:
1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy) phenyl]-3-[2,6-diflurobenzoyl]urea	Novaluron		1/12/04

Codex Status (Maximum Residue Limits)	U. S. Tolerances
☐ No Codex proposal step 6 or above X No Codex proposal step 6 or above for the crops requested	Petition Number: 2F6430 DP #: 297646 Other Identifier:
Residue definition: N/A	Reviewer/Branch: G.F. Kramer
	Residue definition: parent only

Crop (s)	MRL (mg/kg)	Crop(s)	Tolerance (ppm)
		Pome Fruits	2.0
		Apple Pomace	3.0
		Cottonseed	0.6
		Cotton Gin By-Products	30
		Tuberous and Corm Vegetables	0.05
		Cattle, meat	0.4
		Cattle, mbyp	7.0
		Cattle, fat	7.0
		Cattle, liver	0.5
		Cattle, kidney	0.5
		Milk	0.5

Limits for Canada	Limits for Mexico
X No Limits ☐ No Limits for the crops requested	X No Limits ☐ No Limits for the crops requested
Residue definition: N/A	Residue definition: N/A

Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)

Notes/Special Instructions:.S.Funk,01/13/04.

Rev. 1998

U. S. ENVIRONMENTAL PROTECTION AGENCY
Washington, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

016

Date: February 29, 2004
Chemical: Novaluron
PC Code: 124002
DP Barcode: D285477
D285479
D287624
D285479
D297230

MEMORANDUM

SUBJECT: **Environmental Fate and Effects Division Risk Assessment for the Section 3 Registration of Novaluron on Pome Fruit, Cotton, and Potatoes.**

TO: Dan Kenny, Chemical Review Manager
Reregistration Branch II
Special Review and Reregistration Division (7508C)

FROM: William Evans, Biologist
Iwona Maher, Chemist
James Hetrick, Ph D., Senior Environmental Scientist
Edward Odenkirchen, Ph.D., Senior Biologist
Environmental Risk Branch I
Environmental Fate and Effects Division (7507C)

APPROVED BY: Sid Abel, Branch Chief
Environmental Risk Branch I
Environmental Fate and Effects Division (7507C)

This memo summarizes the attached Environmental Fate and Effects Division's (EFED) Novaluron Environmental Risk Assessment for a proposed Section 3 new use on pome fruit, cotton, and potatoes. Novaluron is an insect growth regulating insecticide in the benzoylphenyl urea family which acts on the pest larval stage by inhibiting chitin biosynthesis and blocks the cuticle formation in target pests. It is currently registered for ornamental use in greenhouse and shadehouses.

Novaluron is a chiral compound containing a racemic mixture of two enantiomers (R,S). The available environmental fate and ecological effects data on novaluron represents only the racemic mixture. Additional data on individual enantiomers may be required if the registrant chooses to develop isomeric enriched products of novaluron.

Novaluron is immobile and non-persistent in soil laboratory studies. However, it appears to be more persistent in some field studies under actual use conditions. Novaluron persistence in field soils may be partially explained by temperature effects on metabolism; greater persistence is found in cooler climates. Metabolites of novularon with human-health toxicological concern are chlorophenyl urea (1-[3-chloro-4-(1,1,2-trifluoro-2-trifluroromethoxyethyoxy) phenyl] urea) and chloroaniline (3-chloro-4-(1,1,2-trifluro-trifluroromethoxyethoxy)aniline). Because novaluron can be aerially and ground spray applied as well as exhibits high soil:water partitioning coefficients, novaluron movement from the application site is expected to depend on runoff of entrained sediments and spray drift. Exposure from the use of novaluron on pome fruit, cotton, and potatoes is expected to affect a variety of aquatic and terrestrial ecosystems throughout the south, northwest, and northeast regions as well as the cotton growing regions of California.

Available laboratory toxicology data indicate that novaluron is highly toxic to freshwater and marine invertebrates. A consideration of these data leads EFED to conclude that the potential risk to aquatic systems is likely to be extremely high for freshwater and marine invertebrates, and it will be very difficult to mitigate risks below levels of concern (LOC). However, due to the lack of acute freshwater invertebrate data on the parent, there is some uncertainty with the conclusions on acute risk to freshwater invertebrates. These aquatic invertebrates play a critical role as an important food source in aquatic ecosystems. Prolonged exposure from novaluron could indirectly impact the fish growth, reproduction, and abundance in areas where novaluron is used.

Chronic risk to marine fish remains somewhat uncertain to due a lack of adequate definitive acute and chronic data. There appear not to be acute or chronic risk resulting from applications to any of the use sites for freshwater fish, however, there is some uncertainty concerning acute risk since a definitive LC_{50} could not be determined.

The only data submitted for the major degradate, chlorophenyl urea (275 352 I) was an acute freshwater fish and invertebrate study which indicated that the risk quotients were well below all acute levels of concern. Since no marine fish invertebrate data was submitted on the degradate, there is some uncertainty about the risk to these organisms.

Since novaluron and its degradate have a tendency to strongly adsorb to soil and sediment, sediment testing, as described in EPA protocols, is recommended in order to evaluate risks to sediment dwelling organisms from novaluron.

Although acute risks to birds and mammals did not exceed levels of concern, chronic risk quotients for birds ranged from 19.5 on short grass to 2.9 to 0.3 on fruit, pods, seeds, and large

insects. To further investigate the chronic avian risk for birds, EFED evaluated the impact of foliar dissipation half-lives of 1, 5 and 35 days (default) on novaluron residues concentrations and its impact on reducing risk as well as predicted maximum and mean residues for single applications. Although risk quotients were reduced, in most cases the risk quotients were still above the chronic levels of concern.

Proposed banded applications to cotton only exceeded levels of concern for endangered species for 15 gram birds when the application rates were not adjusted for band width. If the rates were adjusted for band width, the acute risk resulting from banded applications could be effectively mitigated

Although data on honeybees classifies novaluron and Rimon 10EC as practically non-toxic to honey bees, additional non-target insect studies were submitted which demonstrated adverse effects on brood development at all growth stages and significant effects on wasp and predatory mite populations. These effects demonstrate that beneficial non-target insects may be at risk, at least immediately after spray applications. Due to the conflicting conclusions of the available data, risk to non-target beneficial insects is uncertain at this time.

Risk quotients for aquatic and terrestrial plants as well as earthworms did not trigger any acute level of concern. Further data analysis will not be required at this time.

Data Gaps

Environmental Fate: Fate data submitted for the novaluron degradate chlorophenyl urea (275-352I) was limited to the adsorption/desorption study. The degradate appears to have low to slight mobility in soil (K_{oc} values range from 1950 to 2563 L/kg; 163-1; MRID 45638201). It exhibits moderate persistence ($t_{1/2}$= 26 to 46 days) in terrestrial and aquatic environments.

No data was submitted for chloroaniline degradate. This degradate has the potential to be volatile (i.e., its estimated vapor pressure exceeds 10^{-4} mmHg), more mobile (K_{oc} (an estimated value) = 5899) and more persistent than the parent. If there are any toxicological concerns or/and human health affects associated with chloroaniline additional environmental fate data may be required. The submitted aerobic soil metabolism study and an anaerobic aquatic metabolism study lacked the formation and decline data for chloroaniline degradate. Additionally, the submission lacked any physico-chemical and fate data for this degradate.

Ecological Effects: The ecological toxicity data base is fairly complete, however, there are some key studies which need to be repeated to reduce the uncertainties in this risk assessment. In addition, sediment toxicity studies must also be performed. The details are summarized below.

- **Estuarine fish** - The submitted study with the parent novaluron was not tested at or above the limits of solubility (0.003 mg/L). The highest level tested was 0.002 mg/L and no effects were observed. The study does not provide an endpoint sufficient for

comparative purposes with other pesticides. However, it is unlikely that repeat of the study will generate an acute lethality endpoint consistent with screening risk assessment methods that would be at environmentally relevant concentrations. Repeat of the study would only serve the purpose of providing for toxicity endpoint that could be compared with other

- **Freshwater invertebrate** - Valid freshwater invertebrate data are lacking for the parent novaluron as well as the formulated product. Data on the technical should be submitted to better characterize the risk to freshwater invertebrates. If data are to be submitted on the formulated product it is highly recommended that measured concentrations be centrifuged to ensure a more accurate measurement of the active ingredient novaluron rather than the emulsifier(s) added to keep the product in suspension.

- **Sediment dwelling organisms** - Risk to sediment dwelling organisms can not be directly assessed using available screening level assessment techniques at this time because no single-species sediment toxicity data was submitted. Available environmental fate data (Koc = 6,680 - 11,813) on soil suggest that novaluron strongly adsorbs to soil and sediment. Furthermore, available microcosm data suggest that novaluron can significantly impair benthic invertebrates at environmentally relevant concentrations. Toxicity data that demonstrate the measured toxicity of the sediment and the surrounding interstitial water to invertebrate species would allow for the assessment of sediment invertebrate risks using screening-level techniques. To obtain this data, studies which follow the EPA protocols resulting from the direct spiking of the sediment, and in which pore (interstitial) water as well as sediment concentrations are measured, are warranted.

Suggested Label Language

For the management of spray drift EFED suggests the following label language statement to minimize the potential for surface water contamination for all non-granular end-use products:

"This product may contaminate water through drift of spray in wind. This product has a potential for runoff for several weeks after application. Poorly draining soils and soils with shallow watertables are more prone to produce runoff that contains this product. A level, well maintained vegetative buffer strip between areas to which this product is applied and surface water features such as ponds, streams, and springs will reduce the potential for contamination of water from rainfall-runoff (See manual at the following Internet address: http://www.nrcs.usda.gov/water/quality/common/pestmgt/files/core4.html). Runoff of this product will be reduced by avoiding applications when rainfall is forecasted to occur within 48 hours. Sound erosion control practices will reduce this products contribution to surface water contamination."

In addition, the following environmental hazard label language should be included in the

appropriate labels.

Manufacturing Use:

"This pesticide is toxic to fish and aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a 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 treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA. Do not contaminate water when disposing of equipment washwaters."

End Use Products:

"This pesticide may be toxic to fish and invertebrates. Do not apply directly to water, to areas where surface water is present, or to intertidal areas below the mean high water mark **except as noted on appropriate labels**. Drift and runoff may be hazardous to aquatic organisms in water adjacent to treated areas. Do not contaminate water when disposing of equipment wash waters or rinsate. Drift and runoff may be hazardous to aquatic organisms in water adjacent to treated areas. Do not contaminate water when disposing of equipment washwaters or rinsate."

Statement to minimize the potential for surface water contamination for all non-granular end-use products:

"This product may contaminate water through drift of spray in wind. This product has a potential for runoff for several days to weeks after application. Poorly draining soil with shallow water tables are more prone to produce runoff that contains this product. A level, well maintained vegetative (grass) buffer strip between areas to which this product is applied and the surface water features such as ponds, streams, and springs will reduce the potential for contamination of water from rainfall-runoff. Runoff of this product will be reduced by avoiding applications when rainfall is forecasted to occur within 48 hours. Sound erosion control practices will reduce this product's contribution to surface water contamination."

Environmental Fate and Effects Division's Risk Assessment for the Section 3 Use of Novaluron on Cotton, Pome Fruit and Potatoes

Table of Contents

I. Environmental Risk Conclusions 1
Environmental Fate and Risk Summary 1
Pesticide Chemistry and Environmental Fate 1
Aquatic Organism Risks of Concern 1
Terrestrial Vertebrate Risks of Concern 2
Terrestrial Invertebrate Risks of Concern 2
Drinking Water Summary 3

II. Introduction 3
Physical and Chemical Properties of the Pesticide 3
Pesticide Mode of Action 4
Proposed Uses and Use Characterization 4
Risk Assessment Approach 5
Assessment Chemicals of Concern 5
Assessment Endpoints 5
Measures of Effects 5
Measures of Exposure 7
Aquatic Organisms 7
Active Ingredient and Degradate Aquatic Organism Exposure Approach 7
Formulated Product Aquatic Organsim Exposure Approach 8
Terrestrial Animals 8
Risk Characterization Approach 8

III. Integrated Environmental Risk Characterization 8
Risks to Aquatic Organisms 8
Aquatic Invertebrates 9
Sediment-Dwelling Organisms 11
Fish 12
Aquatic Plants 13
Risk to Birds 13
Acute Risks - Birds 13
Chronic Risk - Birds 14
Risks to Mammals 15
Risks to Non-Target Insects 15
Risks to Terrestrial Plants 16
Endangered Species Assessment 16

IV. Environmental Fate Assessment 17

V. Drinking Water Assessment Summary 19
Surface Water Assessment 20
Ground Water Assessment 21

VI. Aquatic Hazard, Exposure, and Risk Quotient Calculation 21
Toxicity to Fish 21
Toxicity to Aquatic Invertebrates 23
Toxicity to Aquatic Plants 24
Community Effects Studies 24
Aquatic Exposure 25
Risk Quotients 29

VI. Terrestrial Hazard, Exposure, and Risk Quotient Calculation 29
Toxicity to Birds 29
Toxicity to Mammals 29
Toxicity to Non-target Insects 30
Toxicity to Earthworms 30
Toxicity to Non-target Plants 31
Exposure 31
Birds and Mammals 31
Risk Quotients 33

APPENDIX LIST

APPENDIX A: Detailed Drinking Water Assessment Memo 34
APPENDIX B: PRZM/EXAMS Input & Output Files for Ecological Assessment 53
APPENDIX C: Ecological Hazard Data 67
APPENDIX D: The Risk Quotient Method 79
APPENDIX E: Detailed Risk Quotients 82
APPENDIX F: Data Requirements for Novaluron 98

I. Environmental Risk Conclusions

Environmental Fate and Risk Summary

Pesticide Chemistry and Environmental Fate

The risk assessment is based on supplemental and acceptable environmental fate and ecological effects data. Novaluron is a chiral compound containing a racemic mixture of two enantiomers (R,S). The available environmental fate and ecological effects data on novaluron represents only the racemic mixture. Additional data on individual enantiomers may be required if the registrant chooses to develop isomeric enriched products of novaluron.

Novaluron is immobile and non-persistent in soil laboratory studies. However, it appears to be more persistent in some field studies under actual use conditions. Novaluron persistence in field soils may be partially explained by temperature effects on metabolism; greater persistence is found in cooler climates. Metabolites of novularon with human-health toxicological concern are chlorophenyl urea (1-[3-chloro-4-(1,1,2-trifluoro-2-trifluroromethoxyethyoxy) phenyl] urea) (termed chlorophenyl urea (275-352I)) in this risk assessment and chloroaniline (3-chloro-4-(1,1,2-trifluro-trifluroromethoxyethoxy)aniline). Because novaluron can be aerially and ground spray applied as well as exhibits high soil:water partitioning coefficients, novaluron movement from the application site is expected to depend on runoff of entrained sediments and spray drift.

Aquatic Organism Risks of Concern

Available laboratory toxicology data indicate that novaluron is highly toxic to freshwater and marine invertebrates. A comparison of these data with estimated levels of aquatic exposure leads EFED to conclude that there is a concern for the potential acute risks to freshwater and marine invertebrates for all crops considered in the risk assessment (cotton, pome fruits, and potatoes). The same conclusions have been reached for chronic risks to freshwater and estuarine/marine invertebrates. Furthermore, a comparison of formulated product toxicity data and formulated product concentrations in surface waters receiving spray drift indicates that short term exposures of formulated product may also be a risk concern for aquatic invertebrates.

Because of the potential for novaluron degradation and dissipation in aquatic systems, the risk assessment considered a number of averaging times for water concentration modeling purposes and compared the results of the exposure model output with long-term lethality testing results for aquatic invertebrates. This approach found that risk concerns for lethal effects in aquatic invertebrates were upheld regardless of the averaging time considered. Furthermore, available aquatic invertebrate microcosm studies, performed at environmentally relevant novaluron concentrations, show reductions in aquatic invertebrate populations, some of the taxa affected never recovered for weeks following initial pesticide exposure.

Aquatic invertebrates play a critical role as an important food source for aquatic vertebrates (eg. fish) in aquatic ecosystems. The observations of significant community disruptions in microcosm studies and the high magnitude of risk quotient results suggests that impacts to aquatic invertebrate communities may be of sufficient severity and at times of prolonged duration

to indirectly impact the fish growth, reproduction, and abundance in areas where novaluron is used. The proposed target crops pome fruit, cotton, and potatoes would suggest that novaluron has the potential for widespread use, though market considerations of novaluron use are not the subject of this risk assessment. As a consequence of the variety of geographical areas encompassed by these target crops, a variety of aquatic ecosystems can be expected to be at risk of novaluron exposure.

Novaluron physical chemical properties suggest that the compound has a tendency to adsorb to soil and sediment. The risk assessment considered the results of benthic invertebrate microcosm testing to evaluate the potential for adverse effects on such invertebrates. The microcosm data indicated that environmentally relevant novaluron concentrations, even below the level of detection, can produce severe and long-lasting impairment of populations of benthic invertebrates. Laboratory testing of novaluron effects on sediment organisms may be very useful for further quantifying the potential risk of the compound to benthic invertebrates.

Terrestrial Vertebrate Risks of Concern

Acute risks to birds and mammals did not exceed levels of concern. However, chronic risk quotients for birds ranged from 19.5 on short grass to 2.9 to 0.3 on fruit, pods, seeds, and large insects. To further evaluate the chronic avian LOC exceedance for birds, EFED evaluated the impact of various foliar dissipation half-lives of (1, 5 and 35 days (default)) on novaluron residue concentrations and their impact on risk conclusions Chronic avian LOCs are exceeded for all crops at all avian food sites (except the fruits, pods, seeds, and large insects site) regardless of the assumed foliar half-life. However, the chronic avian risk for tall grass forage site was reduced below the level of concern using a 1 day foliar half-life. The results of this analysis suggest that additional data on residue dissipation in avian food sources may not be significant to alter screening level assessment conclusions of potential avian chronic risk, but such data may be valuable should more species-specific assessments be conducted that would require consideration of specific dietary behaviors.

Chronic avian risk was also evaluated for single applications of novaluron and assumptions of maximum and mean residues. For maximum residue assumptions, risk quotients exceeding the chronic LOCs for all food categories except the fruit, pod, seed, and large insect category for maximum residues for all crops. Risk quotients ranged from 0.12 to 7.4. The chronic LOCs were exceeded for the short grass, tall grass, and broadleaf/forage plants and small insects categories only for pome fruit for mean residue assumptions. These risk quotients ranged from 1.2 to 2.3. The confidence in the chronic avian risk conclusion is buttressed by these findings.

Proposed banded applications of novaluron to cotton only exceeded levels of concern for endangered species for 15 gram birds when the application rates were not adjusted for band width. If the rates were adjusted for band width, the acute risk resulting from banded applications could be effectively mitigated

Terrestrial Invertebrate Risks of Concern

Available data for adult honeybees classifies novaluron (Rimon technical) and the formulated

product as practically non-toxic to honeybees. The LD_{50} for the technical novaluron was > 100 µg/bee while that of the Rimon 10EC formulated product was LD_{50} >200 µg/bee. EFED currently does not estimate risk quotients for terrestrial non-target insects, however when a LD_{50} is < 11 µg/bee an appropriate label statement is required to protect foraging honeybees. Additional non-target insect studies were submitted which demonstrated adverse effects on honey bee brood development at all growth stages and significant effects on wasp and predatory mite populations. These effects demonstrate that beneficial non-target insects may be at risk, at least immediately after spray applications.

Drinking Water Summary

Tier II PRZM/EMAXS modeling was performed for novaluron to estimate drinking water concentrations for the human health dietary risk assessment. Because of limited environmental fate data , a Tier I drinking water assessment was performed for novaluron degradates, 1-[3-Chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea (275-352I) and 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline (275-309I).

The most conservative estimates were obtained for airblast applications of novaluron to PA apples at the maximum annual application rate of 0.96 lb a.i./acre, applied three times at 0.32 lb a.i./acre with an interval between applications of ten days. The predicted 1 in 10 year annual peak concentrations of novaluron in surface source water was 11.4 µg/L. It is important to note the predicted peak exceeds the solubility of the compound (3 µg/L), which is likely to be an upper bound concentration in drinking water. The estimated 1 in 10 year annual mean concentration of novaluron in drinking water is 1.8 µg/L. The 30-year annual mean concentration is 1.2 µg/L. Both peak and annual average concentrations for all other scenarios were lower.

An estimated peak drinking water concentration in surface water sources is 4.6 µg/L for chlorophenyl urea and 11.4 µg/L for chloroaniline based on novaluron's maximum application rate of 0.32 lb ai/acre applied 3 times a season (0.96 lbs ai/year; apples). The estimated annual average concentration is 0.86 µg/L for chlorophenyl urea (275-352I) and 2.6 µg/L for chloroaniline.

II. Introduction

Novaluron is an insect growth regulating insecticide in the benzoylphenyl urea family which acts on the pest larval stage by inhibiting chitin biosynthesis and blocking the cuticle formation in target pests. It is currently registered for ornamental use in greenhouse and shadehouses. The current registration application is for a Section 3 use on pome fruit, cotton, and potatoes. Specific information about this proposed registration is presented below.

Physical and Chemical Properties of the Pesticide

Common name:	Novaluron
PC Code:	124002
IUPAC name:	1-[3-chloro-4-(1,1,2-trifluoro-methoxyethoxy)phenyl]-3-(2,6-

	difluorobenzoyl)urea	
CAS Name:	N-[[[3-Chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]-amino]carbonyl]-2,6-difluorobenzamide	
CAS Number:	116714-46-6	
Molecular formula:	$C_{17}H_9ClF_8N_2O_4$	
Molecular weight g/mole):	492.7	
Water Solubility:	0.003 mg/L @ 25 ^{0}C	(MRID 45638203)
Vapor pressure:	1.2 x 10^{-7} mm Hg	
Henry's Law Constant:	2.0 Pa m^3/mol^{-1}	
Log K_{ow}:	4.3	(MRID 45638405)

Chemical structure of Novaluron:

Pesticide Mode of Action

Novaluron is a benzoylphenyl urea insect growth regulating insecticide. Its larvacidal action results from the inhibition of chitin biosynthesis and interference in the cuticle formation in target pests. To be fully effective novaluron must be ingested by insect larvae. Rimon™ has no effect on adult insects that have completed all successive molts, and hence implies that the product could be used concurrently with insects released for biocontrol of plant pests. However, the label points out that the compatibility with such integrated pest management approaches has not been established.

Proposed Uses and Use Characterization

For food use, the registrant proposed two novaluron formulations: 7.5% water dispersible granule (RimOn 7.5WDG) insect growth regulator for control of insect pests on apples and pears and 10% emulsifiable concentrate (RimOn 10EC) insect growth regulator for use on cotton and potatoes. Application by chemigation is prohibited for all proposed uses.

The insecticide is applied to the foliage of apples and pears by conventional ground sprayer or airblast sprayer at increased pressure and high volume. According to the proposed label no more

than 0.96 lbs a.i. (RimOn 7.5WDG) may be applied per acre per season, with the maximum rate per application 0.32 lbs a.i., the minimum intervals of 10 to 14 days between applications, and up to 3 applications per season are allowed. No application should be made within 14 days of fruit harvest.

RimOn 10EC is applied to cotton via conventional ground or aerial sprayer, or via band application when cotton plants are small. The maximum proposed application rate is 0.27 lb a.i. (RimOn 10EC) per acre per season, with the maximum rate per application of 0.09 lbs a.i., a minimum interval of 7 to 14 days between applications, and up to 3 applications per season. No instructions were on the label concerning the band width and its corresponding application rate within the band or the width of the untreated areas between the rows. Therefore, an assumption of 6 inch bands with 30 inch row spacing was assumed for the purposes of this risk assessment. No application should be made within 30 days of cotton harvest.

RimOn 10EC is applied to potatoes by conventional ground spray or aerial equipment. The maximum proposed application rate is 0.23 lb ai/A per season, with the maximum rate for a single application rate of 0.078 lb ai/A. Up to three applications per season could be applied at intervals of 10 to 14 days between applications.

Risk Assessment Approach

Assessment Chemicals of Concern

The risk assessment considers aquatic and terrestrial risks for the active ingredient novaluron. In addition, the assessment considers risks posed to aquatic organisms from the chlorophenyl urea degradate (275-352I), and the formulated product Rimon 10EC.

Assessment Endpoints

The typical assessment endpoints for screening-level pesticide ecological risks are reduced survival and reproductive impairment for both aquatic and terrestrial animal species. These effects extend to a consideration of direct acute and direct chronic exposures. While these endpoints are measured at the individual level, they do provide insight about risks at higher levels of biological organization (e.g. populations).

Measures of Effects

The screening level risk assessment process relies on a suite of toxicity studies performed on a limited number of organisms in the following broad groupings:

- Birds (mallard duck and bobwhite quail) (see Toxicity to Birds section)
  - Acute and chronic data complete for this risk assessment
- Mammals (laboratory rat)(see Toxicity to Mammals section)
  - Acute and chronic data set complete for this risk assessment
- Freshwater fish (bluegill sunfish, rainbow trout, and fathead minnow)(see Toxicity to Fish section)

- Acute data set is available for novaluron, however the endpoints available are uncertain
- Acute data are available for formulated product, these data are incorporated into risk assessment through analysis of drift exposure risks
- Acute data are available for chlorophenyl urea degradate 275-352I
- Chronic freshwater fish data are available for novaluron

- Freshwater invertebrates (*Daphnia magna*)(see Toxicity to Aquatic Invertebrates section)
  - Acute data are not available for novaluron, extrapolations are made from other data
  - Acute data are available for formulated product
  - Chronic data set is available
  - Acute data are available for chlorophenyl urea degradate 275-352I
- Estuarine/marine fish (sheepshead minnow)(see Toxicity to Fish section)
  - Acute data are available for novaluron, however the endpoints available are uncertain
  - No chronic data were available
- Estuarine/marine invertebrates (*Crassostrea virginica* and *Mysidopsis bahia*)(see Toxicity to Aquatic Invertebrates section)
  - Acute data are available for novaluron and formulated product
  - Chronic data are available for novaluron
- Terrestrial plants (corn, soybean, carrot (radish or sugar beet), oat (wheat or ryegrass), tomato, onion, cabbage (cauliflower or brussels sprout), lettuce, cucumber)
  - No data were available, quantitative assessment of risks thus not performed
- Algae and aquatic plants
  - Data were available for green algae and aquatic vascular macrophytes for novaluron, formulated product, and chlorophenyl urea degradate 275-352I

Within each of these very broad taxonomic groups, an acute and chronic endpoint is selected from the available test data, as the data sets allow. The selection is made from the most sensitive species tested within that organism group.

Additional effects data were available for other taxa and for aquatic community effects measures. These have been incorporated into the risk characterization as other lines of evidence. These data include:

- Microcosm studies of primary production and invertebrate responses in a small-scale aquatic community
- Acute laboratory toxicity study of technical and formulated product with oligochaete worms
- Toxicity data on beneficial insects
  - laboratory tests for honeybee contact toxicity
  - honey bee brood development studies under field conditions
  - non-target arthropod study in citrus groves

A complete discussion of all toxicity data available for this risk assessment and the resulting measurement endpoints selected for each taxonomic group are included in the Sections VI and

VII of this document.

Measures of Exposure

Exposures estimated in the screening level risk assessment for non-target organisms are not specific to a given species. Rather, general taxonomic exposure assumptions are made that provide separate exposure measures for aquatic and terrestrial plants and animals. The approaches for each are discussed separately below.

Aquatic Organisms

The principal exposure concern for novaluron is the exposure of aquatic organisms to the active ingredient. However, additional data are available for the degradate chlorophenyl urea (275-352 I) in fish and aquatic invertebrates, suggesting that exposure modeling for these degradates is warranted. In addition, acute toxicity data for Rimon 10 EC, the formulated product are available and suggest that one or more constituents of the formulated product may exert toxic effects on fish. Therefore formulated product exposure modeling was also included in the risk assessment. The following sections describe the general analysis approach used for active ingredient, degradate and formulated product exposure assessment.

Active Ingredient and Degradate Aquatic Organism Exposure Approach

This risk assessment considers novaluron exposure in aquatic organisms (animals and plants) via the fraction of pesticide dissolved in the water column. Novaluron is assumed to be introduced to surface waters via runoff and spray drift. Because novaluron is a new pesticide, no monitoring data are available that would provide information on novaluron levels in surface water bodies receiving runoff or spray drift from agricultural fields treated with the pesticide. Consequently, aquatic organism exposure is estimated through the use of runoff and drift models, using a standardized surface water body. Aquatic organism exposures are based on a set of standardized water body assumptions (water body size, watershed size, proximity to field, etc.) that result in high-end estimates of exposure. For this risk assessment the PRZM/EXAMS model was used for making these exposure estimates. Crop scenarios were selected to provide high-end concentrations in drinking water and aquatic environments for each crop and represent the geographic locations where the specific crops are grown in large quantities. Runoff scenarios for novaluron were Pennsylvania, North Carolina and Oregon apples (airblast application), Mississippi cotton (ground and aerial application), and potato in Maine (ground and aerial application).

Degradate exposure analysis is similar to that performed for active ingredient, except the GENEEC model is used because of the limited fate data set for the degradate. The initial production of degradate in the field is determined though analysis of available environmental fate studies that track the formation of the degradate from various degradation pathways.

For acute aquatic risk assessment purposes, no averaging time for exposure was assumed. An instantaneous peak concentration, with a 1 in 10 year return frequency, is used. The use of the instantaneous peak assumes that instantaneous exposure is of sufficient duration to elicit acute

effects on par with those observed over more protracted exposure periods tested in the laboratory, typically 48 to 96 hours. For assessment of chronic aquatic invertebrate risks with novaluron, the peak water concentration was again used. This is a departure from the normal assessment where peak 21-day average,1 in 10 year return frequency value are the measurement endpoint for aquatic invertebrate chronic risk assessment. The decision to use a peak concentration exposure measure was predicated on data available for another chitin inhibiting insect growth regulators, of similar chemical structure and mode of action (diflubenzuron) that suggest effects observed in most chronic invertebrate tests with such pesticides are actually the product of short-term exposures of developing organisms at critical periods of the development cycle (i.e. molting).

Formulated Product Aquatic Organsim Exposure Approach

Rimon 10 EC exposures for acute aquatic risk assessment were assessed for the aerial drift pathway to surface water. Drifted formulated product mass is assumed to be instantaneously mixed with the surface water in a standardized water body with a volume of 20 million liters.

Terrestrial Animals

The focus of terrestrial wildlife exposure estimates is for birds and mammals with an exposure route emphasis on uptake through the diet. For exposure to terrestrial organisms, such as birds and small mammals, OPP mostly looks at the residues of pesticides on food items and assumes that organisms are exposed to a single pesticide residue in a given exposure scenario. For novaluron spray applications, estimation of pesticide concentrations in wildlife food items focuses on quantifying possible dietary ingestion of residues on vegetative matter and insects. The residue estimates are based on a nomogram that relates food item residues to pesticide application rate. Residues may be compared directly with dietary toxicity data or converted to an oral dose, as is the case for small mammals. The screening-level risk assessment for novaluron uses upper bound predicted residues as the measure of exposure. For mammals, the residue concentration is converted to daily oral dose based on fractions of body weight consumed daily as estimated through mammalian allometric relationships

Risk Characterization Approach

For this assessment of novaluron risks, the risk quotient (RQ) method is used to compare exposure and measured toxicity. Estimated environmental concentrations (EECs) are divided by acute and chronic toxicity values. The RQs are compared to the Agency's levels of concern (LOCs). These LOCs are the Agency's interpretative policy and are used to analyze potential risk to non-target organisms and the need to consider regulatory action. These criteria are used to indicate when a pesticide use as directed on the label has the potential to cause adverse effects on non-target organisms. Appendix D of this document summarize the LOCs employed in this risk assessment.

III. Integrated Environmental Risk Characterization

Risks to Aquatic Organisms

Novaluron is immobile and non-persistent to moderately persistent in soil and aquatic environments. Because novaluron has a high sorption affinity to soil/sediment, it is expected sorb strongly to soil and sediment and so may constitute a route of exposure (sediment to pore water to organism) for benthic organisms. It is expected to move from the target application site on entrained sediments in runoff and spray drift.

The results of the risk assessment suggests that acute and chronic risk to freshwater and marine invertebrates are the principal concern for direct toxic effects in aquatic ecosystems. All the calculated risk quotient values (RQs) for these invertebrates were above the acute risk and chronic risk levels of concern established by the Agency for screening-level risk assessment. The chronic invertebrate risk quotients range from 3 on potatoes to 194 on pome fruit. Acute invertebrate quotients range from 0.6 to 42. In addition, the expected potential for novaluron to adsorb to sediments, combined with microcosm observations of benthic invertebrate community effects at environmentally relevant novaluron loadings, suggest that concerns for risks to invertebrates extends to the benthic community as well. The risks associated with all the aquatic organism groups are outlined in more detail below.

Aquatic Invertebrates

Risk quotients (Appedix E) for acute risks to freshwater invertebrates range from 6 to 34, all crop scenarios modeled were in excess of acute risk concern levels. These RQs were based on an extrapolated toxicity value because the available acute aquatic invertebrate toxicity study using parent novaluron was found to be invalid. The freshwater invertebrate toxicity of novaluron was extrapolated from an available chronic endpoint for daphnids, modified by an established acute to chronic ratio for marine invertebrate toxicity endpoints. Attributing an acute to chronic ratio from estuarine/marine invertebrate test data to freshwater invertebrates is uncertain. However, the extrapolated freshwater invertebrate toxicity endpoint would have to be assumed to conservative by more than an order of magnitude for resulting risk quotients to be below the acute toxic risk level of concern. It is therefore concluded that predictions for acute effects in freshwater invertebrates are not likely to be grossly overestimated by the toxicity extrapolation approach employed in this risk assessment.

Estuarine/marine invertebrate acute RQs (Appedix E) for parent novaluron (7 to 39) indicate that the acute risk level of concern is exceeded at all proposed use sites._Of course, a potential source of uncertainty associated with the estuarine/marine risk assessment is the degree to which existing water models adequately represent estuarine/marine environments. It is conceivable that loadings to estuarine/marine environments may differ from freshwater systems. However, loadings to near-shore, shallow water systems, important to the productivity of estuarine systems would have to be more than 10 times lower than those modeled for there not to be a concern.

Previous review (MRID 44460701 and 44460702) of another chitin inhibitor, diflubenzuron, established that there is a "narrow window of sensitivity in the molt cycle that is highly susceptible to inhibition of chitin formation" and that acute LC50s for specific life or molt stages are similar to chronic NOEC values. Analyses of diflubenzuron risks to aquatic invertebrates considered the effects of exposure averaging time on the conclusions of the risk assessment, taking into account the likely acute sensitivity of invertebrates at critical stages of the life cycle.

While not from a standard guideline testing procedure, the registrant data submissions included 28-day LC50s for freshwater and marine invertebrates: 0.0000579 and 0.0001 mg/L, respectively. These LC50 values are remarkably close to the chronic toxicity thresholds measured for freshwater and estuarine/marine organisms, suggesting that the critical life stage observation for diflubenzuron may also occur for novaluron. These 28-day LC50 endpoints likely are of sufficient duration to cover multiple stages of the test organism life cycle and can be used to investigate the potential for other exposure averaging time assumptions (beyond the single day instantaneous peak), on the risk assessment conclusions for aquatic invertebrate mortality risks. Appendix E aquatic organism RQ tables can provide peak, 21-day and 60-day surface water concentration estimates for each use site modeled. Using the peak concentrations of 0.00094 mg/L for potatoes, a use site with the lowest use rate, the water concentrations would far exceed the LC50 values by factors of 16 for freshwater and 9.4 for estuarine/marine invertebrates. When considering the peak water concentrations for the pome fruit scenario, exposures would exceed these LC50s by factors of 87 to 50 for freshwater and estuarine/marine invertebrates, respectively. To further investigate the potential effects of exposure concentration averaging time on the risk conclusions, these 28-day toxicity values can also be compared with other time-weighted average concentrations from the modeling output. Such a comparison with the potato scenario 21-day average concentrations shows that exposures exceed the freshwater and estuarine/marine 28-day LC50 values by factors 11 to 7, respectively. Similar analysis with the higher use rate scenarios for cotton and pome fruits would yield exposures even higher than the demonstrated toxicity endpoints. Indeed, even a comparison of the estimated 60-day average novaluron concentrations in water show exposure exceeding the 28-day LC50s . This analysis further supports the risk assessment conclusions that freshwater and estuarine/marine invertebrates are at potential acute risk.

Valid chronic data were submitted for freshwater invertebrates as well as marine/estuarine invertebrates for parent novaluron. The chronic risk quotients for freshwater and marine invertebrates that are based on this toxicity data and modeled surface water concentrations range from 31 to 194. All use scenarios modeled are included in this range. Even though the mechanism of novaluron would suggest that chronic endpoints reflect acute responses at critical developmental periods in the invertebrate life cycle, the effect of exposure model averaging time was considered. In the manner described for the long-term lethality methods described above. Employing longer averaging times for RQ calculation did not result in RQ values below concern levels for freshwater invertebrates, and for estuarine/marine invertebrates had no effect on the risk assessment conclusions until a two month averaging time was considered. Owing to the high magnitude of the RQ values, it appears that steps to reduce exposure below chronic concern levels would require substantial reductions in loading rates to surface waters.

The risk assessment's RQ results for acute and chronic risk quotients suggest a concern for aquatic invertebrates. An additional line of information is also available to further characterize these risk concerns. Available microcosm data indicate that significant impacts to aquatic zooplankton and benthic macroinvertebrates can occur at nominal initial water concentrations of 0.00005 to 0.005 mg/L. This range of concentrations encompasses all peak, 21-day and most 60-day (except the potato scenario involving ground application) 1 in 10 year return frequency estimates of novaluron in surface waters. Effects in this microcosm study include but are not limited to:

- Total measured zooplankton populations exhibited negative responses to novaluron, as compared to controls for all dose levels, with statistically significant population reductions ($p<0.01$) at the 0.00015 through 0.005 mg/L dose levels (NOEC.0.00005 mg/L);
- Statistically significant ($P<0.01$ or $P<0.05$) reductions in population indices (NOEC< 0.00005 mg/L) for the following zooplankton taxa: Cyclopoidae (recovery after 84 days at this dose level), Chaoboridae (recovery by day 70), and Chirocephalidae;
- Statistically significant ($P<0.01$ or $P<0.05$) reductions in population indices (NOEC 0.00015 mg/L) for the following zooplankton taxa: Chydoridae, Lecanidae, and Diaptomidae;
- Benthic invertebrate community response (taxonomic response weighting) show statistically significant ($p<0.05$) community level effects at the 0.00015 mg/L dose level, with a community level response NOEC of 0.00005 mg/L; and
- Complete eradication of all Gammaridae amphipod crustacean populations, at all novaluron concentrations tested NOEC< 0.00005 mg/L.

The aquatic habitats potentially affected by the proposed uses of novaluron on pome fruit, cotton, and potatoes may be extensive. Runoff and drift from spray applications to pome fruit could affect freshwater or marine invertebrate structure in near-by streams, marshes, ponds, wetlands, tidal pools, and other water bodies. The aquatic invertebrates that may be exposed to novaluron play an important role as a primary food source for fish and other aquatic fauna. Though the available toxicity and exposure information preclude a quantitative assessment of the overall impacts, the demonstrated toxicity of novaluron to a variety of crustacean species and the observed impacts to invertebrate communities in microcosm studies at environmentally relevant novaluron concentrations suggests the potential for commercial crustacean fisheries (e.g. crabs, shrimp, etc.) impacts in the Gulf Coast region if cotton production use of novaluron resulted in the drift or runoff to important fishery habitat. Use in the cotton growing areas of California could potentially impact the ecological aquatic niches of healthy streams, ponds, wetlands, or other aquatic habitats that support healthy fisheries.

A aquatic invertebrates communities play a critical role as an important food source for aquatic vertebrates. Prolonged exposure from novaluron and its associated disruption of aquatic communities may have the potential to impact the fish growth, reproduction, and abundance. However, the level of analysis in this risk assessment cannot quantify the extent to which invertebrate community effects would impact aquatic vertebrates through food source impairment.

Sediment-Dwelling Organisms

Because novaluron is strongly sorbed to sediments and soils (K_{oc} = 6,680 - 11,813) it may be expected to partition to benthic substrates. No single-species toxicity data are available to quantitatively assess risks to individual benthic invertebrate species. However, data available for microcosms effects experiments (MRID 458858-01) suggest that populations of benthic invertebrates can be significantly reduced (up to total eradication in the case of Gammaridea) in aquatic systems where sediment concentrations of novaluron are below levels of detection (detection limit 5 ng/g). Observed impacts to some members of the benthic community were not

followed by population recovery, suggesting wither low potential for recruitment of new individuals or residual activity of novaluron when partitioned to sediments. Sediment toxicity data, which demonstrate the measured toxicity of novaluron in the sediment and interstitial water, would enable a more quantitative analysis of novaluron risks to sediment dwelling organisms.

Fish

While acute RQs (Appedix E) can be tentatively calculated for fish, the interpretive value of these quotients has some limitations. The principal limitations to the interpreting these RQs are the quality of the acute toxicity data available and the peak surface water model estimates of concentration that, in certain use scenarios considered, exceed measured solubility limits in pure water. However, consideration of the actual observations of effects within each acute toxicity study (or lack of observed effects) and modeled surface water concentrations as compared to measured water solubility suggest that acute risks of novaluron, the formulated product Rimon 10 EC, and degradates for which toxicity data are available are not at levels of concern. These analyses are summarized below.

A definitive LC50 for marine fish was not determined for parent novaluron. However, the available toxicity data show no mortality and no signs of toxicity at the highest concentration tested (NOEC 0.002 mg/L), a value close to but not exceeding the reported solubility limit of novaluron. For exposure scenarios involving cotton and potatoes, acute water concentrations are well below this NOEC and so there is not a concern for acute effects. In contrast, the estimated water concentrations associated with the apples application scenario exceed the available NOEC. Because there are no available measurements of potential effects at higher novaluron concentrations, the available toxicity endpoints for estuarine/marine fish are insufficient to provide an RQ that could be compared with Agency concern levels to define the extent of the acute risks for the surface water concentrations estimated for the apple scenario. It is important to note that the peak water concentration estimated for the apple scenario is above the likely water solubility of novaluron (an artifact of the use of solubility information in the water models). The facts that (1) the NOEC is so close to the solubility limit and (2) the apple scenario modeled surface water concentrations may actually exceed the solubility of novaluron suggest that concerns for significant acute estuarine/marine risks for the apple scenario are remote.

An acute freshwater fish toxicity classification (toxic, highly toxic, very highly toxic, etc.) for novaluron cannot be definitively established because available acute toxicity data (MRID 45499004) do not establish an LC50 (the endpoint critical to classification). However, the available data for parent novaluron do establish an acute NOEC (no observed mortality nor signs of intoxication) at the highest concentration tested 0.96 mg/L. It should be noted that this acute NOEC of 0.96 mg/L is orders of magnitude greater than the water solubility of novaluron (0.003 mg/L). Combining the results of the existing toxicity data with the likely solubility limit of parent novaluron suggests that the compound is not acutely toxic to freshwater fish at the limit of the compound's solubility in water. A comparison of the NOEC from this study with estimated surface water concentrations (Appedix E) confirms the assertion that surface water exposure would be well below levels that would trigger concern for acute risks to freshwater fish.

Additional long-term novaluron mortality data were available for freshwater fish. The LC50 from a 28-day study for freshwater fish was 7.14 mg/L. A comparison of this toxicity endpoint with the PRZM/EXAMS peak novaluron concentration of 0.00504 mg/L for pome fruit (a use site with the highest use rate and a conservative exposure assumption given the likely degradation and sediment-partitioning potential of novaluron in surface waters) indicated that exposures estimates are well below concern levels for acute mortality.

Toxicity data were submitted for the formulated product Rimon 10 EC, which indicted that the LC_{50} is 62.4 mg product/L for freshwater fish. Because typical aquatic modeling scenarios such as PRZM/EXAMS do not model formulated products, this acute formulated product fish toxicity endpoint was used in a separate assessment of formulated product drift risks. The LC50 value for Rimon 10EC was compared to surface water concentrations based on 1% and 5% drift assumptions (ground and aerial applications) of Rimon 10 EC to a standard surface water body (20 million liters). The resulting RQs (Appedix E) were all substantially below levels of concern ($<10^{-4}$) and even higher assumption of drift would be insufficient to yield water concentrations of formulated product that equal or exceed acute risk concern levels.

The freshwater fish LC50 for chlorophenyl urea degradate (275351 I) is 0.53 mg /L. Comparison of this toxicity value with GENEEC estimates for degradate concentrations in water (Appedix E) yielded risk quotients for freshwater fish well below all levels of concern.

Valid chronic freshwater fish toxicity data were submitted for parent novaluron. Chronic risk estimates for freshwater fish are below chronic levels of concern (Appedix E). No fish marine/estuarine chronic data were submitted for parent novaluron, the formulated product, or the chlorophenyl urea degradate. As a result, risk quotients cannot be estimated for these organisms. Extrapolation from freshwater chronic responses to estuarine/marine responses is possible and would suggest that estuarine/marine fish would not be at chronic risk if sensitivities were similar. However such an assertion would be quite uncertain, given that no common fish toxicity endpoints are available that enable establishment of a quantifiable a taxonomic sensitivity factor between the two broad fish categories.

Aquatic Plants

Aquatic plant risk to non-vascular plants was evaluated based on the marine diatom study (*Selenastrum capricornatum*) on parent novaluron, the formulated product, and the chlorophenyl urea. Vascular plant risk was based on the duckweed (*Lemna gibba*) which was performed solely on the formulated product. No acute non-endangered or endangered species LOCs were exceeded for the species tested (Appedix E).

Risk to Birds

Acute Risks - Birds

Acute risk to birds utilizes exposure data from Hoeger and Kenaga (1972) as modified by Fletcher et. al. (1994) which determines residue levels on various terrestrial food items following an application in the field. Predicted maximum and mean residue levels are determined based on

an application of 1 lb ai/A on short grass, tall grass, broad-leaved plants/small insects, and seeds/large insects.

Toxicant concentrations on food items following multiple applications are predicted using a first-order residue decline method, EFED's "FATE5" model, which allows determination of residue dissipation over time incorporating degradation half-life. Predicted maximum and mean EECs resulting from multiple applications estimates the highest one-day residue, based on the maximum or mean initial EEC from the first application, the total number of applications, interval between applications, and a first-order degradation rate, consistent with EFED policy. The input parameters for the pome fruit scenario were based on a maximum single application of 0.32 lb ai/A with a maximum of 3 applications per year and a 10 day interval between applications. The input parameters for the cotton scenario was a maximum single application of 0.09 lb ai/A 3 times per year with a 7 day interval between applications. Parameters used for the potato scenario were based on a single maximum application rate of 0.78 lb ai./A 3 times per year at minimum intervals of 10 days between applications. Initially, all the above scenarios used the 35 day foliar dissipation half-life since limited data was available on foliar half-life.

Acute data submitted for parent novaluron indicates that the dietary LC50s were greater than 5200 mg/kg-diet for bobwhite quail and greater than 5310 mg/kg-diet for mallard duck. The LD50s were greater than 2000 mg/kg-bw for both species. Since the results from both the dietary LC50 and the oral gavage LD50 classify novaluron as practically non-toxic to birds and the formulations are non-granular, the dietary LC50 for bobwhite quail was selected for risk quotient calculations.

The resulting risk quotients (Appedix E) showed that acute risk quotients at all sites were below all levels of concern from all use sites using the most sensitive LC50 of >5200 mg/kg-diet. The highest RQ of <0.04 was observed for birds foraging in short grass at the highest use site (pome fruit).

The risk quotient results from banded applications to cotton (Appedix E), based on a 6 inch band width and 30 inch row space indicated that the levels of concern are not exceeded for any bird weight classes except for the endangered species LOC for 15 gram birds when rates were not adjusted by band width. If the rates were adjusted for band width, the acute risk resulting from banded applications could be effectively mitigated.

Chronic Risk - Birds

Chronic risk to birds were evaluated using a mallard duck NOAEC of 9.8 mg/kg-diet based on the reproductive effect of viable eggs set. Use of this endpoint triggered level of concern exceedances at all use sites with the exception of fruit, pod, seeds, and large insect food categories on cotton and potatoes (Appedix E). The risk quotients ranged from 0.3 to 19.5.

Since chronic risks to birds exceeded the chronic LOCs at most of the bird forage sites using a 35-day foliar dissipation half-life, chronic LOC exceedances were estimated if shorter foliar dissipation half-lives were likley. To justify the use of shorter dissipation half-lives, EFED reviewed data from the Health Effects Division (HED) on available foliar dissipation half-life.

Limited information was available from on foliar half-lives (MRID 456384-12, 456384-20). A cursory review of these DERs revealed that only a handful of data for cotton and pome fruit reported results for Time 0 thru study termination (45 days), and many of the trials reported only one measurement point. With one exception, the data were variable throughout the studies for those reporting more than one result due perhaps to the multiple applications applied over the study period. Data from the studies with sufficient data points suggest that a decline in residues over the 45 day period is rapid for food sources of non-target animals. However, the variability of concentrations (some later sampling points were higher than earlier sampling) limit estimation of reliable foliar half-lives. To investigate the importance of the issue of alternative foliar dissipation half-lives in the avian chronic risk assessment, EFED ran the FATE 5 model using 1 and 5-day half-lives to assess the foliar dissipation half-life required to reduce chronic avian risk quotients below LOCs. Risk quotients for the additional FATE 5 analysis are presented in Appendix E. LOCs are exceeded for all crops at all avian food sources (except the fruits, pods, seeds, and large insects) for the 5 day foliar half-life. These results are also true even if the foliar half-life is assumed to be 1 day (with the exception of the tall grass food source which would be below chronic LOCs). Because chronic risk quotients are still exceeded regardless of the foliar dissipation rate assumed, chronic avian risk is an issue for the proposed multiple applications uses of novaluron. However, because the consideration of alternative foliar dissipation half-lives has the potential to reduce the scope of food sources with novaluron residues of chronic risk concern, the availability of reliable foliar dissipation data may be important, should any refined species-specific risk assessments (e.g., listed bird species assessments) be performed that would specifically address dietary behavior contributions to risk.

Chronic risk was also evaluated for single applications for maximum Fletcher values for predicted maximum and mean residues (Appedix E). This resulted in risk quotients exceeding the chronic LOCs for all food categories except the fruit, pod, seed, and large insect category for maximum residues for all crops. These risk quotients ranged from 0.1 to 7. The chronic LOCs were exceeded for the short grass, tall grass, and broadleaf/forage plants and small insects categories only for pome fruit for mean residues. These risk quotients ranged from 1.2 to 2.3.

Given the scenarios discussed above for the evaluation of chronic risk, it is doubtful that chronic risk can be mitigated below the chronic LOCs without substantial modifications to the prosed label use rates, number of applications and intervals.

Risks to Mammals

Acute risks to mammals were evaluated using the rat LD50 of > 5000 mg/kg-bw. There were no acute exceedances of the LOCs (Appedix E). The 2-generation rat study with a NOAEC of 1000 mg/kg-bw was used to evaluate mammalian chronic risk. No LOCs were exceeded for any of the use sites, and there are no chronic risk issues.

Risks to Non-Target Insects

EFED currently does not estimate risk quotients for terrestrial non-target insects. Whenever a LD_{50} is < 11 μg/bee an appropriate label statement is required to protect foraging honeybees. The acute contact toxicity study to honeybees revealed a contact LD_{50} > 100 μg/bee for the

technical novaluron and a contact LD_{50} >200 µg/bee for the Rimon 10EC product. This classifies novaluron (Rimon technical) and the formulated product as practically non-toxic to honeybees. However, additional non-target insect studies were submitted. These additional studies demonstrated adverse effects on brood development at all growth stages and significant effects on wasp and predatory mite populations. These effects demonstrate that beneficial non-target insects may be at risk, at least immediately after spray applications. Due to the conflicting conclusions of the available data, general risks to non-target beneficial insects is uncertain at this time across all species.

Risks to Terrestrial Plants

Since terrestrial plant testing is not required for pesticides other than herbicides except on a case-by-case basis (*e.g.*, labeling bears phytotoxicity warnings incident data or literature that demonstrate phytotoxicity), risk quotients for terrestrial plants were not calculated.

Endangered Species Assessment

The Agency's level of concern for endangered and threatened freshwater and marine invertebrates, marine fish, and birds is exceeded for the use of novaluron. The Agency recognizes that there are no Federally listed estuarine/marine invertebrates. The registrant must provide information on the proximity of Federally listed freshwater vascular plants, birds, mammals, and non-target terrestrial plants (there are no listed estuarine/marine invertebrates) to the novaluron use sites. This requirement may be satisfied in one of three ways: 1) having membership in the FIFRA Endangered Species Task Force (Pesticide Registration [PR] Notice 2000-2); 2) citing FIFRA Endangered Species Task Force data; or 3) independently producing these data, provided the information is of sufficient quality to meet FIFRA requirements. The information will be used by the OPP Endangered Species Protection Program to develop recommendations to avoid adverse effects to listed species.

The preliminary risk assessment for endangered species indicates that Novaluron exceeds the endangered species LOCs for the following combinations of analyzed uses and species:

- Use of Novaluron on pome fruit, cotton, and potatoes indicate an exceedance of the endangered species LOCs for freshwater and marine/estuarine invertebrates. However, there are currently no endangered estuarine/marine invertebrates. Exceedances for freshwater invertebrates were based on the acute to chronic toxicity ratios of marine invertebrate data since the acute data for freshwater invertebrates is invalid. However, when the LC50s from the chronic studies are used, the risk quotients indicate LOC exceedances.

- Use of Novaluron on pome fruit, cotton, and potatoes indicate endangered LOC exceedances for marine fish. However the results are very uncertain because a definitive LC50 was not obtained.

- Use of novaluron on pome fruit, cotton, and potatoes indicate that chronic LOCs are exceeded for birds foraging in all food categories except the fruit, pods, seeds, and large

insect categories. No acute risk LOCs are exceeded.

- Use of novaluron applied on cotton in banded applications trigger endangered species risks for 15 g birds. These risks could be easily mitigated by reducing the use rates for banded applications.

IV. Environmental Fate Assessment

The environmental fate assessment for novaluron is based on acceptable and supplemental environmental fate data. Novaluron is a chiral compound containing a racemic mixture of two enantiomers (R,S). The available environmental fate and ecological effects data on novaluron represents only the racemic mixture. Additional data on individual enantiomers may be required if the registrant chooses to develop isomeric enriched products of novaluron.

Novaluron is immobile and non-persistent in soil laboratory studies. However, it appears to be more persistent in some field studies under actual use conditions. Novaluron persistence in field soils may be partially explained by temperature effects on metabolism; greater persistence is expected in cooler climates. Laboratory studies suggest that novaluron's major route of disappearance is microbially-mediated degradation. The chemical tends to strongly adsorb to soil and sediment, and it is stable to abiotic processes. Novaluron has a very low potential to reach ground water. During surface runoff conditions, novaluron may reach water bodies as bound to soil particles and will likely partition into sediments once in surface water. Additionally, contribution to surface water contamination may occur from spray drift.

Novaluron degradation rates in aerobic soil appear to be dependent on temperature. At 20 °C, novaluron metabolizes with half-lives from 7 to 14.5 days to form chlorophenyl urea (275-352I) and chloroaniline (MRIDs: 44961009 and 44961010). At 10 °C, novaluron degrades slower ($t_{1/2}$= 31.9 days) (MRID 44961009). In aquatic environments under stratified redox conditions (aerobic conditions in water and anaerobic conditions in soil) the chemical metabolizes with total system half-lives of 9.7 and 19.7 days (MRID 45638206). Under anaerobic conditions in water-soil systems, novaluron degrades slower with total system half-lives of 49 and 51 days (MRIDs: 45638205 and 45789203). A proposed transformation pathway in aquatic environments indicates novaluron forms 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl urea (275-352I) and 2,6-difluorobenzoic acid (275-158I, DFBA) through amide hydrolysis. Further hydrolysis of 275-352I yields 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline (275-309I) and hydrolysis of 275-158I yields 2,6-difluorobenzamide (275-157I) (MRID 5638206).

Novaluron was stable to hydrolysis at pH 5, 7, and 9 (pH 9 $t_{1/2}$ (25 °C) = 101 days; MRID 44961008) and stable to both soil and aqueous photolysis (soil photolysis $t_{1/2}$ = 257 days, MRID 45638204; aqueous photolysis $t_{1/2}$ = 187 days, MRID 45638203). At 50 °C in pH 9 buffer solution, however, novaluron appears to hydrolyze rapidly with a half-life of 1.2 days. Novaluron tends to adsorb strongly to soil and sediment. The mean simple K_d values ranged from 95 to 247 ml/g, and K_{oc} values from 6,650 to 11,813 (MRID 44961012). There was no linear relationship between the soil organic carbon content and the K_d values for different soils thus the K_{oc} model may not be appropriate. Because novaluron was tested only at one concentration Freundlich

adsorption/desorption coefficients could not be calculated.

The high sorptive properties of novaluron indicate a low potential for leaching to ground water. In the field dissipation study conducted in North America, sites located in CA, LA, NY, WA, Nova Scotia, and Ontario, novaluron residues were not detected above 0.0851 ppm (Nova Scotia) in the 15-30 cm soil depth and above 0.0606 ppm (Ontario) in the 30-45 cm soil depths (MRID 45789204). In all sites, total water inputs (rainfall plus irrigation) were greater than the 10-year average rainfall except for the Nova Scotia site. Novaluron (RimOn 10EC) was not detected above the LOQ (10 ppb) at any sampling interval or in any replicate sample in the 10-20 cm soil depth when applied to bare soil in Spain and Germany (GLN 164-1; MRID 45638403). In these foreign studies pan evaporation data were not reported to assess whether sufficient moisture was present in the soil to facilitate leaching of the test substance. Irrigation was not applied to any of the test plots during the study trials and monthly rainfall data indicated that in the first 3 to 7 months rainfall was below historical average.

Novaluron (RimOn 10EC and RimOn 6.7WDG) dissipated with half-lives ranging from 20 to 178 days (i.e., in CA with a half-life of 20 days, in WA with a half-life of 61 days, in Nova Scotia with a half-life of 89 days, and in NY with a half-life of 178 days (valid $t_{1/2}$ could not be determined for the LA and Ontario sites)). There is, however, a great deal of uncertainty associated with the half-lives calculated at the NY and Nova Scotia sites due to high data variability, both between replicates and over time. In the field dissipation studies conducted in Spain and Germany, novaluron (RimOn 10EC) dissipated with half-lives ranging from 52 to 178 days (MRID 45638403). In five out of six sites in the North American field studies chlorophenyl (275-352I) urea was detected as a major transformation product (MRID 45789204).

In a microcosm study, novaluron exhibited water column DT_{90} values ranging from 12 to 20 days for three different test concentrations (i.e., 5, 15, and 50 g a.i./ha treatment level; MRID 45785801). Only low concentrations of novaluron were detected in sediment, demonstrating potential for microbial degradation. This was confirmed by the presence of the main degradate, chlorophenyl urea (275-352I), in the water column of three out of five tested concentration and in soil of the highest tested concentration. Chlorophenyl urea (275-352I) was the only degradate analyzed in water and sediment.

Novaluron appears to accumulate in edible and nonedible fish tissues. In a standard bioconcentration study using the bluegill sunfish, the highest mean bioconcentration factor (BCF) in whole fish was 14,431 x. The half-life for clearance of residues in the bluegill was 3.9 to 7.3 days for whole fish (MRID 45638215).

The major novaluron degradate, 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluorometh oxyethoxy) phenyl]urea (275-352I), was formed in aerobic soil metabolism at a maximum rate of 26.6% of the applied parent at 7 days posttreatment (MRID 44961009). Based on the McCall et al., 1980 classification system the degradate appears to have low to slight mobility in soil (K_{oc} values range from 1950 to 2563 L/kg; 163-1; MRID 45638201). The Freundlich isotherm, however, may not adequately represent adsorption of the compound across all concentrations (the 1/n values were not within the range of 0.9 to 1.1). Based on a laboratory study, novaluron degradates appear to have a very low potential for leaching into ground water. Chlorophenyl urea (275-352I) has the

potential to reach surface water through runoff. Its aerobic soil metabolism half-lives estimated from the formation and decline curves (MRID 44961009) are 46.5 and 45.9 days. The degradate may be moderately persistent in the aquatic environment. The half-life was determined from the first-order degradation rate from the maximum concentration in the aerobic aquatic metabolism study (MRID 4538206). The aerobic aquatic metabolism half-life is 26.6 days in a Houghton Meadow water-loamy sand sediment.

Another novaluron degradate of potential concern is 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline (chloroaniline, 275-309I) which was formed in the aerobic soil metabolism study at a maximum rate of 8.5% of the applied at 120 days posttreatment, the last sampling interval (MRID 44961009). Additionally, it is expected that chloroaniline is formed from the further degradation of the major degradate, chlorophenyl urea (275-352I) (MRIDs: 45638205 and 45789203). In the anaerobic aquatic metabolism study, at the last sampling interval, i.e. 363 days posttreatment, the maximum of 32% of the applied was formed in the soil and 49.8% in the total system. This includes soil and volatilized chloroaniline. This degradate has the potential to be volatile (i.e., its estimated vapor pressure exceeds 10^{-4} mmHg), more mobile (K_{oc} (an estimated value) = 5899) and more persistent than the parent. Degradation rates for chloroaniline could not be calculated due to the lack of formation and decline data.

V. Drinking Water Assessment Summary

Monitoring data for novaluron, chlorophenyl urea (275-352I) and chloroaniline in surface water and ground water were not found. Concentrations of novaluron and its degradates, chlorophenyl urea (275-352I) and chloroaniline in surface water and ground water were estimated via modeling.

Surface Water Assessment

A few crop scenarios were selected for novaluron Tier II PRZM-EXAMS modeling to provide high-end drinking water concentrations for each crop and represent the geographic locations where the specific crops are grown in large quantities. These scenarios were: apples in PA, NC and OR to represent the pome fruit group, cotton in MS, and potatoes in ME. The drinking water assessment was based on the maximum annual application rates on apples, cotton, and potatoes as specified on the labels.

The highest EECs were obtained for airblast application of novaluron to PA apples at the maximum annual application rate of 0.96 lb a.i./acre, applied three times at 0.32 lb a.i./acre with an interval between applications of ten days. Table 1 lists estimated drinking water concentrations from surface water sources for all modeled scenarios. For the modeling input parameters and modeling uncertainties refer to the Drinking Water Memorandum in Appendix A.

Table 1. Novaluron estimated drinking water concentrations for surface water sources.

Scenario	Application Type	Estimated Drinking Water Concentrations from Surface Water Sources (ppb)		
		1 in 10 year annual peak	1 in 10 year annual mean	36 year annual mean
PA apples (PCA = 0.87)	airblast	11.4*	1.8	1.2
NC apples (PCA = 0.87)	airblast	4.24*	0.6	0.38
OR apples (PCA = 0.87)	airblast	1.6	0.38	0.31
MS cotton (PCA = 0.20)	ground aerial	0.70 0.78	0.07 0.08	0.04 0.05
ME potato (PCA = 0.87)	ground aerial	2.15 2.43	0.38 0.45	0.24 0.32

*These values exceed the measured water solubility of novaluron of 3 µg/L (3 ppb).

The HED MARC concluded that parent, chlorophenyl urea (1 -[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy) phenyl] urea) (275-352I), and chloroaniline (3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline) are residues of potential concern to be included in the drinking water assessment hence a Tier I drinking water assessment was performed for these degradates. Chlorophenyl urea and chloroaniline scenarios were based on the following: (1) assuming 26.6% (MRID 44961009) conversion from parent to chlorophenyl urea (275-352I) and 100% conversion from parent to chloroaniline, and (2) using molecular weight conversion to adjust from parent application rate to the degradate application rate. Table 2 lists estimated drinking water concentrations for both degradates for all novaluron proposed maximum uses. For the modeling input parameters and more details on assumptions, and modeling uncertainties, refer to the Drinking Water Memorandum in Appendix A.

Table 2. Degradates' estimated drinking water concentrations for surface water sources based on Tier I modeling.

Novaluron Metabolite	Crop	Application Rate	Estimated Drinking Water Concentrations from Surface Water Sources (ppb)	
			Peak	Annual Average
chlorophenyl urea	apples:	3 X 0.32 lb a.i./acre	4.56	0.86
	cotton	3 X 0.09 lb a.i./acre	0.3	0.057
	potato	3 X 0.078 lb a.i./acre	1.12	0.21
chloroaniline	apples	3 X 0.32 lb a.i./acre	11.4	2.61
	cotton	3 X 0.09 lb a.i./acre	0.75	0.17
	potato	3 X 0.078 lb a.i./acre	2.8	0.64

Ground Water Assessment

SCI-GROW modeling predicted a ground water concentration for novaluron at the annual application rate of 0.96 lb a.i./acre (i.e., three applications of 0.32 lb a.i./acre) of 5.5×10^{-3} µg/L in drinking water from shallow ground water sources. The predicted ground water concentration is 4.5×10^{-3} µg/L for chlorophenyl urea and 9.0×10^{-3} µg/L for chloroaniline from novaluron's maximum application rate (0.96 lb a.i./acre). Both concentrations were estimated with the same assumption used for surface water modeling. These concentrations may be considered as both the peak and annual average upper bound exposures.

VI. Aquatic Hazard, Exposure, and Risk Quotient Calculation

Appendix C summarizes the results for toxicity studies material to this risk assessment. Discussions of the effects of novaluron, formulated product, and degradates on aquatic taxonomic grous are presented in the following sections.

Toxicity to Fish

An acute freshwater fish toxicity classification (toxic, highly toxic, very highly toxic, etc.) for novaluron cannot be definitively established because available acute toxicity data (MRID 45499004) do not establish an LC50 (the endpoint critical to classification). However, the available data for parent novaluron do establish an acute NOEC (no observed mortality nor signs of intoxication) at the highest concentration tested 0.96 mg/L. It should be noted that this acute NOEC of 0.96 mg/L is orders of magnitude greater than the water solubility of novaluron (0.003 mg/L). Combining the results of the existing toxicity data with the likely solubility limit of parent novaluron suggests that the compound is not acutely toxic to freshwater fish at the limit of the compound's solubility in water. A repeat of the acute fish toxicity test, conducted using methods to test above the solubility limit (a supersaturated system), might establish an LC50 for classification purposes, but would be of questionable utility in freshwater fish risk assessment.

An acute freshwater fish study submitted for the Rimon 10 EC formulated product indicted that the LC_{50} is 62.4 mg product/L (5.74 mg ai/L) for freshwater fish (MRID 456383-14). This endpoint is well in excess of the water solubility limit of novaluron. Three explanations for these observations are possible. First, novaluron itself is responsible for the acute toxicity observed in this study and the formulated product has resulted in a super saturated condition in the test system. This explanation is unlikely because the parent novaluron concentration is over 3 orders of magnitude higher than the solubility limit (a remarkable saturation not likely to be achieved); and systems with as much as 0.96 mg/L novaluron (discussed above) resulted in no toxic effects. Second, the toxicity observed in the study is the result of the inherent toxicity of constituents of the formulation other than novaluron, a possibility that cannot be dismissed because novaluron alone is of demonstrably low toxicity. Third, both novaluron and other formulation constituents are responsible for the observed toxicity, a hypothesis that available data cannot exclude. Because typical aquatic modeling scenarios such as PRZM/EXAMS do not model formulated products, this acute formulated product fish toxicity endpoint was used in a separate assessment of formulated product drift risks.

As for freshwater fish, the acute novaluron LC_{50} for marine fish was not determined by available toxicity data (MRID 45638210). This lack of an LC_{50} , precluded a toxicity classification of novaluron. However, the data do suggest that the NOEC for novaluron is at least as high as the highest dose tested (0.002 mg/L), which is very close to the established solubility limit of the compound (0.003 mg/L). No sub-lethal effects were observed in this study. Because of the lack of a reported LOEC, the NOEC result from this study is uncertain. There are no data for either the formulated product or the metabolite. To better characterize the toxicity to marine fish the LC50 for the parent novaluron should be repeated above the level of solubility.

A chronic toxicity study was submitted for freshwater fish early life-stage (rainbow trout) for parent novaluron. Although this study was not based on the EPA guideline specifications, it does provide useful information for assessing chronic risk. The NOAEC of the parent was 0.00616 mg/L based on terminal growth and mortality (MRID 456382-16). Additionally, a chronic fish early life-stage test was submitted for the fathead minnow (MRID 456382-13), but was found to be invalid due to numerous deviations from the EPA protocol (most notably variations in stability measurements at all test levels).

A chronic full life cycle test was submitted for freshwater fish (fathead minnow) on the parent novaluron (MRID 457858-05), but was found to be invalid because adequate raw data pertaining to survival of both generations and growth of the F_0 generation were not provided to verify the results of the study. Additionally, several endpoints were not measured such as time to hatch for the F_0 and F_1 generations, lengths of the F_0 fish at 4 and 8 weeks post-hatch, and survival of F_0 fish at 4 weeks post-hatch. The measured NOEC was 0.003 mg/L, and this study could be up-graded to supplemental status if the missing raw data were submitted.

Chronic freshwater fish toxicity testing was also submitted for the formulated product Rimon 10 EC (MRID 456384-06) and indicated a chronic NOAEC of 1.21 mg/L (0.11132 mg ai/L when adjusted to the percent active ingredient) and a 28-day survival LC_{50} of 7.14 mg/L (0.66 mg ai/L adjusted). However, as with the case of acute testing of this formulated product, the novaluron active ingredient-based NOAEC is well in excess of the water solubility limit of the active ingredient. The potential explanations for this observation are similar to those discussed for the acute testing of the formulated product. Additionally, this study does not meet USEPA guideline requirements and can not be used to calculate chronic risk quotients because this test was initiated with 5-month old juvenile rainbow. The USEPA fish early life stage test requires that the test be initiated with fish embryos and terminate at swim-up. No chronic data was submitted for marine fish.

Toxicity to Aquatic Invertebrates

Acute freshwater invertebrate data for parent novaluron has been classified as invalid due to the high variability of the measured concentrations during the test (MRID 454768-02). A valid acute toxicity test will be required to properly address the risk.

Acute aquatic invertebrate data are available for the formulated product Rimon 10 EC for freshwater invertebrates (MRID 456383-13). Data for Rimon 10 EC indicates that the EC_{50} is 0.00431 mg/L (0.0004 mg ai/L when adjusted to the percent active ingredient) and very highly

toxic to freshwater aquatic invertebrates. However, as discussed above for fish, there may some uncertainty with these results since it appears that the measured concentrations were not centrifuged as required under the current EPA pesticide Reregistration Rejection Rate Analysis. This may account for the higher measured concentrations (hence, lower toxicity) in the water column. There is uncertainty with regards to the contribution of novaluron to the toxicity of this study. This uncertainty could be reduced if a valid study for parent novaluron was submitted. Therefore, a valid toxicity test will be required for the parent novaluron.

In the absence of a valid acute toxicity test for freshwater invertebrates the ratios of the acute to chronic toxicities were assumed to be the same as those for marine invertebrates. The following equation was used to derive an estimated acute LC_{50} of 0.00015 mg ai/L for freshwater invertebrates.

$$\textit{Acute toxicity}_{fw} = \textit{Chronic toxicity}_{fw} \times \textit{Acute toxicity}_{est} / \textit{Chronic toxicity}_{est}$$

The 275-352 I degradate of Novaluron is practically non-toxic to freshwater invertebrates (EC_{50} = 1.91 mg/L) (MRID 454990-07).

Marine aquatic data on the technical grade of the active ingredient indicate that novaluron is very highly toxic to shrimp (MRID 456382-09) and oyster (MRID 456382-08) (LC_{50} =0.00013 and 0.0015 mg/L respectively). Additional acute data on the formulated product Rimon 10 EC (460862-03) demonstrate that novaluron is very highly toxic to shrimp (LC_{50} = 0.00012 mg ai/L). No data are available for the major degradate chlorophenyl urea (275-352 I) for marine invertebrates. Such data might help to better characterize the risk and reduce associated uncertainties.

Chronic data were conducted for freshwater and marine invertebrates with the technical grade of the active ingredient and demonstrates that both the daphnid and the mysid shrimp are very sensitive to Novaluron. The NOAEC of 0.0000299 mg/L for the daphnid was based on survival of the parents and the production of offspring (MRID 456382-11). The most sensitive endpoint for the mysid shrimp was for reductions in the terminal male body length, with a NOAEC of 0.000026 mg/L (MRID 456382-12).

Toxicity to Aquatic Plants

Tier 1 Aquatic plant testing was conducted for the marine diatom *Selenastrum capricornutum* and found that the EC_{50} for cell density was >9.68 mg ai/L (MRID # 456382-21).

A Tier 2 study of *Selenastrum capricornutum* for the 275-352 I metabolite revealed an EC_{50} of 0.33 mg/L based on cell density (MRID # 456382-22). Further testing of the formulated product indicated that the EC_{50} of 39 mg ai/L for the same alga (MRID 456384-11). Further tier 2 formulated product testing of the vascular plant *Lemna gibba* (duckweed) indicated an EC_{50} based on biomass of 0.777 mg ai/L (MRID 456382-23).

Community Effects Studies

A microcosm study involving a community of selected algae and aquatic invertebrates was submitted for review (MRID 458858-01). The principle objectives of the study was to assess the potential biological effects of novaluron in invertebrate communities and define the no effect concentration and ecologically acceptable concentration (EAC; µg ai/L). No fish were included in the community structure.

Duplicate microcosm chambers were dosed with 0.05, 0.15, 0.5, 1.5, or 5 µg/L of novaluron (initial nominal application) in the form of Rimon 10 EC. Applications were made twice to each chamber, with a 14-day application interval.

Water concentrations were measured immediately after application (periodically thereafter to 84 days after initial application) from samples collected at 10 and 45 cm depth. Initial measurements confirmed the nominal application rates. The mean times for 90% disappearance (DT_{90}) at 0.5 and 1.5 µg/L subsequent to the second application were 18 and 12 days, respectively. It is important to note that the nominally exposed chambers at 5 µg/L exhibited measured initial concentrations of novaluron in excess of the solubility limit. Because the samples were unfiltered collections, measured concentrations in excess of solubility may reflect a combination of dissolved and colloidal/particulate associated novaluron in the water column.

Sediment (upper 1 cm) concentrations of novaluron were measured starting 3 days after application with periodic sampling events extending out 84 days after initial pesticide application. Novaluron was not detected in sediment (detection limit 5 ng/g) in the two lowest doses, novaluron was detected in only two sediment samples (max 10 ng/g at day 35) at the 0.5 µg/L dose. Peak sediment concentrations of novaluron were 24 ng/g (14 days after 2nd application) and 72 ng/g (35 days after 2nd application) for the 1.5 µg/L and 5 µg/L dose levels, respectively.

Primary production measurement endpoints consisted of phytoplankton chlorophyll a and phaeophytin levels, periphyton biomass, and mascrophyte species counts. Chlorophyll-a levels were elevated post application for the three highest dose groups., with peak chlorophyll a concentrations 28 days after the first application (14-days after 2nd application).

Zooplankton measurements included measures of taxa numbers, initially at the family level with a subsequent analysis of discrete genera and species for those organisms defining system response to novaluron. In general, total measured zooplankton populations exhibited negative responses to novaluron, as compared to controls for all dose levels, with statistically significant population reductions ($p<0.01$) at the 0.15 though 5 ug/L dose levels. Individual taxonomic family responses are summarized as follows:

Taxa	**NOEC for Population Reductions ug/L**
Chydoridae	0.15 (day 84)
Cyclopoidae	<0.05 (recovery after 84 days at this dose level)
Nauplii	<0.05 (recovery after 84 days at this dose level)
Synchaetidae	0.5 (day 84)
Daphnidae	> 5.0 (significant reductions in 2nd phase)

Lecanidae	1.5 (significant increases in numbers at day 84)
Brachionidae	5.0 (significant increases in numbers at day 84)
Chaoboridae	<0.05 (day 42, recovery by day 70)
Chirocephalidae	<0.05 (day 56)
Diaptomidae	0.15 (day 56)

Analysis of benthic invertebrate populations were conducted primarily at the family level, with subsequent analysis to more refined taxonomic levels for those organisms showing definitive responses to novaluron treatment. Analysis of benthic invertebrate community response (taxonomic response weighting) shows statistically significant ($p<0.05$) community level effects at the 0.15 ug/L dose level, with a community level response NOEC of 0.05 ug/L. It should be noted that the Gammaridea showed statistically adverse response ($p<0.01$) below that observed for the community as whole, with a NOEC <0.05 and complete eradication of the family at all dose groups by study termination.

It is important to realize that all NOEC's from this study are presented in terms of the initial nominal novaluron concentration. However, many of the effects observed in the study progress over considerable time periods following initial novaluron application. Concurrent with the emergence of observable effects over the course of the study, measurements of water column concentrations of novaluron are declining with time. Consequently the study cannot provide definitive information on the actual water concentration over time that can be associated with an observed adverse effect. Reliance on the nominal concentrations for establishment of NOECs likely underestimates the toxic potential of novaluron.

Aquatic Exposure

Tier II modeling (PRZM 3.12 and EXAMS 2.975 coupled with a graphical interface shell, the PE4V01.pl program dated 8/8/2003) was used to estimate the concentrations of novaluron in surface water from the proposed food uses. For the purpose of the modeling, the maximum annual application rate, maximum number of applications per season, and the minimum intervals between the applications were selected to estimate the aquatic exposure concentrations. The crops scenarios were selected to provide a high-end scenario for aquatic EECs for each crop and represents the geographic locations where the specific crops are grown in large quantities. The scenarios that were modeled are Pennsylvania apples (airblast application), Mississippi cotton (ground and aerial application), and Maine potato (ground and aerial application). The input parameters used for the aquatic exposure modeling are provided in Tables 3 and 4. The output files for aquatic exposure modeling are provided in Appendix B.

Table 3. Environmental Fate and Chemistry Input Parameters for Novaluron

Parameters	Input Value and Unit	Source of Info/Reference
Maximum Application Rates [1]	apples = 0.359 kg ai/ha cotton = 0.100 kg ai/ha potato = 0.087 kg ai/ha	Product Labels: RimOn 7.5WDG; EPA Reg. No. 66222-LT RimOn 10EC; EPA Reg. No. 66222-35 RimOn 10EC; EPA Reg. No. 66222-35 (?)
Maximum Number of Applications	apples = 3 cotton = 3 potato = 3	Product Labels as above
Minimum Interval Between Applications	apples = 10 days cotton = 7 days potato = 10 days	Product Labels as above
Soil Partition Coefficient (K_d)[2]	133	MRID 44961012
Molecular Weight	492.7	Registrant data
Solubility (at 25 °C) x 100	0.3 ppm	Registrant data (MRID 45638203)
Vapor Pressure	1.2×10^{-7} mm Hg	Registrant data
Henry's Constant at 25 °C	1.974×10^{-13} atm•m^3/mol	Registrant data
Aerobic Soil Metabolism $T_{1/2}$[3]	15.6 days	MRIDs: 44961009 and 44961010
Foliar Dissipation $T_{1/2}$	-	was not considered in the modeling
Aqueous Photolysis (pH 5) $T_{1/2}$[4]	187 days	MRID 45638203
Hydrolysis $T_{1/2}$ (pH7)	stable	MRID 44961008
Aerobic Aquatic Metabolism Half-life[5]	30.1 days	MRID 45638206
Anaerobic Aquatic Metabolism Half-life[5]	52.1 days	MRIDs: 45638205 and 45789203

[1] - One planting per year was assumed and the annual rate is assumed to be the seasonal rate

[2] - The lowest non-sand K_d for sandy loam with sand content < 70% was used. Out of four K_f values (133, 247, 184, and 95) the lowest non-sand K_f
for sandy loam was used (K_{oc} model was not valid).

[3] Solubilitity was adjusted to 0.3 ppm for Tier II modeling according to EFED input parameter guidance.

[4] - Since n=4: to account for the inherent variability the constant rate of the upper confidence bound on the mean (mean half-life (of 14.5, 13.7, 7, and 11.5) + (t_{90} σ)/$\sqrt{n}$ (single tail student's t, α=0.1 where n = number of values)) aerobic soil metabolism half-life was used

[5] - individual data points were very variable so the accuracy of the half-life is uncertain

[6] - since n=2 (aerobic $T_{1/2}$: 19.7 and 9.7 days; anaerobic $T_{1/2}$: 50.6 and 49.2 days), the upper confidence bound on the mean aquatic metabolism half-life was used.

Table 4. Additional PRZM-EXAM Input Parameters for Pond Scenario for Novaluron

Parameters	Input Value and Unit	Source of Info/Reference
First Application Date (day-month)	apples = PA: 25-07 cotton = 20-07 potato = 15-06	assumed based on crop profiles and probable target insect infestation
Rainfall Data (Metfile)	apples = PA: W14737.dvf cotton = MS: W03940.dvf potato = ME: W14607.dvf	Individual crops' scenarios
Application Fraction	apples airblast = 0.99 cotton & potato aerial = 0.95 cotton & potato ground = 0.99	Guidance for Selecting Input Parameters in Modeling the Environmental Fate and Transport of Pesticides; Feb. 28, 2002
Spray Drift Fraction	apples airblast = 0.01 cotton & potato aerial = 0.05 cotton & potato ground = 0.01	as above

The one in 10 year concentrations for acute peak, 21-, 60-, and 90-days and for annual durations are provided in Table 5.

Table 5. PRZM/EXAMS Estimated EECs for Novaluron - Aquatic Exposure

Crops or Crop Groups and Application Information	One in Ten Year Surface Water Concentrations (ppb)				
	Peak	21 days	60 days	90 days	Yearly
Apples in PA (airblast, 0.32 lb/acre, 3x, 10 days)	5.04	3.18	2.24	1.93	0.77
Cotton in MS (aerial, 0.09 lb/acre, 3x, 7 days)	1.58	0.93	0.62	0.51	0.19
Cotton in MS (ground, 0.09 lb/acre, 3x, 7 days)	1.39	0.85	0.52	0.43	0.16
Potato in ME (aerial, 0.078 lb/acre, 3x, 10 days)	1.09	0.78	0.54	0.45	0.21
Potato in ME (ground, 0.078 lb/acre, 3x, 10 days)	0.94	0.65	0.43	0.36	0.16

Exposure issues associated with the formulated product were addressed assuming exposure through spray drift alone. This exposure assessment assumes the impact of formulated product from runoff on aquatic exposure would be negligible due to microbial degradation and soil sorption of the formulated product. Therefore, the exposure scenario assumes 5% drift of formulated product into the standard pond would yield the highest concentration of formulated product. Estimated concentrations are provided in the table below.

Table 6. Estimated Environmental Concentrations from Direct Applications of Rimon 10EC to Surface Water

Crop	Application Rate (lb ai/A)	Percent Active Ingredient	Application Rate of Formulated Product (lb/A)	Mass of drifted Formulated Product (mg)	Conc. of Formulated Product (mg/L) in Farm Pond
Pome fruit	0.32	0.092	3.478	78956.5	0.00395
Cotton	0.09	0.092	0.9783	22206.5	0.00111
Potato	0.078	0.092	0.8478	19245.65	0.00096

Additionally, for the degradate chlorophenyl urea Tier I drinking water analysis was performed. For the surface water modeling the GENEEC model was used as if chlorophenyl urea was "granular" applied to the field with no spray drift and no foliar interception. The degradate scenario was based on the following: (1) assuming 26.6% (MRID 44961009) conversion from parent to chlorophenyl urea and (2) using molecular weight conversion to adjust from parent application rate to chlorophenyl urea application rate. Table 7 lists GENEEC input parameters for the degradate.

Table 7. GENEEC Input Parameters for 1-[3-Chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea

Parameters	Input Value and Unit	Source of Info/Reference
Maximum Application Rates [1]	apples = 0.061 lb/acre cotton = 0.017 lb/acre potato = 0.015 lb/acre	$rate_{der} = rate_{par} * (MW_{deg}/MW_{par}) *$ (max. % form. rate/100)
Maximum Number of Applications	apples = 3 cotton = 3 potato = 3	Product Labels: RimOn 7.5WDG; EPA Reg. No. 66222-LT RimOn 10EC; EPA Reg. No. 66222-35 RimOn 10EC; EPA Reg. No. 66222-35
Minimum interval between applications	apples = 10 days cotton = 7 days potato = 10 days	Product Labels as above
Soil Partition Coefficient (K_d)[2]	16.7	MRID 45638201 (GLN 163-1)
Aerobic Soil Metabolism $T_{1/2}$[3]	47.1 days	MRID 44961009
Wetted in	No	Product Label
Depth of incorporation (inches)	0	Product Label
Method of application	granular	assumed; a degradate formed in soil
Solubility in water at 20 °C	33 ppm	MRID 45638201
Aerobic aquatic metabolism half-life[4]	26.6 days	MRID 45638206
Aqueous Photolysis (pH 5) $T_{1/2}$	stable	assumed; data not available

[1] – Application rate of 275-352I is based on the maximum formation rate of 26.6 % from parent novaluron found in the aerobic soil metabolism study (MIRD 44961009) and molecular weigh conversion (MW_{par} = 492.7; MW_{deg} = 352.6).
[2] - the lowest non-sand K_f(sandy loam) was used. Out of four K_f values (35.1; 16.7; 61.5; and 47.6) the lowest non-sand K_f for sandy loam was used (K_f may not equal K_d).
[3] - 275-352I first order non-linear half-lives were estimated from formation and decline curves using the maximum concentration as the initial concentration; since there were two valid half-lives estimated, i.e. 46.5 and 45.9 days, therefore the upper confidence bound on the mean metabolism half-life was used as the model input value.
[4] - a first order non-linear half-life was calculated from formation and decline curve using the maximum concentration as the initial concentration;

The aquatic EECs for 275-352I are provided in Table 8. The output files for aquatic exposure modeling for the degradate are provided in Appendix B.

Table 8. GENEEC Estimated EECs for 275-352I - Aquatic Exposure

Crop	Aquatic EECs in ppb				
	Peak	4 days	21 days	60 days	90 days
Apples	2.39	2.33	2.00	1.47	1.19
Cotton	0.69	0.67	0.58	0.43	0.34
Potato	0.59	0.57	0.49	0.36	0.29

Risk Quotients

The methodology for calculating RQs is presented in Appendix D. The resulting RQs for the parent toxicity values are presented in detail in Appendix E.

VI. Terrestrial Hazard, Exposure, and Risk Quotient Calculation

Appendix C provides tabular summaries of the toxicity studies material to the risk assessment for novaluron. The toxicity of novaluron, formulated products, and degradates are discussed below for each terrestrial taxonomic group studied.

Toxicity to Birds

Acute testing through oral gavage of technical Novaluron (GR 572) to bobwhite quail and mallard duck indicates that the LD_{50} is > 2000 mg/kg-body weight. The dietary LC_{50} for both species is > 5200 mg/kg-diet. No sub-lethal effects or other treatment related effects were observed in any of these studies with the exception of the bobwhite dietary study (MRID 454990-02) which recorded two mortalities in the 5200 mg a.i./kg treatment group, while body weight and food consumption were not affected by treatment. This classifies technical novaluron as practically non-toxic to birds. Details of the results are tabulated in Appendix C.

Chronic testing of Rimon technical to the bobwhite quail indicates a NOEAC of 301 mg/kg-diet based on the number of viable and live embryos, the number of hatchlings/hen, the number of 14 day old survivors/hen, and the number of 14-day old survivors of hatchlings. Test results from Rimon technical indicates that the mallard duck is more sensitive then the bobwhite quail. The mallard duck NOEAC is 9.8 mg/kg-diet based on the number of viable embryos/pen and viable 14-day embryos of eggs set.

Toxicity to Mammals

Acute testing through oral gavage of technical Novaluron (GR 572) to laboratory rats indicates that the LD_{50} is > 5000 mg/kg-body weight. This classifies the technical novaluron as practically non-toxic to birds. Data were not submitted for the major chlorophenyl urea (275 352 I) .

For chronic mammalian testing the two generation rat or mouse studies, and/or the developmental rabbit study are more relevant than the longer term mammalian carcinogenicity/ongocenicity studies. Accordingly, EFED has obtained the rat two generation rat toxicity study for the

novaluron technical (GR 572). The results from the two generation rat study indicates a NOEAC of 1000 mg/kg-diet (72.4 mg/kg bw/da) based on the epididymal sperm counts in the male F_1 generation. The reproductive NOAEL in females was≥12,000 ppm (1009.8 mg/kg bw/day). In addition, the parental systemic LOAEL was 1000 ppm (74.2 mg/kg bw/day in males, 84.0 mg/kg bw/day in females), based on increased absolute and relative spleen weights. Finally, the offspring LOAEL was 1000 ppm (74.2 mg/kg bw/day in males, 84.0 mg/kg bw/day in females), based on increased absolute and relative spleen weights. The parental offspring NOAELs were not identified.

Toxicity to Non-target Insects

An acute contact toxicity study to honeybees revealed a contact LD_{50} > 100 µg/bee. This classifies novaluron (Rimon technical) as practically non-toxic to non-target insects. However, three other non-target insect studies were submitted.

Honeybee hives fed sucrose solutions containing RIMON 10E C 3.3 (mL/L) showed significant ($p<0.05$) adverse effects on honey bee brood development at the egg, young larvae, and old larvae developmental stages(MRID # 456384-07). Overall failure rate of eggs in Rimon-treated hives was more that twice that of controls (100% failure for Rimon 10 EC treatment vs 49 % for control). Young larvae failure in Rimon-treated hives was almost 3 times that of controls (98% failure for Rimon 10 EC treatment vs 39% for control). Old larvae failure for Rimon-treated hives was 4 times greater than controls (79% failure for Rimon 10 EC treatment vs 19 % for control). The Rimon 10 EC dose was selected to represent the field application rate for the formulated product under field conditions. For comparison, review of the product labels for this risk assessment indicate that 14.4 mL/L Rimon 10 EC in the spray volume is the maximum formulated product concentration in spray.

A field study was conducted to evaluate the effects of Rimon 10 EC on honeybee application to citrus groves in Israel(MRID 45638409). Formulated product was applied at a rate equivalent to 0.2 lb/acre twide with an interval of 7 days. Applications were made during grove flowering. Bee hives were located within the test plots. Honeybee brood development was significantly impaired ($p<0.05$) at the egg, young larvae, and old larvae stages following the first application of pesticide. However, in cases where the hive subsequently removed the affected eggs of larvae, neew eggs had been laid and this second generation proceeded with normal development. Removal of hives after the test peridod and subsequent analysis of hive status over a further month showed no residual impairment of hive foraging activity nor adverse effects on the number of bees.

A field study designed to assess the impact of Rimon 10 EC on non-target arthropod insect populations in citrus groves in Sicily was submitted. Two applications were made at an interval of 7 days when oranges were reaching the end of flowering and the fruit was beginning to set. The organophosphate, diazanon was applied at sampling intervals to kill and collect all arthroods present by drop-net sampling. In addition, a control treatment of water, an IGR reference product (Cascade 50 DC) applied at 150 mL product/hL, and a conventional insecticide standard (Danitol) applied at a rate of 75 mL product/hL. Three plots of trees were treated for water control and Rimon 10 EC.treatments. One plot was used for each of the Cascade 50 DC and

Danitol treatments. Each plot consisted of 7 rows of 8 trees with 6m row spacing. The plots were separated by 1 row of untreated trees. Sampling methods consisted of drop netting to collect arboreal invertebrate fauna, and samples were taken one day before the first application and on days 0, 1, 2, 4, 6, 7, 9, 11, 13, 28, 42, 70, 99, and 176. Aat regular intervals up to 176 days after leaf inspection, aphid parasitoid sampling, and pitfall traps.to had significant effects on wasp and predatory mite populations, however, complete recovery occurred within two days and 2 months, respectively, after the second application (MRID # 456384-10). No other effects were observed in any of the other taxa collected throughout the study.

Toxicity to Earthworms

Acute toxicity studies to earthworms (*Fisenia foetida*) in accordance with OECD guidelines were performed for the Rimon technical novaluron and the degradate chlorophenyl urea (MRID# 456382-24 and 456382-25). The LC_{50} of the technical and the chlorophenyl urea degradate is >1000 and 447 mg/kg respectively. No sub-lethal effects were observed in these studies.

Toxicity to Non-target Plants

Terrestrial plant testing (seedling emergence and vegetative vigor) is required for herbicides that have terrestrial non-residential outdoor use patterns and that may move off the application site through volatilization (vapor pressure $>1.0 \times 10^{-5}$mm Hg at 25°C) or drift (aerial or irrigation) and/or that may have endangered or threatened plant species associated with the application site. Currently, terrestrial plant testing is not required for pesticides other than herbicides except on a case-by-case basis (*e.g.*, labeling bears phytotoxicity warnings incident data or literature that demonstrate phytotoxicity). Since novaluron is a new chemical insecticide and meets none of the above criteria, data will not be required at this time.

Exposure

Terrestrial exposure estimations differ for the groups of terrestrial organisms. One major difference in the way in which exposure scenarios are evaluated for terrestrial species is the methodology used for non-granular and granular applications. Since the proposed uses for novaluron is limited to a water dispersable granular and an emulsifiable concentrate, exposure scenarios were only considered for non-granular applications.

Birds and Mammals

Toxicant concentrations on terrestrial food items are based on data from by Hoerger and Kenaga (1972) as modified by Fletcher et al. (1994) that determined residue levels on various terrestrial items immediately following toxicant application in the field. These values are summarized in the table below.

Estimated Environmental Concentrations on Avian and Mammalian Food Items (ppm) Following a Single Application at 1 lb ai/A)

Food Items	EEC (ppm) Predicted Maximum Residue[1]	EEC (ppm) Predicted Mean Residue[1]
Short grass	240	85
Tall grass	110	36
Broadleaf/forage plants and small insects	135	45
Fruits, pods, seeds, and large insects	15	7

[1] Predicted maximum and mean residues are for a 1 lb ai/a application rate and are based on Hoerger and Kenaga (1972) as modified by Fletcher *et al.* (1994).

Toxicant concentrations on food items following multiple applications are predicted using a first-order residue decline method, EFED's "FATE5" model, which allows determination of residue dissipation over time incorporating a degradation half-life. Predicted maximum and mean EECs resulting from multiple applications estimates the highest one-day residue, based on the maximum or mean initial EEC from the first application, the total number of applications, interval between applications, and a first-order degradation rate, consistent with EFED policy. The input parameters for the pome fruit scenario were based on a maximum single application of 0.32 lb ai/A with a maximum of 3 applications per year and a 10 day interval between applications. The input parameters for the cotton scenario was a maximum single application of 0.09 lb ai/A applied 3 times per year with a 7 day interval between applications. Parameters used for the potato scenario were based on a single maximum application rate of 0.78 lb ai./A applied 3 times per year at minimum intervals of 10 days between applications. Initially, all the above scenarios used the 35 day foliar dissipation half-life since limited data were available on foliar residue studies.

Dietary exposure to mammals from liquid sprays is based upon EFEDs draft 1995 SOP for mammalian risk assessments and methods used by Hoerger and Kenaga (1972) as modified by Fletcher *et al.* (1994). The concentration of novaluron in the diet that is expected to be acutely lethal to 50% of the test population (LC_{50}) is determined by dividing the LD_{50} value (usually rat LD_{50}) by the amount of food, as percent (decimal of) body weight consumed. A risk quotient is then determined by dividing the EEC by the derived LC_{50} value. Acute RQs are calculated for three separate weight classes of mammals (15, 35, and 1000 g), each presumed to consume four different kinds of food (grass, forage, insects, and seeds). Chronic mammalian RQs are calculated using the most sensitive NOEC from the 2-generation rat study and the residue concentration expected on food items from Hoerger and Kenaga (1972) as modified by Fletcher *et al.* (1994).

According to proposed labeling banded, applications of sprays to cotton do not make adjustments to the application rate and the resulting treatment concentrates the per acre application rate into a narrow band. Banded applications are commonly adjusted to concentrate the treatment on the

plant rather than the surrounding soil between the rows. Therefore, the total per acre application rate can be adjusted (reduced) in proportion to the ratio of the treated to untreated bands. Birds, at least in theory, could be exposed to the higher concentration of toxicant by foraging or wandering into the treated band. EFED evaluated the banded risk to cotton by comparing the RQs from unadjusted band rates to those using the adjusted band rates to illustrate the increased risk. EFED assumed a 6 inch band and 30 inch row space as a typical banded application. The RQs indicate that levels of concern are not exceeded for either the adjusted or unadjusted rates with the exception of the endangered species LOC for 15 g birds when rates have not been adjusted.

The proposed label for use on cotton allows unincorporated banded treatments. Exposure to birds increases for banded applications since birds may forage within and between the treated bands unless the application rates are adjusted. Many labels require the formulators to reduce the application rate according to the following formula.

$$\frac{\textit{band width in inches}}{\textit{row width in inches}} \quad X \quad \textit{Broadcast rate per acre} \quad = \quad \textit{Rate per banded acre}$$

Since the registrant has opted not to adjust the banded application rate per label instructions, EFED will assume a 6 inch band and 30 inch row space as a typical banded application and the following formulas were used to calculate LD_{50} s per square foot.

$$\text{mg ai per ft}^2 = \text{App. Rate lbs ae/Acre} \times 453{,}590 \text{ mg/lbs} \times \text{Acre}/43{,}560 \text{ ft}^2 \times \%\text{unincorporated} \times \text{untreated row space (ft)/Bandwidth (ft)}$$

$$RQ = \frac{\text{mg ai}}{\text{ft}^2} \times \frac{1}{\text{Weight of Animal (g)}} \times \frac{1000 \text{ g}}{\text{kg}} \times \frac{\text{kg}}{\text{LD50 mg}}$$

Risk Quotients

The methodology for calculating RQs is presented in Appendix D. The resulting RQs for the parent toxicity values are presented in detail in Appendix E.

APPENDIX A: Detailed Drinking Water Assessment Memo

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

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

017

February 11,2004

MEMORANDUM

SUBJECT: Novaluron Estimated Drinking Water Concentration for Use in the Human Health Drinking Water Risk Assessment.
PC Code: 124002
DP Barcode: D285477 and D285479

FROM: Iwona L. Maher, Chemist
James Hetrick, Ph.D., Senior Scientist
Sid Abel, Branch Chief
Pat Jennings, Risk Assessment Process Leader
Environmental Risk Branch 1
Environmental Fate and Effects Division (7507C)

TO: Kathleen Martin, Chemist
Health Effects Division (7509C)

Tier II PRZM/EMAXS modeling was performed to estimate drinking water concentrations for the human health dietary risk assessment. The crops scenarios were selected to provide high-end drinking water concentrations for each crop and represent the geographic locations where the specific crops are grown in large quantities. The scenarios that were modeled are Pennsylvania, North Carolina and Oregon apples (airblast application), Mississippi cotton (ground and aerial application), and potato in Maine (ground and aerial application). The most conservative estimates were obtained for airblast applications of novaluron to PA apples at the maximum annual application rate of 0.96 lb a.i./acre, applied three times at 0.32 lb a.i./acre with an interval between applications of ten days. The predicted 1 in 10 year annual peak concentrations of novaluron in drinking water from surface water for PA apples of 11.4 µg/L exceeds the solubility of the compound (3 µg/L) , which is expected to be an upper bound environmental concentration. The estimated 1 in 10 year annual mean concentration of novaluron in drinking water is 1.8

µg/L. The 30-year annual mean concentration is 1.2 µg/L. Both peak and annual average concentrations for all other scenarios were lower. Table 1 lists estimated drinking water concentrations from surface water sources for all modeled scenarios.

Novaluran is an insect growth regulator that must be ingested by insect larvae to be fully effective. The pesticide is registered for insect pest control on ornamentals grown in greenhouses and nurseries. The registrant submitted a petition for Novaluran first food use on pome fruits (apples and pears), cotton, and potato. Novaluron, the active ingredient in RimOn, is a benzoylphenyl urea compound whose mode of action results from the inhibition of chitin biosynthesis. RimOn is applied at a maximum rate of 0.09 lb ai/A by either ground or aerial applications up to 3 times per year (0.27 lb ai/yr.) on cotton, at a maximum rate of 0.078 lb ai/A by ground or aerial application up to 3 times per year (0.23 lb ai/) on potato, and at a rate of 0.32 lb ai/A by airblast up to 3 times per year (0.96 lb ai/yr.) on large orchard trees.

A complete set of fate and transport data were submitted for novaluron. Fate data submitted for the novaluron degradate chlorophenyl urea (275-352I) was limited to the adsorption/desorption study. No data were submitted for chloroaniline degradate. Based on laboratory and field studies, novaluron appears to be immobile and ranges from moderately persistent to persistent in the field. It biodegrades in soil under aerobic conditions with half-lives of 7 to14.5 days, strongly adsorbs to soil and sediment (simple K_d values ranged from 95 to 247), and is stable to hydrolysis and photodegradation. Due to its high sorptive properties (Koc = 6,680-11,813) on soil the chemical has low potential for leaching into ground water. In the field, novaluron appears to degrade with half-lives ranging from 20 to 178 days. The laboratory and field data suggest that novaluron may be more persistent in colder climates. At 50 °C and pH 9 novaluron hydrolyzes very rapidly with a half-life of 1.2 days. In aerobic soils it degrades slower at 10 °C (i.e., half-life 31.9 days) than at 20 °C (i.e., half-lives from 7 to 14.5 days). Novaluron has the potential to reach surface water through runoff weeks to months following application, and through spray drift during application.

The HED MARC concluded that parent, chlorophenyl urea (1 -[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy) phenyl] urea) (275-352I), and chloroaniline (3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline) are residues of potential concern to be included in the drinking water assessment. Chlorophenyl urea (275-352I) is a major degradate of novaluron formed in aerobic soil metabolism and aquatic anaerobic metabolism. The degradate appears to be mobile (Kds = 16.7 - 61.5), moderately persistent in soil (decline curve estimated $t_{1/2}$ = 46.5 and 45.6 days; GLN 162-1), and moderately persistent in aquatic environment (decline curve estimated $t_{1/2}$ = 26.6 days; GLN 162-4). It has potential to reach surface water through runoff and has low potential to reach ground water resources. The cloroaniline degradate formed in aerobic soil metabolism. Although formation of chloroaniline in soil didn't exceed 10% of the applied dose (i.e., the maximum concentration was 8.5% at 120 days posttreatemnt). the major degradate chlorophenyl urea (275-352I) is expected to further degrade in the environment to form chloroaniline.

Table 1. Novaluron estimated drinking water concentrations for surface water sources.

Scenario	Application Type	Estimated Drinking Water Concentrations from Surface Water Sources (ppb)		
		1 in 10 year annual peak	1 in 10 year annual mean	36 year annual mean
PA apples (PCA = 0.87)	airblast	11.4*	1.8	1.2
NC apples (PCA = 0.87)	airblast	4.24*	0.6	0.38
OR apples (PCA = 0.87)	airblast	1.6	0.38	0.31
MS cotton (PCA = 0.20)	ground aerial	0.70 0.78	0.07 0.08	0.04 0.05
ME potato (PCA = 0.87)	ground aerial	2.15 2.43	0.38 0.45	0.24 0.32

*These values exceed the measured water solubility of novaluron of 3 µg/L (3 ppb).

Additionally, for novaluron degradates, 1-[3-Chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea (275-352I) and 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline (275-309I) a Tier I drinking water assessment was performed. An estimated peak drinking water concentration of 275-352I from surface water sources is 4.6 µg/L and 11.4 µg/L for 275-309I based on novaluron's maximum application rate of 0.32 lb ai/acre applied 3 times a season (0.96 lbs ai/year; apples). An estimated annual average concentration of chlorophenyl urea (275-352I) is 0.86 µg/L and for the chloroaniline is 2.6 µg/L from the same novaluron application rate. Table 2 lists estimated drinking water concentrations for both degradates for all novaluron proposed maximum uses. For modeling assumptions and conversion from the parent to the degradate, refer to the Surface Water Assessment section.

Table 2. Degradates' estimated drinking water concentrations for surface water sources based on Tier I modeling.

Novaluron Metabolite	Crop	Application Rate	Estimated Drinking Water Concentrations from Surface Water Sources (ppb)	
			Peak	Annual Average
chlorophenyl urea	apples:	3 X 0.32 lb a.i./acre	4.56	0.86
	cotton	3 X 0.09 lb a.i./acre	0.3	0.057
	potato	3 X 0.078 lb a.i./acre	1.12	0.21
chloroaniline	apples	3 X 0.32 lb a.i./acre	11.4	2.61
	cotton	3 X 0.09 lb a.i./acre	0.75	0.17
	potato	3 X 0.078 lb a.i./acre	2.8	0.64

SCI-GROW modeling predicted a ground water concentration for novaluron at the annual application rate of 0.96 lb a.i./acre (i.e., three applications of 0.32 lb a.i./acre) of 5.5×10^{-3} µg/L

in drinking water from shallow ground water sources. The predicted ground water concentration is 4.5×10^{-3} µg/L for chlorophenyl urea and 9.0×10^{-3} µg/L for chloroaniline from novaluron's maximum application rate (0.96 lb a.i./acre). Both concentrations were estimated with the same assumption used for surface water modeling. These concentrations may be considered as both the peak and annual average upper bound exposures.

INTRODUCTION

Mode of Action

Novaluron is a benzoylphenyl urea insect growth regulating insecticide. Its larvalcidal action results from the inhibition of chitin biosynthesis and interference in the cuticle formation in target pests.

Proposed uses

For food use the registrant proposed two novaluran formulations: 7.5% water dispersible granule (RimOn 7.5WDG) insect growth regulator for control of insect pests on apples and pears, and 10% emulsifiable concentrate (RimOn 10EC) insect growth regulator for use on cotton and potato. The insecticide should be applied to foliage by conventional ground or airblast sprayer. According to the proposed label no more than 0.96 lbs a.i. (RimOn 7.5WDG) may be applied per acre per year, with the maximum rate per application of 0.32 lbs a.i., a minimum intervals of 10 to 14 days between applications, and up to 3 applications per year. No application should be made within 14 days of fruit harvest. RimOn 10EC should be applied via conventional ground or aerial sprayer to cotton and potatoes, or when cotton plants are small, via band application. On cotton, the maximum proposed application rate is 0.27 lb a.i. (RimOn 10EC) per acre per year, with the maximum rate per application of 0.09 lbs a.i., a minimum intervals of 7 to 14 days between applications, and up to 3 applications per year. On potatoes the maximum proposed application rate is 0.23 lb a.i. (RimOn 10EC) per acre per year, a maximum rate per application of 0.078 lbs a.i., a minimum intervals of 10 to 14 days between applications, and up to 3 applications per year. No application should be made within 30 days of harvest (cotton and potatoes).

Table 3. Pesticide Name, Identification Number, Structure, and its Physical/Chemical Properties

Common Name:	Novaluron	
PC Code:	124002	
IUPAC Name:	1-[3-Chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	
CAS Name:	N-[[[3-Chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]-amino]carbonyl]-2,6-difluorobenzamide	
CAS Number	116714-46-6	
Molecular Formula:	$C_{17}H_9ClF_8N_2O_4$	
Molecular Weight (g/mole):	492.7	
Water Solubility:	0.003 mg/L at 25 °C	(MRID 45638203)
Vapor Pressure:	1.2×10^{-7} mm Hg	
Henry's Law Constant:	2.0 Pa m^3 Mol^{-1}	
log K_{ow}:	4.3	(MRID 45638405)

Structure:

ENVIRONMENTAL FATE SUMMARY

Environmental fate data indicate that novaluron is immobile and moderately persistent to persistent in the field. Laboratory studies suggest that novaluron's major route of disappearance is microbially-mediated degradation. The chemical tends to strongly adsorb to soil and sediment, and it is stable to abiotic processes. Novaluron has a very low potential to reach ground water. During surface runoff conditions, novaluron may reach water bodies as bound to soil particles and will likely partition into sediments once in surface water. Additionally, contribution to surface water contamination may occur from spray drift.

At 20 °C, in soil under aerobic conditions novaluron metabolizes to form chlorophenyl urea (275-352I) with half-lives ranging from 7 to 14.5 days (20 °C, MRIDs: 44961009 and 44961010) and chloroaniline. At lower temperatures (i.e.,10 °C), novaluron degrades slower (i.e., half-life of 31.9 days (MRID 44961009)) than at 20 °C. In aquatic environments under stratified redox conditions (aerobic conditions in water and anaerobic conditions in soil) the chemical metabolizes with total system half-lives of 9.7 and 19.7 days (MRID 45638206). In laboratory studies it rapidly dissipates from the water column with a half-life of 1.2 days under aerobic conditions and less than 3 days under anaerobic condition. Under anaerobic conditions in water-soil systems it biodegrades slower with half-life a total system half-lives of 49 and 51 days (MRIDs: 45638205 and 45789203). A proposed transformation pathway indicates that in aquatic environments novaluron forms 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl urea (275-352I) and 2,6-difluorobenzoic acid (275-158I, DFBA) through amide hydrolysis. Further hydrolysis of 275-352I yields 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline (275-309I) and hydrolysis of 275-158I yields 2,6-difluorobenzamide (275-157I) (MRID 5638206).

Novaluron appears to be stable to hydrolysis at pH 5, 7, and 9 (pH 9 $t_{1/2}$ (25 °C) = 101 days; MRID 44961008) and stable to both soil and aqueous photolysis (soil photolysis $t_{1/2}$ = 257 days, MRID 45638204; aqueous photolysis $t_{1/2}$ = 187 days, MRID 45638203). At 50 °C at pH 9, however, novaluron appears to hydrolyze rapidly with a half-life of 1.2 days. Novaluron tends to adsorb strongly to soil and sediment. The mean simple K_d values ranged from 95 to 247 ml/g, and K_{oc} values from 6,650 to 11,813 (MRID 44961012). There was no linear relationship between the soil organic carbon content and the K_d values for different soils thus the K_{oc} model may not be appropriate. Because novaluron was tested only at one concentration the Freundlich adsorption/desorption coefficients could not be calculated.

The high sorptive properties of novaluron indicate a low potential for leaching to ground water. In the field dissipation study conducted in North America, sites located in CA, LA, NY, WA, Nova Scotia, and Ontario, novaluron residues were not detected above 0.0851 ppm (Nova Scotia) in the 15-30 cm soil depth and above 0.0606 ppm (Ontario) in the 30-45 cm soil depths (MRID 45789204). In all sites, total water inputs (rainfall plus irrigation) were greater than the 10-year average rainfall except for the Nova Scotia site. Novaluron (RimOn 10EC) was not detected above the LOQ (10 ppb) at any sampling interval or in any replicate sample in the 10-20 cm soil depth when applied to bare soil in Spain and Germany (GLN 164-1; MRID 45638403). In these foreign studies pan evaporation data were not reported to assess whether sufficient moisture was present in the soil to facilitate leaching of the test substance. Irrigation was not applied to any of the test plots during the study trials and monthly rainfall data indicated that in the first 3 to 7 months rainfall was below historical average.

In the domestic terrestrial field dissipation studies novaluron (RimOn 10EC and RimOn 6.7WDG) dissipated with half-lives ranging from 20 to 178 days (i.e., in CA with a half-life of 20 days, in WA with a half-life of 61 days, in Nova Scotia with a 89 days, and in NY with a half-life of 178 days (valid $t_{1/2}$ could not be determined for the LA and Ontario sites)). There is, however, a great deal of uncertainty associated with the half-lives calculated at the NY and Nova Scotia sites due to high data variability, both between replicates and over time. In the field dissipation studies conducted in Spain and Germany, novaluron (RimOn 10EC) dissipated with half-lives ranging from 52 to 178 days (MRID 45638403). In five out of six sites in the North American field studies chlorophenyl (275-352I) urea was detected as a major transformation product (MRID 45789204).

In a microcosm study, novaluron exhibited water column DT9O values ranging from 12 to 20 days for three different test concentrations (i.e., 5, 15, and 50 g a.i./ha treatment level; MRID 45785801). Only low concentrations of novaluron were detected in sediment, demonstrating potential for microbial degradation. This was confirmed by the presence of the main degradate, chlorophenyl urea (275-352I), in the water column of three out of five tested concentration and in soil of the highest tested concentration. Chlorophenyl urea (275-352I) was the only degradate analyzed in water and sediment.

Novaluron appears to accumulate in edible and nonedible fish tissues. In a standard bioconcentration study using the bluegill sunfish, the highest mean bioconcentration factor (BCF) in whole fish was 14,431 x. The half-life for clearance of residues in the bluegill was 3.9 to 7.3 days for whole fish (MRID 45638215).

The major novaluron degradate, 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluorometh oxyethoxy) phenyl]urea (275-352I), was formed in aerobic soil metabolism at a maximum rate of 26.6% of the applied parent at 7 days posttreatment (MRID 44961009). Based on the McCall et al., 1980 classification system the degradate appears to have low to slight mobility in soil (K_{oc} values range from 1950 to 2563 L/kg; 163-1; MRID 45638201). The Freundlich isotherm, however, may not adequately represent adsorption of the compound across all concentrations (the 1/n values were not within the range of 0.9 to 1.1). Based on a laboratory study, novaluron degradates appear to have a very low potential for leaching into ground water. Chlorophenyl urea (275-352I) has the potential to reach surface water through runoff. Its aerobic soil

metabolism half-lives estimated from the formation and decline curves (MRID 44961009) are 46.5 and 45.9 days. The degradate may be moderately persistent in the aquatic environment. The half-life was determined from the first-order degradation rate from the maximum concentration in the aerobic aquatic metabolism study (MRID 4538206). The aerobic aquatic metabolism half-life is 26.6 days in a Houghton Meadow water-loamy sand sediment.

Another novaluron degradate of potential concern is 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline (chloroaniline, 275-309I) was formed in the aerobic soil metabolism study at a maximum rate of 8.5% of the applied at 120 days posttreatment, the last sampling interval (MRID 44961009). Additionally, it is expected that chloroaniline is formed from the further degradation of the major degradate chlorophenyl urea (275-352I) (MRIDs: 45638205 and 45789203). In the anaerobic aquatic metabolism study, at the last sampling interval, i.e. 363 days posttreatment, the maximum of 32% of the applied was formed in the soil and 49.8% in the total system, this includes soil and volatilized chloroaniline. This degradate has the potential to be volatile (i.e., its estimated vapor pressure exceeds 10^{-4} mmHg), more mobile (K_{oc} (an estimated value) = 5899) and more persistent than the parent. Degradation rates for chloroaniline could not be calculated due to the lack of formation and decline data.

DRINKING WATER ASSESSMENT

Fate and transport data submitted for novaluron were sufficient to characterize drinking water exposures. Fate data submitted for the novaluron degradate chlorophenyl urea (275-352I) was limited to the adsorption/desorption study. For modeling purpose, chlorophenyl urea (275-352I) aerobic soil mentalism and aerobic aquatic metabolism rates were estimated based on the formation and decline curves from the laboratory studies submitted for the parent (MRIDs: 44961009 and 45638206). No data were submitted for the chloroaniline degradate. Its physico-chemical properties were estimated using structure activity relationships (SAR) (Howard and Meylan, 2001).

Monitoring data for novaluron, chlorophenyl urea (275-352I) and chloroaniline in surface water and ground water were not found. Novaluron is not included in the USGS National Water-Quality Assessment (NAWQA) Program, the Pesticides in Ground Water Database (USEPA, 1992), and it was not an analyte in the National Pesticide Survey (USEPA, 1990). Concentrations of novaluron and its degradates, chlorophenyl urea (275-352I) and chloroaniline in surface water and ground water were estimated using modeling. The drinking water assessment was based on the maximum annual application rates on apples, cotton, and potatoes as specified on the labels. These uses are the only food uses registered or proposed to date.

Surface Water Assessment

For the drinking water assessment, a Tier II PRZM-EXAMS (PRZM 3.12 and EXAMS 2.975) modeling simulation was performed using the index reservoir (IR) scenario and the percent crop area (PCA) adjustment factor for the use of novaluron on apples in PA, NC and OR to represent

to pome friut group, cotton in MS, and potatoes in ME. The crops scenarios were selected to provide high-end drinking water concentrations for each crop and represent the geographic locations where the specific crops are grown in large quantities. For the GIS maps refer to Attachment 1. These graphics indicate that for several of the scenarios, ME potatoes and MS cotton, major combined and single crop production areas are well represented. In addition, several scenarios, OR, PA and NC apples are in productions areas with a high density of community drinking water systems. There are several areas where single or combined crop productions is greater than those areas selected for modeling. These areas have been determined to be less vulnerable to runoff. The East and West coast apple scenarios simulated three applications of 0.32 lbs ai/acre with a 10-day interval between applications per label. The MS cotton scenario simulated three application of 0.09 lbs ai/acre with a 7-day interval between applications per label. The ME potato scenario simulated three applications of 0.078 lbs ai/acre with 10-day interval between applications per label. A graphical interface shell, PE4V01.pl (dated 8/8/2003), was used to facilitate in input of use-specific information in the PRZM input (inp) and the EXAMS chemical files.

There are some uncertainties associated with the results of several input parameters. The half-life of photodegradation in water half-life was estimated from extremely variable data within and between labeled study concentration data (r^2 ranged from 0.0039 to 0.6516). However, because novaluron has a very long photodegradation half-life, it is not expected to impact the confidence in estimating environmental concentrations. The soil adsorption/desorption coefficient was based on supplemental adsorption/desorption data. Novaluron was tested at a single concentration and the Freundlich adsorption/desorption coefficients (K_{ads} and K_{des}) could not be calculated. Additionally, instead of being measured, the concentrations of novaluron adsorbed to the soil were calculated. Aerobic aquatic metabolism data were only available for water/sediment systems tested under stratified redox potential where water was under aerobic and sediment under anaerobic conditions throughout the test. Moreover, foliar dissipation half-lives were not considered in the modeling. Tables 4 and 5 list the PRZM/EXAMS modeling input parameters.

Table 4. Environmental Fate and Chemistry Input Parameters for Novaluron

Parameters	Input Value and Unit	Source of Info/Reference
Maximum Application Rates [1]	apples = 0.359 kg ai/ha cotton = 0.100 kg ai/ha potato = 0.087 kg ai/ha	Product Labels: RimOn 7.5WDG; EPA Reg. No. 66222-LT RimOn 10EC; EPA Reg. No. 66222-35 RimOn 10EC; EPA Reg. No. 66222-35
Maximum Number of Applications	apples = 3 cotton = 3 potato = 3	Product Labels as above
Minimum Interval Between Applications	apples = 10 days cotton = 7 days potato = 10 days	Product Labels as above
Soil Partition Coefficient (K_d)[2]	133 ml/g	MRID 44961012
Molecular Weight	492.7	Registrant data
Solubility (at 25 °C) x 100	0.3 ppm	Registrant data (MRID 45638203)
Vapor Pressure	1.2×10^{-7} mm Hg	Registrant data
Henry's Constant at 25 °C	1.974×10^{-13} atm•m³/mol	Registrant data
Aerobic Soil Metabolism $T_{1/2}$[3]	15.6 days	MRIDs: 44961009 and 44961010
Foliar Dissipation $T_{1/2}$	-	was not considered in the modeling
Aqueous Photolysis (pH 5) $T_{1/2}$[4]	187 days	MRID 45638203
Hydrolysis $T_{1/2}$ (pH7)	stable	MRID 44961008
Aerobic Aquatic Metabolism Half-life[5]	30.1 days	MRID 45638206
Anaerobic Aquatic Metabolism Half-life[5]	52.1 days	MRIDs: 45638205 and 45789203

[1] - One planting per year was assumed and the annual rate is assumed to be the seasonal rate

[2] - The lowest non-sand K_d for sandy loam with sand content < 70% was used. Out of four K_f values (133, 247, 184, and 95) the lowest non-sand K_f for sandy loam was used (K_{oc} model was not valid).

[3] - Since n=4: to account for the inherent variability the constant rate of the upper confidence bound on the mean (mean half-life (of 14.5, 13.7, 7, and 11.5) + $(t_{90}\ \sigma)/\sqrt{n}$ (single tail student's t, α=0.1 where n = number of values)) aerobic soil metabolism half-life was used

[4] - individual data points were very variable so the accuracy of the half-life is uncertain

[5] - since n=2 (aerobic $T_{1/2}$: 19.7 and 9.7 days; anaerobic $T_{1/2}$: 50.6 and 49.2 days), the upper confidence bound on the mean aquatic metabolism half-life was used.

Table 5. Additional PRZM-EXAM Input Parameters for Novaluron

Parameters	Input Value and Unit	Source of Info/Reference
First Application Date (day-month)	apples = PA: 25-07 NC: 20-05 OR: 05-08 cotton = MS:20-07 potato = ME:15-06	assumed based on crop profiles and probable target insect infestation
Rainfall Data (Metfile)	apples = PA: W14737.dvf NC: W03812.dvf OR: W24229.dvf cotton = MS: W03940.dvf potato = ME: W14607.dvf	Individual crops' scenarios
Application Fraction	apples airblast = 0.99 cotton & potato aerial = 0.95 cotton & potato ground = 0.99	Guidance for Selecting Input Parameters in Modeling the Environmental Fate and Transport of Pesticides; Feb. 28, 2002
Spray Drift Fraction	apples airblast = 0.063 cotton & potato aerial = 0.16 cotton & potato ground = 0.064	as above

The highest EECs were obtained for airblast application of novaluron to PA apples at the maximum annual application rate of 0.96 lb a.i./acre, applied three times at 0.32 lb a.i./acre with an interval between applications of ten days. The simulated 1 in 10 year annual peak concentration of novaluron in drinking water was 11.4 µg/L in a PA apples index reservoir scenario adjusted for a default PCA factor of 0.87. The annual peak concentration in drinking water from surface water estimated by PRZM/EXAMS exceeded the water solubility of novaluron of 3 µg/L. The simulated 1 in 10 year annual mean concentration of novaluron in drinking water was 1.8 µg/L and 30 year annual mean concentration was 1.2 µg/L in the same scenario. Table 1 lists estimated drinking water concentrations from surface water sources for all modeled scenarios. The PRZM/EXAMS output files for novaluron are presented in Appendix B.

For the degradate chlorophenyl urea (275-352I) Tier I drinking water analysis was performed. For the surface water modeling the FIRST model was used as if chlorophenyl urea (275-352I) was "ground" applied, i.e. as granular, to the field with no spray drift and no foliar interception as the degradate is formed in the top soil layer from the parent. The FIRST model estimates a peak and an annual average value based on the Index Reservoir scenario. It uses a percent cropped area factor (PCA) to adjust the Estimated Environmental Concentrations (EECs) for the fraction of the watershed which is planted in the modeled crop. A default value of 0.87 was used for apples and potato, and estimated 0.20 for cotton cropped area factor. The degradate scenario was based on the following: (1) assuming 26.6% (MRID 44961009) conversion from parent to chlorophenyl urea (275-352I) and (2) using molecular weight conversion to adjust from parent application rate to chlorophenyl urea (275-352I) application rate. Table 6 lists the modeling

input parameters.

Table 6. FIRST Input Parameters for 1-[3-Chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea

Parameters	Input Value and Unit	Source of Info/Reference
Maximum Application Rates [1]	apples = 0.061 lb/acre cotton = 0.017 lb/acre potato = 0.015 lb/acre	$rate_{der} = rate_{par} * (MW_{deg}/MW_{par}) * (max.\ \%\ form.\ rate/100)$
Maximum Number of Applications	apples = 3 cotton = 3 potato = 3	Product Labels: RimOn 7.5WDG; EPA Reg. No. 66222-LT RimOn 10EC; EPA Reg. No. 66222-35 RimOn 10EC; EPA Reg. No. 66222-35
Minimum interval between applications	apples = 10 days cotton = 7 days potato = 10 days	Product Labels as above
Soil Partition Coefficient (K_d)[2]	16.7	MRID 45638201 (GLN 163-1)
Aerobic Soil Metabolism $T_{1/2}$[3]	47.1 days	MRID 44961009
Wetted in	No	Product Label
Depth of incorporation (inches)	0	Product Label
Method of application	granular	assumed; a degradate formed in soil
Solubility in water at 20 °C	33 ppm	MRID 45638201
Aerobic aquatic metabolism half-life[4]	79.8 days	MRID 45638206
Aqueous Photolysis $T_{1/2}$	stable	assumed; data not available

[1] – Application rate of 275-352I is based on the maximum formation rate of 26.6 % from parent novaluron found in the aerobic soil metabolism study (MIRD 44961009) and molecular weigh conversion (MW_{par} = 492.7; MW_{deg} = 352.6).
[2] - the lowest non-sand K_f(sandy loam) was used. Out of four K_f values (35.1; 16.7; 61.5; and 47.6) the lowest non-sand K_f for sandy loam was used (K_f may not equal K_d).
[3] - 275-352I first order non-linear half-lives were estimated from formation and decline curves using the maximum concentration as the initial concentration; since there were two valid half-lives estimated, i.e. 46.5 and 45.9 days, therefore the upper confidence bound on the mean metabolism half-life was used as the model input value.
[4] - a first order non-linear half-life was calculated from formation and decline curve using the maximum concentration as the initial concentration; since there was only one valid half-life (26.6 days; in Houghton Meadow water-loamy sand sediment) available as a model input value $t_{1/2}$ x3 = 79.8 was used.

An estimated peak drinking water concentration of chlorophenyl urea (275-352I) from surface water sources is 4.6 µg/L from novaluron use on apples at the maximum application rate of 0.32 lb ai/acre applied 3 times a season (0.96 lbs ai/year; RimOn 7.5WDG). An estimated annual average concentration of chlorophenyl urea (275-352I) is 0.86 µg/L from the same use rate.

From novaluron use on cotton at the maximum application rate of 0.09 lb ai/acre applied 3 times a season (0.27 lbs ai/year; RimOn 10EC) the estimated peak drinking water concentration of chlorophenyl urea (275-352I) is 0.30 µg/L. From the same use on cotton an estimated annual average concentration is 0.06 µg/L. An estimated peak concentration of chlorophenyl urea (275-352I) is 1.1 µg/L and an estimated annual average concentration is 0.21 µg/L from novaluron use on potato at the maximum application rate of 0.078 lbs ai/acre applied 3 times a season (0.23 lbs ai/year; RimOn 10EC). The FIRST output files for chlorophenyl urea (275-352I) are presented in Appendix II.

Additionally, Tier I drinking water analysis were performed for chloroaniline. Because non of the laboratory studies submitted for novaluron were conducted long enough to establish the pattern of formation and decline of chloroaniline the maximum formation rate is unknown. Therefore, the degradate scenario was based on the following: (1) assuming 100% conversion from parent to chloroaniline and (2) using molecular weight conversion to adjust from parent application rate to chloroaniline application rate. Table 7 lists the modeling input parameters.

Table 7. FIRST Input Parameters for 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline

Parameters	Input Value and Unit	Source of Info/Reference
Maximum Application Rates [1]	apples = 0.20 lb/acre cotton = 0.057 lb/acre potato = 0.049 lb/acre	$rate_{der} = rate_{par} * (MW_{deg}/MW_{par}) *$ (max. % form. rate/100)
Maximum Number of Applications	apples = 3 cotton = 3 potato = 3	Product Labels: RimOn 7.5WDG; EPA Reg. No. 66222-LT RimOn 10EC; EPA Reg. No. 66222-35 RimOn 10EC; EPA Reg. No. 66222-35
Minimum interval between applications	apples = 10 days cotton = 7 days potato = 10 days	Product Labels as above
Soil Partition Coefficient (K_{oc})	5899	Estimated [2]
Aerobic Soil Metabolism $T_{1/2}$	stable	assumed; data not available
Wetted in	No	Product Label
Depth of incorporation (inches)	0	Product Label
Method of application	granular	assumed; a degradate formed in soil
Solubility in water at 25 °C	10.6 ppm	Estimated [2]
Aerobic aquatic metabolism half-life	stable	assumed; data not available
Hydrolysis $T_{1/2}$ (pH7)	stable	assumed; data not available
Aqueous Photolysis $T_{1/2}$	stable	assumed; data not available

– Application rate of 275-309I is based on 100% formation from parent novaluron and molecular weigh conversion (MW_{par} = 492.7; MW_{deg} = 310.6).

[2] - Estimated using substructure physical/chemical property computer program (Howard and Meylan, 1995).

The estimated peak and annual average drinking water concentrations for chloroaniline are provided in Table 8.

Table 8. FIRST Estimated Peak and Annual Avg. Drinking Water Concentrations for 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline

Crops and Novaluron Application Information (type, max single application rate, max no of applications, min interval between applications)	Chloroaniline Drinking Water Concentrations (ppb)	
	Peak	Annual Average
Apples (airblast, 0.32 lb/acre, 3x, 10 days)	11.4	2.6
Cotton (ground and aerial, 0.09 lb/acre, 3x, 7 days)	0.75	0.17
Potato (ground and aerial, 0.078 lb/acre, 3x, 10 days)	2.8	0.64

The FIRST output files for chloroaniline are presented in Appendix B.

Assumptions and Uncertainties

Due to a lack of physico-chemical properties and fate data for chloroaniline degradate the Tier I modeling is likely a bounding exposure scenario for drinking water. In addition, the assumed 100% conversion from parent to chloroaniline further increases uncertainty of the estimated drinking water concentrations and is likely to result in higher concentrations.

The modeling for chlorphenyl urea (275-352I) was performed based on its maximum formation in soil in the aerobic soil metabolism study (i.e., 26.6% of the applied parent at 7 days posttreatment; MRID 44961009). Novaluron, however, will potentially form up to 33.2% of chlorophenyl urea (275-352I) in sediment as shown by an anaerobic aquatic metabolism study (MRID 45789203). Therefore, the predicted drinking water concentrations for 275-352I may be underestimated.

A change of date of insect treatment may also change the estimates for novaluran drinking water concentrations. Application dates will vary greatly, depending on time of year, weather conditions, stage of crop growth, and when insect outbreaks occur.

Ground Water Assessment

According to the McCall classification (McCall *et al.*, 1980) novaluron appears to be immobile in soils. It is unlikely that novaluron would reach potable ground water resources. In the field dissipation studies conducted in North America, the residues were detected in the 15-30 cm soil depth at maximum concentrations of 0.0851 ppm (Nova Scotia) and 0.0606 ppm in the 30-45 cm soil depths (Ontario) (MRID 45789204). Total water inputs (i.e., rainfall plus irrigation), in these studies were greater than the 10-year average at all sites with the exception of Nova Scotia where water input was 81.5% of the 10-year average. Novaluron (RimOn 10EC) was not detected above the LOQ (10 ppb) at any sampling interval or in any replicate sample in the 10-20 cm soil depth when applied to bare soil in Spain and Germany (GLN 164-1; MRID 45638403). In these studies, however, rainfall, in general, was below historical average during the first three to seven months following application.

Based on a laboratory aged column leaching study novaluron degradates appear to have a very low potential for leaching into ground water. No radiolabeled residues were identified below the treated 0-8 cm soil layer. An adsorption-desorption study indicates that chlorophenyl urea (275-352I) appears to have low to slight mobility in soil. Laboratory data are not available for chloroaniline. The degradate has potential to be more mobile than novaluron. Chlorophenyl urea (275-352I), the only degradate analyzed in the field studies, was detected above the LOQ (0.01 ppm) at all sites but CA. In three out of six sites, LA, WA, and Ontario, the degradate was not detected above the LOQ below the 0-15 cm soil depth. At the NY site, the degradate was detected once at 0.0266 ppm (single replicate) in the 15-30 cm soil depth and at the Nova Scotia site was sporadically detected at ≤0.0186 ppm (single replicate) in the 15-30 cm soil depth, and was not detected below that depth.

The SCI-GROW (SG23.exe, version 2.3, dated July 29, 2003) screening model was used to estimate ground water concentrations. The model estimates the upper bound ground water concentrations of pesticides likely to occur when the pesticide is used at the maximum allowable rate in areas where ground water is particularly vulnerable to contamination. Table 9 lists the input parameters used to model concentrations of novaluron in ground water.

Table 9. SCI-GROW Input Parameters for Novaluron

Parameter	Input Value and Units	Source of Info/Reference
Maximum Application Rate [1]	apples = 0.32 lb ai/acre cotton = 0.09 lb ai/acre potato = 0.078 lb ai/acre	Product Labels: RimOn 7.5WDG; EPA Reg. No. 66222-LT RimOn 10EC; EPA Reg. No. 66222-35 RimOn 10EC; EPA Reg. No. 66222-35 (??)
Max Number of Applications per year	apples = 3 cotton = 3 potato = 3	Product Labels as above
Partition Coefficient Normalized to Organic Carbon Content [2] - K_{oc}	9965 L kg o.c.$^{-1}$	MRID 44961012 (GLN 163-1)
Aerobic Soil Metabolism nonlinear $t_{1/2}$ [3]	12.6 days	MRIDs: 44961009 and 44961010 (GLN 162-1)

[1] - One planting per year was assumed and the annual rate is assumed to be the seasonal rate.

[2] - The median K_{oc} value from four measurements (10271, 6650, 9658, and 11813 L/kg) was used.

[3] - There were four aerobic soil metabolism $t_{1/2}$ values (14.5, 13.7, 7, and 11.5 days) available so the median half-life value was used.

Estimated concentrations of novaluron in drinking water from shallow ground water sources are 5.5×10^{-3} µg/L for applications on apples at 0.32 lbs ai/A (RimOn 7.5WDG) applied 3 times per year, 1.6×10^{-3} µg/L for applications on cotton at 0.09 lbs ai/A (RimOn 10EC) applied 3 times per year, and 1.35×10^{-3} µg/L for applications on potatoes at 0.078 lbs ai/A (RimOn 10EC) applied 3 times per year. These concentrations may be considered as both peak and annual average upper bound concentrations.

The SCI-GROW model was also used to estimate ground water concentrations of chlorophenyl urea (275-352I) and chloroaniline. The modeling assumptions were the same as for surface water modeling of the degradates (see Surface Water Assessment). Table 10 lists the modeling input parameters for chlorophenyl urea (275-352I) and Table 11 for chloroaniline.

Table 10. SCI-GROW Input Parameters for 1-[3-Chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea

Parameter	Input Value and Units	Source of Info/Reference
Maximum Application Rate [1]	apples = 0.061 lb/acre cotton = 0.017 lb/acre potato = 0.015 lb/acre	$rate_{der} = rate_{par} * (MW_{deg}/MW_{par}) *$ (max. % form. rate/100)
Max Number of Applications per year	apples = 3 cotton = 3 potato = 3	Product Labels: RimOn 7.5WDG; EPA Reg. No. 66222-LT RimOn 10EC; EPA Reg. No. 66222-35 RimOn 10EC; EPA Reg. No. 66222-35 (?)
Partition Coefficient Normalized to Organic Carbon Content [2] - K_{oc}	2297 L kg o.c.$^{-1}$	MRID 45638201 (GLN 163-1)
Aerobic Soil Metabolism nonlinear $t_{1/2}$ [3]	46.2 days	MRID 44961009 (GLN 162-1)

[1] – Application rate of 275-352I is based on the maximum formation rate of 26.6 % from parent novaluron found in the aerobic soil metabolism study (MIRD 44961009) and molecular weigh conversion (MW_{par} = 492.7; MW_{deg} = 352.6).

[2] - The median K_{oc} value from four measurements (1950, 2088, 2563, and 2505 L/kg) was used.

[3] - 275-352I first order non-linear half-lives were estimated from formation and decline curve using the maximum concentration as the initial concentration; since there were two valid half-lives estimated, i.e. 46.5 and 45.9 days, the average value was used as the model input value.

Table 11. SCI-GROW Input Parameters for 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)aniline

Parameter	Input Value and Units	Source of Info/Reference
Maximum Application Rate [1]	apples = 0.20 lb/acre cotton = 0.057 lb/acre potato = 0.049 lb/acre	$rate_{der} = rate_{par} * (MW_{deg}/MW_{par}) *$ (max. % form. rate/100)
Max Number of Applications per year	apples = 3 cotton = 3 potato = 3	Product Labels: RimOn 7.5WDG; EPA Reg. No. 66222-LT RimOn 10EC; EPA Reg. No. 66222-35 RimOn 10EC; EPA Reg. No. 66222-35 (?)
Partition Coefficient Normalized to Organic Carbon Content - K_{oc}	5899 L kg o.c.$^{-1}$	Estimated [2]
Aerobic Soil Metabolism nonlinear $t_{1/2}$ [3]	1000 days	assumed; data not available

[1] – Application rate of 275-309I is based on 100% formation from parent novaluron and molecular weigh conversion (MW_{par} = 492.7; MW_{deg} = 310.6).
[2] - Estimated using substructure physical/chemical property computer program (Howard and Meylan, 1995).
[3] - SCI-GROW was developed using aerobic soil metabolism half-lives from 13-1000 days. Due to the lack of aerobis soil metabolism data the highest value of 1000 days was used.

An estimated concentration of chlorophenyl urea (275-352I) in drinking water from shallow ground water sources is 4.5 x 10^{-3} µg/L from novaluron's maximum application rate (RimOn 7.5WDG use on apples). From the same novaluron maximum application rate, an estimated concentration of chloroaniline in drinking water from shallow ground water sources is 9.0 x 10^{-3} µg/L. The SCI-GROW output files for novaluron and its degradates, chlorophenyl urea (275-352I) and chloroaniline are presented in Appendix B.

Assumptions and Uncertainties

SCI-GROW modeling was conducted using K_{oc} values ranging from 32-180 L/Kg. Extrapolation beyond these values further increases the uncertainty of the ground water EECs. Additionally, Koc values for chloroaniline were estimated from a structural activity model. The K_{oc} input value for novaluron was 9965 L/kg o.c., for chlorophenyl urea 2297 L/kg o.c., and for chloroaniline was 5899 L/kg o.c. Given that the K_{oc} of the parent and its degradates are outside the range of the K_{oc} values used to develop SCI-GROW, there is uncertainty regarding the estimated ground water concentrations. The lack of aerobic soil metabolism data for chloroaniline further increases uncertainty of the estimated drinking water concentrations from ground water sources.

Literature Review

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APPENDIX B: PRZM/EXAMS Input & Output Files for Ecological Assessment

Aquatic Exposure Modeling Output Files
(PRZM/EXAMS)

A. Output File - Apples
stored as novalPAp.out
Chemical: novaluron
PRZM environment: PAappleC.txt modified Monday, 24 November 2003 at 13:49:49
EXAMS environment: pond298.exv modified Thuday, 29 August 2002 at 16:33:30
Metfile: w14737.dvf modified Wedday, 3 July 2002 at 09:06:12
Water segment concentrations (ppb)

Year	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
1961	0.3064	0.2659	0.2007	0.1317	0.1025	0.03282
1962	3.119	2.834	2.032	1.369	1.146	0.3951
1963	2.66	2.394	1.751	1.217	1.056	0.5695
1964	0.6478	0.6437	0.6266	0.5888	0.5598	0.3222
1965	1.806	1.601	1.332	0.9257	0.8013	0.323
1966	2.898	2.545	1.704	1.336	1.164	0.5517
1967	1.819	1.633	1.175	0.8721	0.7604	0.5148
1968	0.4562	0.4236	0.4121	0.3872	0.3678	0.2479
1969	3.859	3.396	2.514	1.602	1.313	0.4848
1970	0.908	0.818	0.62	0.5392	0.4944	0.3839
1971	5.967	5.309	3.889	2.643	2.264	0.9056
1972	1.278	1.203	1.174	1.105	1.053	0.6593
1973	2.434	2.164	1.487	0.9882	0.8471	0.4059
1974	5.043	4.472	3.128	2.238	1.936	0.8516
1975	1.049	0.9802	0.956	0.8996	0.8562	0.5691
1976	4.645	4.213	2.87	1.901	1.63	0.6733
1977	1.417	1.262	0.8781	0.7491	0.708	0.4949
1978	4.544	4.126	3.19	2.057	1.703	0.6713
1979	2.893	2.59	1.934	1.391	1.2	0.6954
1980	0.7037	0.6999	0.6829	0.6429	0.6118	0.3303
1981	0.3872	0.3395	0.2444	0.1869	0.1703	0.106
1982	6.291	5.663	3.968	2.481	2.043	0.6999
1983	1.502	1.371	0.9772	0.8031	0.7624	0.5275
1984	0.8526	0.7512	0.6761	0.4679	0.3871	0.2571
1985	2.54	2.226	1.736	1.252	1.235	0.5115
1986	1.256	1.164	0.9072	0.7013	0.6042	0.4466
1987	4.539	4.022	2.735	2.206	1.902	0.7455
1988	2.425	2.203	1.633	1.225	1.128	0.7753
1989	1.178	1.066	0.7933	0.6013	0.5717	0.4451
1990	5.02	4.412	2.978	1.846	1.521	0.625

Sorted results

Prob.	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
0.032258064516129	6.291	5.663	3.968	2.643	2.264	0.9056
0.0645161290322581	5.967	5.309	3.889	2.481	2.043	0.8516
0.0967741935483871	5.043	4.472	3.19	2.238	1.936	0.7753
0.129032258064516	5.02	4.412	3.128	2.206	1.902	0.7455
0.161290322580645	4.645	4.213	2.978	2.057	1.703	0.6999
0.193548387096774	4.544	4.126	2.87	1.901	1.63	0.6954
0.225806451612903	4.539	4.022	2.735	1.846	1.521	0.6733
0.258064516129032	3.859	3.396	2.514	1.602	1.313	0.6713
0.290322580645161	3.119	2.834	2.032	1.391	1.235	0.6593

0.32258064516129	2.898	2.59	1.934	1.369	1.2	0.625
0.354838709677419	2.893	2.545	1.751	1.336	1.164	0.5695
0.387096774193548	2.66	2.394	1.736	1.252	1.146	0.5691
0.419354838709677	2.54	2.226	1.704	1.225	1.128	0.5517
0.451612903225806	2.434	2.203	1.633	1.217	1.056	0.5275
0.483870967741936	2.425	2.164	1.487	1.105	1.053	0.5148
0.516129032258065	1.819	1.633	1.332	0.9882	0.8562	0.5115
0.548387096774194	1.806	1.601	1.175	0.9257	0.8471	0.4949
0.580645161290323	1.502	1.371	1.174	0.8996	0.8013	0.4848
0.612903225806452	1.417	1.262	0.9772	0.8721	0.7624	0.4466
0.645161290322581	1.278	1.203	0.956	0.8031	0.7604	0.4451
0.67741935483871	1.256	1.164	0.9072	0.7491	0.708	0.4059
0.709677419354839	1.178	1.066	0.8781	0.7013	0.6118	0.3951
0.741935483870968	1.049	0.9802	0.7933	0.6429	0.6042	0.3839
0.774193548387097	0.908	0.818	0.6829	0.6013	0.5717	0.3303
0.806451612903226	0.8526	0.7512	0.6761	0.5888	0.5598	0.323
0.838709677419355	0.7037	0.6999	0.6266	0.5392	0.4944	0.3222
0.870967741935484	0.6478	0.6437	0.62	0.4679	0.3871	0.2571
0.903225806451613	0.4562	0.4236	0.4121	0.3872	0.3678	0.2479
0.935483870967742	0.3872	0.3395	0.2444	0.1869	0.1703	0.106
0.967741935483871	0.3064	0.2659	0.2007	0.1317	0.1025	0.03282
0.1	5.0407	4.466	3.1838	2.2348	1.9326	0.77232

Average of yearly averages: 0.507397333333333

Inputs generated by pe4.pl - 8-August-2003

Data used for this run:
Output File: novalPAp
Metfile: w14737.dvf
PRZM scenario: PAappleC.txt
EXAMS environment file: pond298.exv
Chemical Name: novaluron

Description	Variable Name	Value	Units	Comments
Molecular weight	mwt	492.9	g/mol	
Henry's Law Const.	henry	1.97e-13		atm-m^3/mol
Vapor Pressure	vapr	1.2e-7	torr	
Solubility	sol	0.3	mg/L	
Kd	Kd	133	mg/L	
Koc	Koc		mg/L	
Photolysis half-life	kdp	187	days	Half-life
Aerobic Aquatic Metabolism	kbacw	30.1	days	Halfife
Anaerobic Aquatic Metabolism	kbacs	52.1	days	Halfife
Aerobic Soil Metabolism	asm	15.6	days	Halfife
Hydrolysis:	pH 7	0	days	Half-life
Method:	CAM	2	integer	See PRZM manual
Incorporation Depth:	DEPI	0	cm	
Application Rate:	TAPP	0.359	kg/ha	
Application Efficiency:	APPEFF		0.99	fraction
Spray Drift	DRFT	0.01	fraction of application rate applied to pond	
Application Date	Date	25-07	dd/mm or dd/mmm or dd-mm or dd-mmm	
Interval 1	interval	10	days	Set to 0 or delete line for single app.
Interval 2	interval	10	days	Set to 0 or delete line for single app.
Record 17:	FILTRA			
IPSCND		1		

	UPTKF		
Record 18:	PLVKRT		
	PLDKRT		
	FEXTRC	0.5	
Flag for Index Res. Run	IR	Pond	
Flag for runoff calc.	RUNOFF	none	none, monthly or total(average of entire run)

B. Output File - Cotton - aerial application

stored as novalMSap.out
Chemical: novaluron
PRZM environment: MScottonC.txt modified Monday, 24 November 2003 at 13:49:38
EXAMS environment: pond298.exv modified Thuday, 29 August 2002 at 16:33:30
Metfile: w03940.dvf modified Wedday, 3 July 2002 at 09:05:46
Water segment concentrations (ppb)

Year	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
1961	1.016	0.9044	0.7883	0.5848	0.4733	0.1517
1962	0.7423	0.6349	0.4047	0.2477	0.1978	0.1021
1963	0.4712	0.4018	0.2906	0.1714	0.1284	0.05209
1964	1.234	1.068	0.8452	0.5596	0.4636	0.158
1965	0.5058	0.4476	0.3154	0.2647	0.238	0.1239
1966	1.156	1.016	0.6847	0.4478	0.3626	0.1438
1967	0.8377	0.7417	0.5459	0.4253	0.3719	0.1623
1968	0.4884	0.4193	0.3081	0.2437	0.1957	0.1077
1969	0.7617	0.6641	0.4274	0.317	0.2596	0.1
1970	0.7315	0.6803	0.5679	0.4349	0.3676	0.1463
1971	0.7983	0.716	0.5929	0.359	0.297	0.1288
1972	0.501	0.4277	0.314	0.1923	0.148	0.06493
1973	0.4857	0.4161	0.3122	0.2777	0.2382	0.0871
1974	0.4754	0.4081	0.3276	0.279	0.2366	0.09842
1975	1.31	1.18	0.9321	0.5973	0.4751	0.173
1976	0.852	0.7363	0.5867	0.4787	0.4116	0.1809
1977	0.8554	0.734	0.5416	0.3318	0.267	0.1351
1978	0.4734	0.4044	0.2936	0.1758	0.1433	0.06853
1979	1.787	1.55	1.058	0.7138	0.595	0.2063
1980	0.4882	0.4167	0.3072	0.1836	0.1562	0.1009
1981	0.4649	0.3987	0.2992	0.1986	0.1602	0.06002
1982	1.606	1.479	1.089	0.686	0.5514	0.1885
1983	0.9009	0.7779	0.5146	0.3291	0.2633	0.1307
1984	0.7332	0.66	0.4738	0.3244	0.2603	0.1054
1985	1.65	1.436	0.9233	0.6195	0.5102	0.1862
1986	0.5811	0.5034	0.4271	0.2682	0.2123	0.1125
1987	0.5618	0.4824	0.3772	0.2411	0.1874	0.07338
1988	0.8289	0.7205	0.4861	0.3452	0.2994	0.1163
1989	0.4807	0.4117	0.3002	0.1935	0.1633	0.08574
1990	0.4703	0.401	0.2898	0.1937	0.1707	0.07082

Sorted results

Prob.	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
0.032258064516129	1.787	1.55	1.089	0.7138	0.595	0.2063
0.0645161290322581	1.65	1.479	1.058	0.686	0.5514	0.1885
0.0967741935483871	1.606	1.436	0.9321	0.6195	0.5102	0.1862
0.129032258064516	1.31	1.18	0.9233	0.5973	0.4751	0.1809
0.161290322580645	1.234	1.068	0.8452	0.5848	0.4733	0.173
0.193548387096774	1.156	1.016	0.7883	0.5596	0.4636	0.1623

0.225806451612903	1.016	0.9044	0.6847	0.4787	0.4116	0.158
0.258064516129032	0.9009	0.7779	0.5929	0.4478	0.3719	0.1517
0.290322580645161	0.8554	0.7417	0.5867	0.4349	0.3676	0.1463
0.32258064516129	0.852	0.7363	0.5679	0.4253	0.3626	0.1438
0.354838709677419	0.8377	0.734	0.5459	0.359	0.2994	0.1351
0.387096774193548	0.8289	0.7205	0.5416	0.3452	0.297	0.1307
0.419354838709677	0.7983	0.716	0.5146	0.3318	0.267	0.1288
0.451612903225806	0.7617	0.6803	0.4861	0.3291	0.2633	0.1239
0.483870967741936	0.7423	0.6641	0.4738	0.3244	0.2603	0.1163
0.516129032258065	0.7332	0.66	0.4274	0.317	0.2596	0.1125
0.548387096774194	0.7315	0.6349	0.4271	0.279	0.2382	0.1077
0.580645161290323	0.5811	0.5034	0.4047	0.2777	0.238	0.1054
0.612903225806452	0.5618	0.4824	0.3772	0.2682	0.2366	0.1021
0.645161290322581	0.5058	0.4476	0.3276	0.2647	0.2123	0.1009
0.67741935483871	0.501	0.4277	0.3154	0.2477	0.1978	0.1
0.709677419354839	0.4884	0.4193	0.314	0.2437	0.1957	0.09842
0.741935483870968	0.4882	0.4167	0.3122	0.2411	0.1874	0.0871
0.774193548387097	0.4857	0.4161	0.3081	0.1986	0.1707	0.08574
0.806451612903226	0.4807	0.4117	0.3072	0.1937	0.1633	0.07338
0.838709677419355	0.4754	0.4081	0.3002	0.1935	0.1602	0.07082
0.870967741935484	0.4734	0.4044	0.2992	0.1923	0.1562	0.06853
0.903225806451613	0.4712	0.4018	0.2936	0.1836	0.148	0.06493
0.935483870967742	0.4703	0.401	0.2906	0.1758	0.1433	0.06002
0.967741935483871	0.4649	0.3987	0.2898	0.1714	0.1284	0.05209
0.1	1.5764	1.4104	0.93122	0.61728	0.50669	0.18567

Average of yearly averages: 0.120714333333333

Inputs generated by pe4.pl - 8-August-2003

Data used for this run:
Output File: novalMSap
Metfile: w03940.dvf
PRZM scenario: MScottonC.txt
EXAMS environment file: pond298.exv
Chemical Name: novaluron

Description	Variable Name	Value	Units	Comments
Molecular weight	mwt	492.9	g/mol	
Henry's Law Const.	henry	1.97e-13		atm-m^3/mol
Vapor Pressure	vapr	1.2e-7	torr	
Solubility	sol	0.3	mg/L	
Kd	Kd	133	mg/L	
Koc	Koc		mg/L	
Photolysis half-life	kdp	187	days	Half-life
Aerobic Aquatic Metabolism	kbacw	30.1	days	Halfife
Anaerobic Aquatic Metabolism	kbacs	52.1	days	Halfife
Aerobic Soil Metabolism	asm	15.6	days	Halfife
Hydrolysis:	pH 7	0	days	Half-life
Method:	CAM	2	integer	See PRZM manual
Incorporation Depth:	DEPI	0	cm	
Application Rate:	TAPP	0.10	kg/ha	
Application Efficiency:	APPEFF		0.95	fraction
Spray Drift	DRFT	0.05	fraction of application rate applied to pond	
Application Date	Date	20-07	dd/mm or dd/mmm or dd-mm or dd-mmm	
Interval 1	interval	7	days	Set to 0 or delete line for single app.

Interval 2 interval 7 days Set to 0 or delete line for single app.
Record 17: FILTRA
IPSCND 1
UPTKF
Record 18: PLVKRT
PLDKRT
FEXTRC 0.5
Flag for Index Res. Run IR Pond
Flag for runoff calc. RUNOFF none none, monthly or total(average of entire run)

C. Output File - Cotton - ground applicvation
stored as novalMSpp.out
Chemical: novaluron
PRZM environment: MScottonC.txt modified Monday, 24 November 2003 at 13:49:38
EXAMS environment: pond298.exv modified Thuday, 29 August 2002 at 16:33:30
Metfile: w03940.dvf modified Wedday, 3 July 2002 at 09:05:46
Water segment concentrations (ppb)

Year	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
1961	0.778	0.6911	0.58	0.4677	0.3857	0.1259
1962	0.3849	0.3313	0.2032	0.1249	0.103	0.0702
1963	0.09645	0.0825	0.06024	0.0361	0.02722	0.01816
1964	1.001	0.8729	0.7301	0.4727	0.396	0.1282
1965	0.4729	0.4147	0.2785	0.1739	0.1467	0.09119
1966	0.972	0.8552	0.5533	0.3388	0.2751	0.1101
1967	0.7711	0.6791	0.4955	0.341	0.2869	0.1271
1968	0.2577	0.2308	0.1691	0.1139	0.1066	0.07196
1969	0.6593	0.5717	0.3605	0.2103	0.168	0.06593
1970	0.6346	0.6024	0.4398	0.3415	0.2881	0.1152
1971	0.5374	0.4679	0.3731	0.2408	0.2033	0.0973
1972	0.1268	0.1091	0.0845	0.05866	0.04914	0.03256
1973	0.3527	0.3125	0.2353	0.1754	0.1469	0.05475
1974	0.3086	0.2705	0.2279	0.1682	0.141	0.06465
1975	1.057	0.9773	0.7283	0.487	0.3925	0.1414
1976	0.7361	0.6884	0.551	0.3828	0.335	0.1495
1977	0.5646	0.4876	0.3223	0.2125	0.1745	0.1028
1978	0.1017	0.08747	0.06525	0.05153	0.0483	0.03459
1979	1.465	1.275	0.8944	0.6202	0.5094	0.1763
1980	0.1783	0.1765	0.1696	0.1554	0.1444	0.06908
1981	0.1529	0.1355	0.09417	0.06928	0.06101	0.02628
1982	1.426	1.26	0.9215	0.5769	0.4697	0.1593
1983	0.6561	0.5672	0.3627	0.2122	0.1698	0.09892
1984	0.5763	0.5026	0.3483	0.2059	0.1663	0.07163
1985	1.567	1.361	0.867	0.5283	0.4339	0.1566
1986	0.3227	0.2787	0.2095	0.1369	0.1159	0.08056
1987	0.2673	0.2392	0.1841	0.111	0.08892	0.03967
1988	0.7544	0.6523	0.4354	0.2831	0.2368	0.08446
1989	0.114	0.1027	0.09082	0.08179	0.07526	0.05182
1990	0.2059	0.1817	0.1458	0.09311	0.07774	0.0369

Sorted results

Prob.	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
0.032258064516129	1.567	1.361	0.9215	0.6202	0.5094	0.1763
0.0645161290322581	1.465	1.275	0.8944	0.5769	0.4697	0.1593
0.0967741935483871	1.426	1.26	0.867	0.5283	0.4339	0.1566

0.129032258064516	1.057	0.9773	0.7301	0.487	0.396	0.1495
0.161290322580645	1.001	0.8729	0.7283	0.4727	0.3925	0.1414
0.193548387096774	0.972	0.8552	0.58	0.4677	0.3857	0.1282
0.225806451612903	0.778	0.6911	0.5533	0.3828	0.335	0.1271
0.258064516129032	0.7711	0.6884	0.551	0.3415	0.2881	0.1259
0.290322580645161	0.7544	0.6791	0.4955	0.341	0.2869	0.1152
0.32258064516129	0.7361	0.6523	0.4398	0.3388	0.2751	0.1101
0.354838709677419	0.6593	0.6024	0.4354	0.2831	0.2368	0.1028
0.387096774193548	0.6561	0.5717	0.3731	0.2408	0.2033	0.09892
0.419354838709677	0.6346	0.5672	0.3627	0.2125	0.1745	0.0973
0.451612903225806	0.5763	0.5026	0.3605	0.2122	0.1698	0.09119
0.483870967741936	0.5646	0.4876	0.3483	0.2103	0.168	0.08446
0.516129032258065	0.5374	0.4679	0.3223	0.2059	0.1663	0.08056
0.548387096774194	0.4729	0.4147	0.2785	0.1754	0.1469	0.07196
0.580645161290323	0.3849	0.3313	0.2353	0.1739	0.1467	0.07163
0.612903225806452	0.3527	0.3125	0.2279	0.1682	0.1444	0.0702
0.645161290322581	0.3227	0.2787	0.2095	0.1554	0.141	0.06908
0.67741935483871	0.3086	0.2705	0.2032	0.1369	0.1159	0.06593
0.709677419354839	0.2673	0.2392	0.1841	0.1249	0.1066	0.06465
0.741935483870968	0.2577	0.2308	0.1696	0.1139	0.103	0.05475
0.774193548387097	0.2059	0.1817	0.1691	0.111	0.08892	0.05182
0.806451612903226	0.1783	0.1765	0.1458	0.09311	0.07774	0.03967
0.838709677419355	0.1529	0.1355	0.09417	0.08179	0.07526	0.0369
0.870967741935484	0.1268	0.1091	0.09082	0.06928	0.06101	0.03459
0.903225806451613	0.114	0.1027	0.0845	0.05866	0.04914	0.03256
0.935483870967742	0.1017	0.08747	0.06525	0.05153	0.0483	0.02628
0.967741935483871	0.09645	0.0825	0.06024	0.0361	0.02722	0.01816
0.1	1.3891	1.23173	0.85331	0.52417	0.43011	0.15589

Average of yearly averages: 0.0884336666666667

Inputs generated by pe4.pl - 8-August-2003

Data used for this run:
Output File: novalMSpp
Metfile: w03940.dvf
PRZM scenario: MScottonC.txt
EXAMS environment file: pond298.exv
Chemical Name: novaluron

Description	Variable Name	Value	Units	Comments
Molecular weight	mwt	492.9	g/mol	
Henry's Law Const.	henry	1.97e-13		atm-m^3/mol
Vapor Pressure	vapr	1.2e-7	torr	
Solubility	sol	0.3	mg/L	
Kd	Kd	133	mg/L	
Koc	Koc		mg/L	
Photolysis half-life	kdp	187	days	Half-life
Aerobic Aquatic Metabolism	kbacw	30.1	days	Halfife
Anaerobic Aquatic Metabolism	kbacs	52.1	days	Halfife
Aerobic Soil Metabolism	asm	15.6	days	Halfife
Hydrolysis:	pH 7	0	days	Half-life
Method:	CAM	2	integer	See PRZM manual
Incorporation Depth:	DEPI	0	cm	
Application Rate:	TAPP	0.10	kg/ha	
Application Efficiency:	APPEFF		0.99	fraction

Spray Drift	DRFT	0.01	fraction of application rate applied to pond	
Application Date	Date	20-07	dd/mm or dd/mmm or dd-mm or dd-mmm	
Interval 1	interval	7	days	Set to 0 or delete line for single app.
Interval 2	interval	7	days	Set to 0 or delete line for single app.
Record 17:	FILTRA			
IPSCND		1		
UPTKF				
Record 18:	PLVKRT			
PLDKRT				
FEXTRC		0.5		
Flag for Index Res. Run		IR	Pond	
Flag for runoff calc.		RUNOFF	none	none, monthly or total(average of entire run)

D. Output File - Potato - aerial application

stored as novalMEap.out
Chemical: novaluron
PRZM environment: MEpotatoC.txt modified Monday, 24 November 2003 at 13:49:36
EXAMS environment: pond298.exv modified Thuday, 29 August 2002 at 16:33:30
Metfile: w14607.dvf modified Wedday, 3 July 2002 at 09:05:36
Water segment concentrations (ppb)

Year	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
1961	0.4244	0.3732	0.2989	0.2385	0.2068	0.0792
1962	1.1	0.9895	0.7865	0.5411	0.4565	0.2076
1963	0.6651	0.6059	0.457	0.3344	0.2984	0.1868
1964	0.9946	0.8819	0.5997	0.3988	0.3387	0.176
1965	0.4413	0.393	0.3145	0.2491	0.2132	0.1287
1966	0.4128	0.3645	0.2888	0.2103	0.1714	0.08818
1967	0.8458	0.7501	0.5119	0.3565	0.3053	0.1398
1968	0.6096	0.5477	0.4407	0.3442	0.3013	0.1615
1969	0.4654	0.4152	0.3405	0.2921	0.2633	0.1485
1970	0.4348	0.3916	0.34	0.2715	0.2303	0.1274
1971	0.4621	0.4119	0.3213	0.2258	0.1856	0.09779
1972	0.6385	0.5654	0.4106	0.2869	0.2526	0.121
1973	1.266	1.151	0.8559	0.5383	0.4469	0.2067
1974	0.482	0.431	0.3551	0.2608	0.2231	0.1439
1975	0.4141	0.3644	0.2949	0.2525	0.2154	0.111
1976	0.8836	0.8156	0.6572	0.5004	0.4286	0.1979
1977	0.5516	0.4951	0.4184	0.3479	0.3152	0.1897
1978	1.27	1.131	0.7876	0.5352	0.4512	0.2225
1979	0.4857	0.4316	0.3614	0.2695	0.2361	0.1553
1980	0.5398	0.4797	0.436	0.3331	0.2854	0.1429
1981	0.6521	0.5811	0.4581	0.3527	0.3157	0.1657
1982	0.6428	0.5784	0.4501	0.3496	0.3138	0.1753
1983	0.9062	0.8124	0.5928	0.4483	0.3849	0.2008
1984	0.9356	0.8427	0.7285	0.5556	0.4652	0.2314
1985	0.5653	0.5116	0.4414	0.3381	0.2903	0.1711
1986	0.4333	0.3849	0.3054	0.2555	0.2343	0.1339
1987	0.5815	0.5173	0.4198	0.3051	0.2573	0.1341
1988	0.4712	0.4166	0.3269	0.2394	0.2081	0.1129
1989	0.4151	0.3664	0.3091	0.2495	0.2268	0.1179
1990	0.6505	0.5803	0.5033	0.4287	0.3661	0.1741

Sorted results

Prob.	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
0.032258064516129	1.27	1.151	0.8559	0.5556	0.4652	0.2314
0.0645161290322581	1.266	1.131	0.7876	0.5411	0.4565	0.2225
0.0967741935483871	1.1	0.9895	0.7865	0.5383	0.4512	0.2076
0.129032258064516	0.9946	0.8819	0.7285	0.5352	0.4469	0.2067
0.161290322580645	0.9356	0.8427	0.6572	0.5004	0.4286	0.2008
0.193548387096774	0.9062	0.8156	0.5997	0.4483	0.3849	0.1979
0.225806451612903	0.8836	0.8124	0.5928	0.4287	0.3661	0.1897
0.258064516129032	0.8458	0.7501	0.5119	0.3988	0.3387	0.1868
0.290322580645161	0.6651	0.6059	0.5033	0.3565	0.3157	0.176
0.32258064516129	0.6521	0.5811	0.4581	0.3527	0.3152	0.1753
0.354838709677419	0.6505	0.5803	0.457	0.3496	0.3138	0.1741
0.387096774193548	0.6428	0.5784	0.4501	0.3479	0.3053	0.1711
0.419354838709677	0.6385	0.5654	0.4414	0.3442	0.3013	0.1657
0.451612903225806	0.6096	0.5477	0.4407	0.3381	0.2984	0.1615
0.483870967741936	0.5815	0.5173	0.436	0.3344	0.2903	0.1553
0.516129032258065	0.5653	0.5116	0.4198	0.3331	0.2854	0.1485
0.548387096774194	0.5516	0.4951	0.4184	0.3051	0.2633	0.1439
0.580645161290323	0.5398	0.4797	0.4106	0.2921	0.2573	0.1429
0.612903225806452	0.4857	0.4316	0.3614	0.2869	0.2526	0.1398
0.645161290322581	0.482	0.431	0.3551	0.2715	0.2361	0.1341
0.67741935483871	0.4712	0.4166	0.3405	0.2695	0.2343	0.1339
0.709677419354839	0.4654	0.4152	0.34	0.2608	0.2303	0.1287
0.741935483870968	0.4621	0.4119	0.3269	0.2555	0.2268	0.1274
0.774193548387097	0.4413	0.393	0.3213	0.2525	0.2231	0.121
0.806451612903226	0.4348	0.3916	0.3145	0.2495	0.2154	0.1179
0.838709677419355	0.4333	0.3849	0.3091	0.2491	0.2132	0.1129
0.870967741935484	0.4244	0.3732	0.3054	0.2394	0.2081	0.111
0.903225806451613	0.4151	0.3664	0.2989	0.2385	0.2068	0.09779
0.935483870967742	0.4141	0.3645	0.2949	0.2258	0.1856	0.08818
0.967741935483871	0.4128	0.3644	0.2888	0.2103	0.1714	0.0792
0.1	1.08946	0.97874	0.7807	0.53799	0.45077	0.20751

Average of yearly averages: 0.154985666666667

Inputs generated by pe4.pl - 8-August-2003

Data used for this run:
Output File: novalMEap
Metfile: w14607.dvf
PRZM scenario: MEpotatoC.txt
EXAMS environment file: pond298.exv
Chemical Name: novaluron

Description	Variable Name	Value	Units	Comments
Molecular weight	mwt	492.9	g/mol	
Henry's Law Const.	henry	1.97e-13		atm-m^3/mol
Vapor Pressure	vapr	1.2e-7	torr	
Solubility	sol	0.3	mg/L	
Kd	Kd	133	mg/L	
Koc	Koc		mg/L	
Photolysis half-life	kdp	187	days	Half-life
Aerobic Aquatic Metabolism	kbacw	30.1	days	Halfife
Anaerobic Aquatic Metabolism	kbacs	52.1	days	Halfife
Aerobic Soil Metabolism	asm	13.6	days	Halfife
Hydrolysis:	pH 7	0	days	Half-life

Method:	CAM	2	integer	See PRZM manual
Incorporation Depth:		DEPI	0	cm
Application Rate:		TAPP	0.087	kg/ha
Application Efficiency:		APPEFF		0.95 fraction
Spray Drift	DRFT	0.05	fraction of application rate applied to pond	
Application Date	Date	15-06	dd/mm or dd/mmm or dd-mm or dd-mmm	
Interval 1	interval	10	days	Set to 0 or delete line for single app.
Interval 2	interval	10	days	Set to 0 or delete line for single app.
Record 17:	FILTRA			
IPSCND		1		
UPTKF				
Record 18:	PLVKRT			
PLDKRT				
FEXTRC		0.5		
Flag for Index Res. Run		IR	Pond	
Flag for runoff calc.		RUNOFF		none none, monthly or total(average of entire run)

E. Output File - Potato - ground application

stored as novalMEgp.out
Chemical: novaluron
PRZM environment: MEpotatoC.txt modified Monday, 24 November 2003 at 13:49:36
EXAMS environment: pond298.exv modified Thuday, 29 August 2002 at 16:33:30
Metfile: w14607.dvf modified Wedday, 3 July 2002 at 09:05:36
Water segment concentrations (ppb)

Year	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
1961	0.246	0.2203	0.1556	0.1167	0.108	0.04417
1962	0.9589	0.8604	0.6576	0.4549	0.3831	0.1617
1963	0.4176	0.3876	0.2808	0.2126	0.1915	0.138
1964	0.72	0.64	0.4377	0.2867	0.2427	0.1263
1965	0.1689	0.1576	0.1199	0.1018	0.09538	0.07686
1966	0.09688	0.08773	0.0761	0.06352	0.05453	0.03667
1967	0.6796	0.6005	0.405	0.2624	0.2212	0.09124
1968	0.486	0.434	0.3515	0.2458	0.2077	0.1141
1969	0.2862	0.2633	0.2259	0.1674	0.1493	0.09912
1970	0.3001	0.2688	0.191	0.137	0.122	0.07902
1971	0.1442	0.1322	0.1061	0.0787	0.06825	0.04727
1972	0.3284	0.3063	0.2283	0.1644	0.1487	0.06978
1973	1.046	0.9301	0.7016	0.4458	0.3677	0.1607
1974	0.1788	0.1646	0.1475	0.1311	0.1251	0.09523
1975	0.2209	0.2	0.1647	0.1226	0.1063	0.0615
1976	0.7164	0.6557	0.5166	0.3993	0.3424	0.1513
1977	0.3868	0.3526	0.2746	0.2096	0.204	0.1411
1978	1.063	0.9477	0.6629	0.4302	0.364	0.1761
1979	0.2262	0.2057	0.1633	0.1423	0.1358	0.1076
1980	0.4037	0.3653	0.2809	0.21	0.1798	0.09375
1981	0.3653	0.3287	0.2638	0.2274	0.2136	0.1173
1982	0.5385	0.4812	0.3731	0.2632	0.226	0.1268
1983	0.7599	0.6795	0.4953	0.348	0.2974	0.1538
1984	0.7045	0.6396	0.5348	0.4292	0.365	0.1865
1985	0.4141	0.3743	0.2963	0.2108	0.18	0.123
1986	0.237	0.2169	0.1896	0.1447	0.1269	0.08196
1987	0.3075	0.2757	0.2159	0.1704	0.1462	0.08227
1988	0.1528	0.1373	0.1118	0.1017	0.09493	0.06217
1989	0.2571	0.2349	0.1754	0.1327	0.1207	0.0677

1990	0.4984	0.466	0.3584	0.2998	0.2642	0.1275

Sorted results

Prob.	Peak	96 hr	21 Day	60 Day	90 Day	Yearly
0.032258064516129	1.063	0.9477	0.7016	0.4549	0.3831	0.1865
0.0645161290322581	1.046	0.9301	0.6629	0.4458	0.3677	0.1761
0.0967741935483871	0.9589	0.8604	0.6576	0.4302	0.365	0.1617
0.129032258064516	0.7599	0.6795	0.5348	0.4292	0.364	0.1607
0.161290322580645	0.72	0.6557	0.5166	0.3993	0.3424	0.1538
0.193548387096774	0.7164	0.64	0.4953	0.348	0.2974	0.1513
0.225806451612903	0.7045	0.6396	0.4377	0.2998	0.2642	0.1411
0.258064516129032	0.6796	0.6005	0.405	0.2867	0.2427	0.138
0.290322580645161	0.5385	0.4812	0.3731	0.2632	0.226	0.1275
0.32258064516129	0.4984	0.466	0.3584	0.2624	0.2212	0.1268
0.354838709677419	0.486	0.434	0.3515	0.2458	0.2136	0.1263
0.387096774193548	0.4176	0.3876	0.2963	0.2274	0.2077	0.123
0.419354838709677	0.4141	0.3743	0.2809	0.2126	0.204	0.1173
0.451612903225806	0.4037	0.3653	0.2808	0.2108	0.1915	0.1141
0.483870967741936	0.3868	0.3526	0.2746	0.21	0.18	0.1076
0.516129032258065	0.3653	0.3287	0.2638	0.2096	0.1798	0.09912
0.548387096774194	0.3284	0.3063	0.2283	0.1704	0.1493	0.09523
0.580645161290323	0.3075	0.2757	0.2259	0.1674	0.1487	0.09375
0.612903225806452	0.3001	0.2688	0.2159	0.1644	0.1462	0.09124
0.645161290322581	0.2862	0.2633	0.191	0.1447	0.1358	0.08227
0.67741935483871	0.2571	0.2349	0.1896	0.1423	0.1269	0.08196
0.709677419354839	0.246	0.2203	0.1754	0.137	0.1251	0.07902
0.741935483870968	0.237	0.2169	0.1647	0.1327	0.122	0.07686
0.774193548387097	0.2262	0.2057	0.1633	0.1311	0.1207	0.06978
0.806451612903226	0.2209	0.2	0.1556	0.1226	0.108	0.0677
0.838709677419355	0.1788	0.1646	0.1475	0.1167	0.1063	0.06217
0.870967741935484	0.1689	0.1576	0.1199	0.1018	0.09538	0.0615
0.903225806451613	0.1528	0.1373	0.1118	0.1017	0.09493	0.04727
0.935483870967742	0.1442	0.1322	0.1061	0.0787	0.06825	0.04417
0.967741935483871	0.09688	0.08773	0.0761	0.06352	0.05453	0.03667
0.1	0.939	0.84231	0.64532	0.4301	0.3649	0.1616

Average of yearly averages: 0.106683666666667

Inputs generated by pe4.pl - 8-August-2003

Data used for this run:
Output File: novalMEgp
Metfile: w14607.dvf
PRZM scenario: MEpotatoC.txt
EXAMS environment file: pond298.exv
Chemical Name: novaluron

Description	Variable Name	Value	Units	Comments
Molecular weight	mwt	492.9	g/mol	
Henry's Law Const.	henry	1.97e-13		atm-m^3/mol
Vapor Pressure	vapr	1.2e-7	torr	
Solubility	sol	0.3	mg/L	
Kd Kd	133	mg/L		
Koc Koc		mg/L		
Photolysis half-life	kdp	187	days	Half-life
Aerobic Aquatic Metabolism	kbacw	30.1	days	Halfife

Anaerobic Aquatic Metabolism		kbacs	52.1	days	Halfife
Aerobic Soil Metabolism		asm	15.6	days	Halfife
Hydrolysis:	pH 7	0	days	Half-life	
Method:	CAM	2	integer	See PRZM manual	
Incorporation Depth:		DEPI	0	cm	
Application Rate:		TAPP	0.087	kg/ha	
Application Efficiency:		APPEFF		0.99	fraction
Spray Drift	DRFT	0.01	fraction of application rate applied to pond		
Application Date	Date	15-06	dd/mm or dd/mmm or dd-mm or dd-mmm		
Interval 1	interval	10	days	Set to 0 or delete line for single app.	
Interval 2	interval	10	days	Set to 0 or delete line for single app.	
Record 17:	FILTRA				
IPSCND		1			
UPTKF					
Record 18:	PLVKRT				
PLDKRT					
FEXTRC		0.5			
Flag for Index Res. Run		IR	Pond		
Flag for runoff calc.		RUNOFF		none	none, monthly or total(average of entire run)

APPENDIX II

GENEEC Output Files for 275-352I

```
RUN No. 1.  For 275-352I from novaluron application on apples
                        * INPUT VALUES *
-------------------------------------------------------------------
RATE (#/AC)    No.APPS &    SOIL  SOLUBIL    APPL TYPE  NO-SPRAY INCORP
 ONE(MULT)     INTERVAL      Kd   (PPM )     (%DRIFT)   ZONE(FT)  (IN)
-------------------------------------------------------------------
.061(   .159)   3  10       16.7   33.0    GRANUL(   .0)     .0     .0
```

FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS (POND)	PHOTOLYSIS (POND-EFF)	METABOLIC (POND)	COMBINED (POND)
47.10	2	N/A	.00- .00	26.60	26.60

GENERIC EECs (IN MICROGRAMS/LITER (PPB)) Version 2.0 Aug 1, 2001

PEAK GEEC	MAX 4 DAY AVG GEEC	MAX 21 DAY AVG GEEC	MAX 60 DAY AVG GEEC	MAX 90 DAY AVG GEEC
2.39	2.33	2.00	1.47	1.19

RUN No. 2. For 275-352I from novaluron application on cotton

* INPUT VALUES *

RATE (#/AC) ONE(MULT)	No.APPS & INTERVAL	SOIL Kd	SOLUBIL (PPM)	APPL TYPE (%DRIFT)	NO-SPRAY ZONE(FT)	INCORP (IN)
.017(.046)	3 7	16.7	33.0	GRANUL(.0)	.0	.0

FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS (POND)	PHOTOLYSIS (POND-EFF)	METABOLIC (POND)	COMBINED (POND)
47.10	2	N/A	.00- .00	26.60	26.60

GENERIC EECs (IN NANOGRAMS/LITER (PPTr)) Version 2.0 Aug 1, 2001

PEAK GEEC	MAX 4 DAY AVG GEEC	MAX 21 DAY AVG GEEC	MAX 60 DAY AVG GEEC	MAX 90 DAY AVG GEEC
693.45	674.86	581.39	425.94	344.70

RUN No. 3. For 275-352I from novaluron application on potato

* INPUT VALUES *

RATE (#/AC) ONE(MULT)	No.APPS & INTERVAL	SOIL Kd	SOLUBIL (PPM)	APPL TYPE (%DRIFT)	NO-SPRAY ZONE(FT)	INCORP (IN)
.015(.039)	3 10	16.7	33.0	GRANUL(.0)	.0	.0

FIELD AND STANDARD POND HALFLIFE VALUES (DAYS)

METABOLIC (FIELD)	DAYS UNTIL RAIN/RUNOFF	HYDROLYSIS (POND)	PHOTOLYSIS (POND-EFF)	METABOLIC (POND)	COMBINED (POND)
47.10	2	N/A	.00- .00	26.60	26.60

GENERIC EECs (IN NANOGRAMS/LITER (PPTr)) Version 2.0 Aug 1, 2001

PEAK GEEC	MAX 4 DAY AVG GEEC	MAX 21 DAY AVG GEEC	MAX 60 DAY AVG GEEC	MAX 90 DAY AVG GEEC
587.59	571.84	492.65	360.92	292.08

APPENDIX C: Ecological Hazard Data

Table 1: Acute Toxicity of Novaluron to Freshwater Fish							
Species	% a.i.	96-hr LC_{50}, mg/L (confid. int.)	NOEC (mg/L)	Study Properties[a]	Toxicity Classification	MRID, Autheor, Year	Status
EPA PC Code: 124002 - Novaluron (GR 572 Technical)							
Rainbow trout	94.3	>0.96	0.96	M, F-T	highly toxic	454990-04, Douglas, M.T. et.al., 1989.	Supplemental[b]
Bluegill sunfish	94.3	>0.96	0.96	M, F-T	highly toxic	454990-05, Douglas, M.T. et.al., 1989.	Supplemental[b]
EPA PC Code: 124002 - Rimon 10 EC (formulated product)							
Rainbow trout	9.2 w/w	5.74 (3.97 - 8.31)[c]	0.498	M, F-T	slightly toxic	456383-14, Jenkins, C.A., 1998.	core
EPA PC Code: 124002 - Chlorophenyl urea (275-352 I) (major degradate)							
Rainbow trout	99.3	0.53	0.144	M, S	Highly toxic	454990-06, Jenkins,C., 1999.	core

[a] M=mean-measured chemical concentrations, N=nominal chemical concentrations; F-T=flow-through; S=static.
[b] Despite several deviations from the protocol, the compound was tested above the limits of solubility.
[c] Adjusted to mg ai/L. Study measured concentrations of the formulated product at 62.4 (43.1 - 90.3) mg/L

Table 2: Acute Toxicity of Novaluron to Freshwater Invertebrates							
Species	**% a.i.**	**48-hr EC_{50}, mg/L (confid. int.)**	**NOAEC (mg/L)**	**Study Properties[a]**	**Toxicity Classification**	**MRID, Author, Year**	**Status**
EPA PC Code: 124002 - Rimon 10 EC (formulated product)							
Daphnia magna	9.1 w/w	0.0004 (0.00031 - 0.00052)[c]	0.000115[c]	M, S	very highly toxic	456383-13, Jenkins, C.A., 1998.	core
EPA PC Code: 124002 - Chlorophenyl urea (275-352 I) (major degradate)[b]							
Daphnia magna	96.2	1.91	0.69	M, S	practically non-toxic	454990-07, Jenkins, C.A., 1999.	Supplemental[d]

[a] M=mean-measured chemical concentrations, N=nominal chemical concentrations; F-T=flow-through; S=static.
[b] Data submitted on parent novaluron (MRID # 454768-02) is invalid due to the high variability of the mean measured concentrations and the resulting uncertainty of the actual concentrations that daphnids were exposed to.
[c] Adjusted to mg ai/L. Study measured concentrations of the formulated product at 0.00431 (0.00334 - 0.00577) mg/L
[d] Several deviations from EPA protocols may have impacted the water quality of this study.

Table 3: Acute Toxicity of Novaluron to Estuarine Fish							
Species	**% a.i.**	**96-hr LC_{50} mg/L (confid. int.)**	**NOAEC (mg/L)**	**Study Properties[a]**	**Toxicity Classification**	**MRID, Author, Year**	**Status**
EPA PC Code: 124002 - Novaluron ("Rimon" Technical)							
Sheephead minnow	99.9	>0.002	0.002	M, F-T	very highly toxic	456382-10, Machado, M.W., 2002	Supplemental[b]

[a] M=mean-measured chemical concentrations, N=nominal chemical concentrations; F-T=flow-through; S=static.

[b] Stability measurements not consistent. Can not be determined if test substance degraded, was limited by solubility, or if some other factors were involved.

Table 4: Acute Toxicity of Novaluron to Estuarine/Marine Invertebrates							
Species	**% a.i.**	**96-hr LC_{50} mg/L (confid. int.)**	**NOAEC (mg/L)**	**Study Properties[a]**	**Toxicity Classification**	**MRID, Author, Year**	**Status**
EPA PC Code: 124002 - Novaluron ("Rimon" Technical)							
Mysid shrimp	>97	0.00013 (0.00011 - 0.00016)	0.000087	M, F-T	very highly toxic	456382-09.Machado, M.W., 2002	core
Eastern oyster-larvae/embryo	99.9	0.0015 (0.0012 - 0.0018)	0.00023	M, F-T	very highly toxic	456382-08,Cafarella, M.A., 2002	core
EPA PC Code: 124002 - Rimon 10 EC (formulated product)							
Mysid shrimp	9.4	0.00012 (0.0001 - 0.00014)	0.00003	M, S	very highly toxic	460862-03, Albuquerque, R., 2003	Core

[a] M=mean-measured chemical concentrations, N=nominal chemical concentrations; F-T=flow-through; S=static.

Table 5: Chronic (Early-life) Toxicity of Novaluron to Fish							
Species	**% a.i.**	**NOAEC (mg/L)**	**LOAEC (mg/L)**	**Study Properties[a]**	**Most sensitive parameter**	**MRID , Author, Year**	**Status**
EPA PC Code: 124002 - Novaluron ("Rimon" Technical)							
Rainbow trout	99.3	0.00616	>0.00616	M, F-T	Terminal growth & mortality	456382-16, Jenkins, C.A., 1998.	supplemental[b]
EPA PC Code: 124002 - Rimon 10 EC (formulated product)							
Rainbow trout	9.2 w/w	0.11132[cd]	0.31[d]	M, F-T	Mortality (toxic effects)	456384-06, Jenkins, C.A., 2000	supplemental[b]

[a] M=mean-measured chemical concentrations, N=nominal chemical concentrations; F-T=flow-through; S=static.
[b] Study not performed to US EPA guideline specifications.
[c] 28 day survival LC50 = 7.14 mg/L 95% c.i.: 4.66 - 10.87 mg/L.
[d] Adjusted to mg ai/kg. Study measured concentrations of the formulated product at 1.21 mg/kg

Table 6: Chronic (Life-cycle) Toxicity of Novaluron to Invertebrates							
Species	**% ai**	**NOAEC (mg/L)**	**LOAEC (mg/L)**	**Study Properties[a]**	**Most sensitive parameter**	**MRID, Author, Year**	**Status**
EPA PC Code: 124002 - Novaluron ("Rimon" Technical)							
Daphnid	>99	0.0000299[b]	0	M, S	Parental survival & offspring production	456382-11, Jenkins, C.A., 1998.	Core
Mysid shrimp	99.9	0.000026[c]	0	M, F-T	Reductions on terminal male body length.	456382-12, Lima, W., 2002	Supplemental[d]

[a] M=mean-measured chemical concentrations, N=nominal chemical concentrations; F-T=flow-through; S=static.
[b] 28 day survival LC50 = 0.0000579 mg/L 95% c.i.: 0.0000508 - 0.0000707 mg/L.
[c] 28 day survival LC50 = 0.0001 mg/L 95% c.i.: 0.00009 - 0.00012 mg/L.
[d] Daily survival and mortality data were not provided. The first day of brood release was not reported, and second generation were not observed daily for at least 4 days for survival, development, and behavior. Since second generation were counted and then discarded, this study is not repairable.

Table 7: Acute Toxicity of Novaluron to Aquatic Plants							
Species	%a.i.	EC_{50}, mg/L (mg ai/L)	NOAEC (mg/L) a.i.	Most sensitive parameter	Initial/mean measured concentrations	MRID, Author, Year	Status
EPA PC Code: 124002 - Novaluron ("Rimon" Technical)							
Vascular Plant							
Duckweed (*Lemna gibba*)							
Nonvascular Plants							
Marine diatom (*Selenastrum capricornutum*)	99.3	> 9.68	9.68	cell density	mean	456382-21, Jenkins, 1998.	supplemental[a]
Freshwater diatom (*Navicula pelliculosa*)							
Blue-green algae (*Anabaena flos-aquae*)							
Marine diatom (*Skeletonema costatum*)							
EPA PC Code: 124002 - 275-352 I (a metabolite of Rimon)							
Vascular Plant							
Duck weed (*Lemna gibba*)							
Nonvascular Plants							
Marine diatom (*Selenastrum capricornutum*)	96.2	0.33 (0.28 - 0.39)	0.105	cell density	mean	456382-22, Jenkins, C.A., 1999.	Core
Freshwater diatom (*Navicula pelliculosa*)							
Blue-green algae (*Anabaena flos-aquae*)							
Marine diatom (*Skeletonema costatum*)							
EPA PC Code: 124002 - Rimon 10 EC (formulated product)							
Vascular Plants							
Duck weed (*Lemna gibba*)	9.7	0.777 (0.0754)	0.777 (0.0754)	biomass & no. of fronds	mean	456382-23, Jenkins, C.A., 2001.	Core

Table 7: Acute Toxicity of Novaluron to Aquatic Plants							
Species	%a.i.	EC_{50}, mg/L (mg ai/L)	NOAEC (mg/L) a.i.	Most sensitive parameter	Initial/mean measured concentrations	MRID, Author, Year	Status
Nonvascular plants							
Marine diatom (*Selenastrum capricornutum*)	9.1	39 (16 - 95)	27.2	Cell density and biomass	mean	456384-11, Jenkins, C.A., 1998.	Supplemental[a]
Freshwater diatom (*Navicula pelliculosa*)							
Blue-green algae (*Anabaena flos-aquae*)							
Marine diatom (*Skeletonema costatum*)							

[a] Light intensity not at required 4-5 Klux.

Table 8: Acute Toxicity to Novaluron to Birds (oral administration)							
Species	% a.i.	LD_{50}, mg/kg-bw (conf. interval)	NOAEC, mg/kg-bw	Effects	Toxicity Classification (based on a.i.)	MRID, Author, Year	Status
EPA PC Code: 124002 - Novaluron (GR 572 Technical)							
Bobwhite quail	99.3	>2000	2000	No sub-lethal effects or other treatment related effects were observed.	practically non-toxic	454768-01, Rodgers, M., 1998	core
Mallard duck	94.3	> 2000	2000	No treatment related effects observed.	practically non-toxic	454990-01, Hakin, B, et. al. 1989.	supplemental[a]

[a] Could be up-graded to core if additional information is submitted.

Table 9: Acute Toxicity to Novaluron to Birds (dietary administration)							
Species	% a.i.	LC_{50}, mg/kg-diet (conf. interval)	NOAEC, mg/kg-diet	Effects	Toxicity Classification	MRID, Author, Year	Status
EPA PC Code: 124002 - Novaluron (GR 572 Technical)							
Bobwhite quail	94.3	> 5200	2610	No treatment related effects observed	practically non-toxic	454990-02, Hakin, B. et.al., 1989.	core
Mallard duck	94.3	>5310	5310	No mortalities or sub-lethal treatment related effects	practically non-toxic	454990-03, Hakin, B. et.al., 1988.	core

Table 10: Chronic Toxicity of Novaluron to Birds						
Species	% a.i.	NOAEC (mg/kg-diet) a.i.	LOAEC (mg/kg-diet) a.i.	Effects	MRID #, Author, Year	Status
124002 - Novaluron / Rimon Technical						
Bobwhite quail	99.3	301	1013	Viable & live embryos, # hatchlings,/hen, # 14 day old survivors,/hen, # 14 day old survivors of hatchlings,	456382-18, Rodgers, M.H., 1999.	core
Mallard duck	≥99.3	9.8	30	Viable embryos/pen, viable 14-day embryos of eggs set	456382-19, Rodgers, M.H., 2001.	core

[a] Acid equivalency calculated as: 90.3% for MCPA sodium salt, 81.7% for MCPA DMAS, and 64.1% for MCPA 2-EHE.

Table 11: Mammalian Acute Oral Toxicity to Novaluron					
Species	% a.i.	LD_{50} (mg/kg-diet) a.i.	Toxicity Classification	MRID #, Author, Year	Status[b]
124002 - Novaluron / Rimon Technical					
laboratory rat *(Rattus norvegicus)*	93.5	>5000	Practically non-toxic	449610-01, Cuthbert et.al, 1986.	Acceptable

[a] Acid equivalency calculated as: 90.3% for MCPA sodium salt, 81.7% for MCPA DMAS, and 64.1% for MCPA 2-EHE.

[b] Status (acceptability) based on HEDs guidelines.

Table 12: Mammalian Developmental and Chronic Toxicity to Novaluron						
Test Type	% a.i.	NOAEC (mg/kg-diet) a.i.	LOAEC (mg/kg-diet) a.i.	Effects	MRID #, Author, Year	Status[a]
124002 - Novaluron / Rimon Technical						
2-generation reproductive (rats)	99.3	1000 ppm (74.2 mg/kg bw/da)	4000 (297.5 mg/kg bw/da)[b]	- Decreased F_1 sperm counts at 4000 ppm - Increased P & F_1 swelling of spleen at all levels. - Hemosiderosis of spleen at 12,000 ppm - Mean litter size of F_1 offspring decreased at 12,000 ppm -F_2 offspring body weight decreases at day 7	456515-05, Blee, 1999.	Acceptable

[a] Status (acceptability) based on HEDs guidelines.
[b] Based on decrease epidermal sperm counts.

Table 13: Acute Contact Toxicity of Novaluron to Non-target Insects					
Species	% a.i.	Toxicity endpoint Contact LD50 (µg/bee)	Toxicity classification	MRID, Author, Year	Status
EPA PC Code: 124002 - Novaluron ("Rimon" Technical)					
Honey bee (*Apis mellifera*)	99.3	>100	Practically non-toxic	456382-20, Gray, A.P., 1998.	Core[a]
EPA PC Code: 124002 - Rimon 10 EC (formulated product)					
Honey bee (*Apis mellifera*)	9.1	>200	Practically non-toxic	456382-20, Gray, A.P., 1998.	Core[b]

[a] Supplemental for Oral LD50 of >100 µg/bee.
[b] Supplemental for Oral LD50 of >200 µg/bee.

Table 14: Acute Toxicity of Novaluron to Earthworm (*Eisenia foetida*)					
Species	**% a.i.**	**LC50 (mg/kg) (Conf. Interval)**	**NOAEC (mg/kg)**	**MRID, Author, Year**	**Status**
EPA PC Code: 124002 - Novaluron ("Rimon Technical)					
Earthworm (*Eiseenia foetide*)	99.3	>1000	≥1000	456382-24, Rodgers, M.H., 1998.	Supplemental[a]
EPA PC Code: 124002 - Novaluron (Chlorophenyl urea (soil degreadate))					
Earthworm (*Eiseenia foetide*)	99.3	447 (407 - 485)	171	456382-25, Rodgers, M.H., 2001.	Supplemental[a]

[a] Performed under OECD guidelines. Not required by EPA.

APPENDIX D: The Risk Quotient Method

The Risk Quotient Method is the means used by EFED to integrate the results of exposure and ecotoxicity data. For this method, RQs (RQs) are calculated by dividing exposure estimates by ecotoxicity values (i.e., RQ = EXPOSURE/TOXICITY), both acute and chronic. These RQs are then compared to OPP's levels of concern (LOCs). These LOCs are criteria used by OPP to indicate potential risk to non-target organisms and the need to consider regulatory action. EFED has defined LOCs for acute risk, potential restricted use classification, and for endangered species.

The criteria indicate that a pesticide used as directed has the potential to cause adverse effects on nontarget organisms. LOCs currently address the following risk presumption categories:

(1) acute - there is a potential for acute risk; regulatory action may be warranted in addition to restricted use classification;

(2) acute restricted use - the potential for acute risk is high, but this may be mitigated through restricted use classification

(3) acute endangered species - the potential for acute risk to endangered species is high, regulatory action may be warranted, and

(4) chronic risk - the potential for chronic risk is high, regulatory action may be warranted.

Currently, EFED does not perform assessments for chronic risk to plants, acute or chronic risks to non-target insects, or chronic risk from granular/bait formulations to mammalian or avian species.

The ecotoxicity test values (i.e., measurement endpoints) used in the acute and chronic RQs are derived from required studies. Examples of ecotoxicity values derived from short-term laboratory studies that assess acute effects are: (1) LC_{50} (fish and birds), (2) LD_{50} (birds and mammals), (3) EC_{50} (aquatic plants and aquatic invertebrates), and (4) EC_{25} (terrestrial plants). Examples of toxicity test effect levels derived from the results of long-term laboratory studies that assess chronic effects are: (1) LOEL (birds, fish, and aquatic invertebrates), and (2) NOEL (birds, fish and aquatic invertebrates). The NOEL is generally used as the ecotoxicity test value in assessing chronic effects.

Risk presumptions, along with the corresponding RQs and LOCs are summarized in Table E1.

Table 1: Risk Presumptions and LOCs		
Risk Presumption	**RQ**	**LOC**
Birds[1]		
Acute Risk	EEC/LC_{50} or LD_{50}/sqft or LD_{50}/day	0.5
Acute Restricted Use	EEC/LC_{50} or LD_{50}/sqft or LD_{50}/day (or LD_{50} < 50 mg/kg)	0.2
Acute Endangered Species	EEC/LC_{50} or LD_{50}/sqft or LD_{50}/day	0.1
Chronic Risk	EEC/NOEC	1
Wild Mammals[1]		
Acute Risk	EEC/LC_{50} or LD_{50}/sqft or LD_{50}/day	0.5
Acute Restricted Use	EEC/LC_{50} or LD_{50}/sqft or LD_{50}/day (or LD_{50} < 50 mg/kg)	0.2
Acute Endangered Species	EEC/LC_{50} or LD_{50}/sqft or LD_{50}/day	0.1
Chronic Risk	EEC/NOEC	1
Aquatic Animals[2]		
Acute Risk	EEC/LC_{50} or EC_{50}	0.5
Acute Restricted Use	EEC/LC_{50} or EC_{50}	0.1
Acute Endangered Species	EEC/LC_{50} or EC_{50}	0.05
Chronic Risk	EEC/NOEC	1
Terrestrial and Semi-Aquatic Plants		
Acute Risk	EEC/EC_{25}	1
Acute Endangered Species	EEC/EC_{05} or NOEC	1
Aquatic Plants[2]		
Acute Risk	EEC/EC_{50}	1
Acute Endangered Species	EEC/EC_{05} or NOEC	1

[1] LD_{50}/sqft = (mg/sqft) / (LD_{50} * wt. of animal)
LD_{50}/day = (mg of toxicant consumed/day) / (LD_{50} * wt. of animal)

[2] EEC = (ppm or ppb) in water

APPENDIX E: Detailed Risk Quotients

Table 1: Aquatic Organism Risk Quotient Calculations for Parent Novaluron for Pome fruit, Cotton, and Potatoes.							
Scenario	**Acute Toxicity Threshold, LC_{50} or EC_{50} (mg ai/L)**	**Chronic Toxicity Threshold, NOEC (mg ai/L)**	**Peak Water Conc. (mg ai/L)**	**21-day Average Water Conc. (mg ai/L)**	**60-day Average Water Conc. (mg ai/L)**	**Acute RQ[a]**	**Chronic Species RQ[b]**
Pome Fruit (0.32 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and air blast equipment)							
Freshwater Fish	>0.96 (NOEC value)	0.00616	0.00504	0.00318	0.00224	<NOEC	0.81
Estuarine fish	>0.002 (NOEC value)	No data	0.00504	0.00318	0.00224	<NOEC	-
Freshwater Invert.	0.00015[c]	0.0000299	0.00504	0.00318	0.00224	34***	169[+]
Estuarine Invert. (shrimp)	0.00013	0.000026	0.00504	0.00318	0.00224	38.8***	194[+]
Estuarine Invert. (oyster)	0.0015	0.0003[d]	0.00504	0.00318	0.00224	3.4***	16.8[+]
Cotton (0.09 lb ai/A/App.; 3 app/yr; 7 day intervals; ground equipment)							
Freshwater Fish	>0.96 (NOEC value)	0.00616	0.00139	0.00085	0.00052	<NOEC	0.23
Estuarine fish	>0.002 (NOEC value)	No data	0.00139	0.00085	0.00052	<NOEC	-
Freshwater Invert.	0.00015[c]	0.0000299	0.00139	0.00085	0.00052	9.3***	46.5[+]
Estuarine Invert. (shrimp)	0.00013	0.000026	0.00139	0.00085	0.00052	10.7***	53.5[+]
Estuarine Invert. (oyster)	0.0015	0.0003[d]	0.00139	0.00085	0.00052	0.93***	4.6[+]
Cotton (0.09 lb ai/A/App.; 3 app/yr; 7 day intervals; aerial equipment)							
Freshwater Fish	>0.96 (NOEC value)	0.00616	0.00158	0.00093	0.00062	<NOEC	0.260

Table 1: Aquatic Organism Risk Quotient Calculations for Parent Novaluron for Pome fruit, Cotton, and Potatoes.							
Scenario	**Acute Toxicity Threshold, LC_{50} or EC_{50} (mg ai/L)**	**Chronic Toxicity Threshold, NOEC (mg ai/L)**	**Peak Water Conc. (mg ai/L)**	**21-day Average Water Conc. (mg ai/L)**	**60-day Average Water Conc. (mg ai/L)**	**Acute RQ[a]**	**Chronic Species RQ[b]**
Estuarine fish	>0.002 (NOEC value)	No data	0.00158	0.00093	0.00062	<NOEC	-
Freshwater Invert.	>0.002 (NOEC value)	0.0000299	0.00158	0.00093	0.00062	10.5***	52.8[+]
Estuarine Invert. (shrimp)	0.00013	0.000026	0.00158	0.00093	0.00062	12.2***	60.8[+]
Estuarine Invert. (oyster)	0.0015	0.0003[d]	0.00158	0.00093	0.00062	1.1***	5.3[+]
Potato (0.078 lb ai/A/App.; 3 app/yr; 10 day intervals; aerial equipment)							
Freshwater Fish	>0.96 (NOEC value)	0.00616	0.00109	0.00078	0.00054	<NOEC	0.18
Estuarine fish	>0.002 (NOEC value)	No data	0.00109	0.00078	0.00054	<NOEC	-
Freshwater Invert.	0.00015[c]	0.0000299	0.00109	0.00078	0.00054	7.3***	36.5[+]
Estuarine Invert. (shrimp)	0.00013	0.000026	0.00109	0.00078	0.00054	8.4***	41.9[+]
Estuarine Invert. (oyster0	0.0015	0.0003[d]	0.00109	0.00078	0.00054	0.7***	3.6[+]
Potato (0.078 lb ai/A/App.; 3 app/yr; 10 day intervals; ground equipment)							
Freshwater Fish	>0.96 (NOEC value)	0.00616	0.00094	0.00065	0.00043	<NOEC	0.15
Estuarine fish	>0.002 (NOEC value)	No data	0.00094	0.00065	0.00043	<NOEC	-
Freshwater Invert.	0.00015[c]	0.0000299	0.00094	0.00065	0.00043	6.3***	31.4[+]
Estuarine Invert. (shrimp)	0.00013	0.000026	0.00094	0.00065	0.00043	7.2***	36.2[+]

Table 1: Aquatic Organism Risk Quotient Calculations for Parent Novaluron for Pome fruit, Cotton, and Potatoes.							
Scenario	Acute Toxicity Threshold, LC_{50} or EC_{50} (mg ai/L)	Chronic Toxicity Threshold, NOEC (mg ai/L)	Peak Water Conc. (mg ai/L)	21-day Average Water Conc. (mg ai/L)	60-day Average Water Conc. (mg ai/L)	Acute RQ[a]	Chronic Species RQ[b]
Estuarine Invert. (oyster)	0.0015	0.0003[d]	0.00094	0.00065	0.00043	0.63***	3.1+

[a] * indicates an exceedance of Endangered Species Level of Concern (LOC).
** indicates an exceedance of Acute Restricted Use LOC.
*** indicates an exceedance of Acute Risk LOC.
[b] + indicates an exceedance of Chronic LOC.
[c] Estimated on the assumption that acute to chronic ratio for estuarine invertebrates applies to freshwater invertebrates.
[d] Estimated on the assumption that acute to chronic ratio for oyster is the same as shrimp.

Table 2 : Aquatic Organism Risk Quotient Calculations for RimOn 10 EC (Formulated Product of Novaluron) for Pome fruit, Cotton, and Potatoes.			
Scenario	Acute Toxicity Threshold, LC_{50} or EC_{50} (mg product/L)	Peak Water Conc. (mg ai/L)	Acute RQ[a]
Pome Fruit (3.478 lb product/A; single application air blast equipment 5% drift)			
Freshwater Fish	62.4	0.00395	0.000063
Freshwater Invert.	0.004	0.00395	0.9875
Estuarine Invert.	0.00012	0.00395	32.92
Pome Fruit (3.478 lb product/A; single application ground equipment 1% drift)			
Freshwater Fish	62.4	0.00079	0.000013
Freshwater Invert.	0.004	0.00079	0.1975
Estuarine Invert.	0.00012	0.00079	6.58
Cotton (0. 9783 lb product/A/; single application; ground equipment 1% drift)			
Freshwater Fish	62.4	0.00022	0.000004
Freshwater Invert.	0.004	0.00022	0.06
Estuarine Invert.	0.0012	0.00022	0.18333
Cotton (0.9783 lb product/A/; single application; aerial equipment 5% drift)			
Freshwater Fish	62.4	0.00111	0.000018
Freshwater Invert.	0.004	0.00111	0.28

Table 2 : Aquatic Organism Risk Quotient Calculations for RimOn 10 EC (Formulated Product of Novaluron) for Pome fruit, Cotton, and Potatoes.			
Scenario	Acute Toxicity Threshold, LC_{50} or EC_{50} (mg product/L)	Peak Water Conc. (mg ai/L)	Acute RQ[a]
Estuarine Invert.	0.0012	0.00111	0.92500
Potato (0.8478 lb product/A; single application; ground equipment 1% drift)			
Freshwater Fish	62.4	0.00019	0.000003
Freshwater Invert.	0.004	0.00019	0.05
Estuarine Invert.	0.0012	0.00019	0.16
Potato (0.8478 lb product/A; single application; aerial equipment 5% drift)			
Freshwater Fish	62.4	0.00096	0.00002
Freshwater Invert.	0.004	0.00096	0.24
Estuarine Invert.	0.0012	0.00096	0.80

Table 3: Aquatic Organism Risk Quotient Calculations for Chlorophenyl Urea (275 352 I) for Pome fruit, Cotton, and Potatoes.							
Scenario	Acute Toxicity Threshold, LC_{50} or EC_{50} (mg ai/L)	Chronic Toxicity Threshold, NOEC (mg ai/L)	Peak Water Conc. (mg ai/L)	21-day Average Water Conc. (mg ai/L)	60-day Average Water Conc. (mg ai/L)	Acute RQ[a]	Chronic RQ[b]
Pome Fruit (0.32 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and air blast equipment)							
Freshwater Fish	0.53	No data	0.00239	0.00200	0.00147	0.0045	-
Estuarine fish	No data	No data	0.00239	0.00200	0.00147	-	-
Freshwater Invert.	1.91	No data	0.00239	0.00200	0.00147	0.0013	-
Estuarine Invert.	No data	No data	0.00239	0.00200	0.00147	-	-
Cotton (0.09 lb ai/A/App.; 3 app/yr; 7 day intervals; ground equipment)							
Freshwater Fish	0.53	No data	0.00069	0.00058	0.00043	0.0013	-
Estuarine fish	No data	No data	0.00069	0.00058	0.00043	-	-
Freshwater Invert.	1.91	No data	0.00069	0.00058	0.00043	0.00036	-
Estuarine Invert.	No data	No data	0.00069	0.00058	0.00043	-	-

Table 3: Aquatic Organism Risk Quotient Calculations for Chlorophenyl Urea (275 352 I) for Pome fruit, Cotton, and Potatoes.							
Scenario	**Acute Toxicity Threshold, LC_{50} or EC_{50} (mg ai/L)**	**Chronic Toxicity Threshold, NOEC (mg ai/L)**	**Peak Water Conc. (mg ai/L)**	**21-day Average Water Conc. (mg ai/L)**	**60-day Average Water Conc. (mg ai/L)**	**Acute RQ[a]**	**Chronic RQ[b]**
Potato (0.078 lb ai/A/App.; 3 app/yr; 10 day intervals; aerial equipment)							
Freshwater Fish	0.53	No data	0.00059	0.00049	0.00036	0.001100	-
Estuarine fish	No data	No data	0.00059	0.00049	0.00036	-	-
Freshwater Invert.	1.91	No data	0.00059	0.00049	0.00036	0.000309	-
Estuarine Invert.	No data	No data	0.00059	0.00049	0.00036	-	-

[a] * indicates an exceedance of Endangered Species Level of Concern (LOC).
** indicates an exceedance of Acute Restricted Use LOC.
*** indicates an exceedance of Acute Risk LOC.
[b] + indicates an exceedance of Chronic LOC.

Table 4: Aquatic Plant Risk Quotient Calculations for the Parent Novaluron for Pome Fruit, Cotton, and Potato.					
Scenario	**Acute Toxicity Threshold, LC_{50} or EC_{50} (mg ai/L)**	**Endangered Species Toxicity Threshold, NOEC (mg ai /L)**	**Peak Water Concentration (mg ai/L)**	**Acute RQ[a]**	**Endangered Species RQ[bc]**
Pome Fruit (0.32 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and air blast equipment)					
Aquatic Vascular Plant (*Lemna gibba*)	No data	No data	0.00504	N/A	N/A
Marine diatom (*Selenastrum capricornutum*)	>9.68	9.68	0.00504	<0.00	0.00052
Cotton (0.09 lb ai/A/App.; 3 app/yr; 7 day intervals; ground equipment)					
Aquatic Vascular Plant (*Lemna gibba*)	No data	No data	0.00158	N/A	N/A
Marine diatom (*Selenastrum capricornutum*)	>9.68	9.68	0.00158	<0.00016	0.00016
Potato (0.078 lb ai/A/App.; 3 app/yr; 10 day intervals; aerial equipment)					
Aquatic Vascular Plant (*Lemna gibba*)	No data	No data	0.00109	N/A	N/A

Table 4: Aquatic Plant Risk Quotient Calculations for the Parent Novaluron for Pome Fruit, Cotton, and Potato.					
Scenario	Acute Toxicity Threshold, LC_{50} or EC_{50} (mg ai/L)	Endangered Species Toxicity Threshold, NOEC (mg ai /L)	Peak Water Concentration (mg ai/L)	Acute RQ[a]	Endangered Species RQ[bc]
Marine diatom (*Selenastrum capricornutum*)	>9.68	9.68	0.00109	<0.00011	0.00011

[a] * indicates an exceedence of Acute Risk LOC
[b] ** indicates an exceedence of Endangered Species LOC.
[c] There are currently no endangered nonvascular plant species

Table 5: Aquatic Plant Risk Quotient Calculations for RimOn 10EC (a Formulated Product of Novaluron) for Pome Fruit, Cotton, and Potato.					
Scenario	Acute Toxicity Threshold, LC_{50} or EC_{50} (mg ai/L)	Endangered Species Toxicity Threshold, NOEC (mg ai /L)	Peak Water Concentration (mg ai/L)	Acute RQ[a]	Endangered Species RQ[bc]
Pome Fruit (0.32 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and air blast equipment)					
Aquatic Vascular Plant (*Lemna gibba*)	0.777	0.777	0.00504	0.0065	0.0065
Marine diatom (*Selenastrum capricornutum*)	39	27.2	0.00504	0.00013	0.00019
Cotton (0.09 lb ai/A/App.; 3 app/yr; 7 day intervals; ground equipment)					
Aquatic Vascular Plant (*Lemna gibba*)	0.777	0.777	0.00158	0.00024	0.00024
Marine diatom (*Selenastrum capricornutum*)	39	27.2	0.00158	0.00004	0.00006
Potato (0.078 lb ai/A/App.; 3 app/yr; 10 day intervals; aerial equipment)					
Aquatic Vascular Plant (*Lemna gibba*)	0.777	0.777	0.00109	0.0014	0.0014
Marine diatom (*Selenastrum capricornutum*)	39	27.2	0.00109	0.00003	0.00004

[a] * indicates an exceedence of Acute Risk LOC
[b] ** indicates an exceedence of Endangered Species LOC.
[c] There are currently no endangered nonvascular plant species

Table 6: Aquatic Plant Risk Quotient Calculations for Chlorophenyl Urea (275 352 I) for Pome Fruit, Cotton, and Potato.					
Scenario	**Acute Toxicity Threshold, LC_{50} or EC_{50} (mg ai/L)**	**Endangered Species Toxicity Threshold, NOEC (mg ai/L)**	**Peak Water Concentration (mg ai/L)**	**Acute RQ[a]**	**Endangered Species RQ[bc]**
Pome Fruit (0.32 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and air blast equipment)					
Aquatic Vascular Plant (*Lemna gibba*)	No data	No data	0.00504	-	-
Marine diatom (*Selenastrum capricornutum*)	0.33	0.105	0.00504	0.01530	0.01000
Cotton (0.09 lb ai/A/App.; 3 app/yr; 7 day intervals; ground equipment)					
Aquatic Vascular Plant (*Lemna gibba*)	No data	No data	0.00158	-	-
Marine diatom (*Selenastrum capricornutum*)	0.33	0.105	0.00158	0.00480	0.01500
Potato (0.078 lb ai/A/App.; 3 app/yr; 10 day intervals; aerial equipment)					
Aquatic Vascular Plant (*Lemna gibba*)	No data	No data	0.00109	-	-
Marine diatom (*Selenastrum capricornutum*)	0.33	0.105	0.00109	0.00330	0.01040

a * indicates an exceedence of Acute Risk LOC
b ** indicates an exceedence of Endangered Species LOC.
c There are currently no endangered nonvascular plant species

Table 7: Avian Acute and Chronic Risk Quotient Calculations for Pome Fruit, Cotton, and Potatoes - Multiple Applications					
	Acute Toxicity Threshold, LC_{50} (mg ai /kg-diet)	**Chronic Toxicity Threshold, NOEC (mg ai/kg-diet)**	**Predicted Maximum Residue Levels (EEC)(mg ai/kg-diet)**	**Acute RQ [a]**	**Chronic RQ [b]**
Pome Fruit (0.32 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and air blast equipment)					
Short grass	>5200	9.8	191.48	<0.04	19.5[+]
Tall grass	>5200	962	87.76	<0.02	9.0[+]
Broadleaf forage, small insects	>5200	962	107.71	<0.02	11[+]

Table 9: Chronic Avian Risk Quotients From Maximum Concentration for Selected Foliar Dissipation Half-Life Values (ppm)								
5	32.89	**3.4+**	15.07	**1.5+**	18.5	**1.9+**	2.06	0.21
35	56.77	**5.8+**	26.02	**2.7+**	31.94	**3.3+**	3.55	0.36
Potato								
Foliar Dissipation Half-Life (Days)	**Avian and Mammalian Food Types**							
	Short Grass		**Tall Grass**		**Broadleaf/Forage Plants/Small Insects**		**Fruits, Pods, Seeds, Large Insects**	
	Max. Conc.	**Risk Quot.**	**Max. Conc.**	**Risk Quot.**	**Max. Conc.**	**Risk Quot.**	**Max. Conc.**	**Risk Quot.**
1	18.74	**1.9+**	8.59	0.88	10.54	**1.1+**	1.17	0.13
5	24.57	**2.5+**	11.26	**1.2+**	13.82	**1.4+**	1.54	0.16
35	46.67	**1.9+**	21.39	**2.2+**	26.25	**2.7+**	2.92	0.3

+ indicates an exceedence of Chronic LOC.

Table 10: Avian Acute Risk Quotient Calculations for Banded Spray Applications										
Animal Body Weight (g)	**Band width (ft.)**	**Untreated Row Space (ft)**	**Adjusted Appl. Rate[a]**	**Unadjusted Appl. Rate (from label)**	**Mg ai per ft² [b]**		**Acute Toxicity Threshold, LD_{50} (mg/kg)**	**Acute RQ (LD_{50} per ft²)[c]**		
					Adjusted	**Unadjusted**		**Adjusted**	**Unadjusted**	
Cotton (0.09 lb ai/A/App.; 3 app/yr; 7 day intervals; ground and aerial equipment)										
15	0.5	2	0.018	0.09	0.749736	3.748677686	2000	0.03	0.13	*
35	0.5	2	0.018	0.09	0.749736	3.748677686	2000	0.01	0.05	
1000	0.5	2	0.018	0.09	0.749736	3.748677686	2000	0.00	0.00	

[a] *Rate per banded acre* = $\frac{\text{band width in inches}}{\text{row width in inches}}$ x *Broadcast rate per acre*

[b] *mg ae per ft²* = $\frac{\text{App. Rate lbs ae}}{\text{Acre}}$ x $\frac{453{,}590\text{ mg}}{\text{Lbs}}$ x $\frac{\text{Acre}}{43{,}560\text{ ft}^2}$ x *% unincorporated* x $\frac{\text{untreated row space (ft)}}{\text{Bandwidth (ft)}}$

[c] RQ = $\frac{\text{Mg ae}}{\text{ft}^2}$ x $\frac{1}{\text{Weight of Animal (g)}}$ x $\frac{1000\text{ g}}{\text{kg}}$ x $\frac{\text{kg}}{\text{LD50 mg}}$

* indicates an exceedence of Endangered Species Level of Concern (LOC).
** indicates an exceedence of Acute Restricted Use LOC.
*** indicates an exceedence of Acute Risk LOC.

* indicates an exceedence of Endangered Species Level of Concern (LOC).
** indicates an exceedence of Acute Restricted Use LOC.
*** indicates an exceedence of Acute Risk LOC.

Table 11: Mammalian (Herbivore/Insectivore) Acute Risk Quotient Calculations for Spray Applications

Animal Body Weight (g)	% Body Weight Consumed	Scenario	Acute Toxicity Threshold, LD_{50} (mg/kg-bw)	Predicted Maximum Residue Levels		Predicted Mean Residue Levels	
				EEC (mg/kg-diet)	Acute RQ [a]	EEC (mg/kg-diet)	Acute RQ [a]
Pome Fruit (0.32 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and air blast equipment)							
		Short grass	>5000	191	0.04	68	0
15	95	Broadleaf forage, small insects	>5000	108	0.02	36	0
		Large insects	>5000	12	0.00	5.6	0
		Short grass	>5000	191	0.03	68	0
35	66	Broadleaf forage, small insects	>5000	108	0.01	36	0
		Large insects	>5000	12	0.00	5.6	0
		Short grass	>5000	191	0.01	68	0
1000	15	Broadleaf forage, small insects	>5000	108	0.00	36	0
		Large insects	>5000	12	0.00	5.6	0
Cotton (0.09 lb ai/A/App.; 3 app/yr; 7 day intervals; aerial and ground equipment)							
		Short grass	>5000	57	0.01	20	0.00
15	95	Broadleaf forage, small insects	>5000	32	0.01	11	0.00
		Large insects	>5000	4	0.00	2	0.00
		Short grass	>5000	57	0.01	20	0.00
35	66	Broadleaf forage, small insects	>5000	32	0.00	11	0.00
		Large insects	>5000	4	0.00	2	0.00
		Short grass	>5000	57	0.00	20	0.00
1000	15	Broadleaf forage, small insects	>5000	32	0.00	11	0.00
		Large insects	>5000	4	0.00	2	0.00
Potato (0.078 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and aerial equipment)							

Table 11: Mammalian (Herbivore/Insectivore) Acute Risk Quotient Calculations for Spray Applications							
Animal Body Weight (g)	% Body Weight Consumed	Scenario	Acute Toxicity Threshold, LD_{50} (mg/kg-bw)	Predicted Maximum Residue Levels		Predicted Mean Residue Levels	
				EEC (mg/kg-diet)	Acute RQ	EEC (mg/kg-diet)	Acute RQ [a]
35	66	Large insects	>5000	3	0.00	1.4	0.00
		Short grass	>5000	47	0.01	17	0.00
		Broadleaf forage, small insects	>5000	26	0.00	9	0.00
1000	15	Large insects	>5000	3	0.00	1.4	0.00
		Short grass	>5000	47	0.00	17	0.00
		Broadleaf forage, small insects	>5000	26	0.00	9	0.00
		Large insects	>5000	3	0.00	1.4	0.00

Table 12: Mammalian (Granivore) Acute Risk Quotient Calculations for Spray Applications							
Animal Body Weight (g)	% Body Weight Consumed	Scenario	Acute Toxicity Threshold, LD_{50} (mg/kg-bw)	Predicted Maximum Residue Levels		Predicted Mean Residue Levels	
				EEC (mg/kg-diet)	Acute RQ [a]	EEC (mg/kg-diet)	Acute RQ [a]
Pome Fruit (0.32 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and air blast equipment)							
15	21	Seeds	>5000	191	0.01	5.6	0.00
35	15	Seeds	>5000	12	0.00	5.6	0.00
1000	3	Seeds	>5000	12	0.00	5.6	0.00
Cotton (0.09 lb ai/A/App.; 3 app/yr; 7 day intervals; aerial and ground equipment)							
15	21	Seeds	>5000	3.5	0.00	1.6	0.00
35	15	Seeds	>5000	3.5	0.00	1.6	0.00
1000	3	Seeds	>5000	3.5	0.00	1.6	0.00

Table 12: Mammalian (Granivore) Acute Risk Quotient Calculations for Spray Applications							
Animal Body Weight (g)	% Body Weight Consumed	Scenario	Acute Toxicity Threshold, LD_{50} (mg/kg-bw)	Predicted Maximum Residue Levels		Predicted Mean Residue Levels	
				EEC (mg/kg-diet)	Acute RQ [a]	EEC (mg/kg-diet)	Acute RQ [a]
35	15	Seeds	>5000	3.5	0.00	1.6	0.00
1000	3	Seeds	>5000	3.5	0.00	1.6	0.00
Potato (0.078 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and aerial equipment)							
15	21	Seeds	>5000	2.9	0.00	1.4	0.00
35	15	Seeds	>5000	2.9	0.00	1.4	0.00
1000	3	Seeds	>5000	2.9	0.00	1.4	0.00

[a] $RQ = \frac{EEC}{LD_{50} / \% \text{ Body wt. consumed}}$

* indicates an exceedence of Endangered Species Level of Concern (LOC).
** indicates an exceedence of Acute Restricted Use LOC.
*** indicates an exceedence of Acute Risk LOC.

Table 13 : Mammalian Chronic Risk Quotient Calculations for Spray Applications					
Scenario	Chronic Toxicity Threshold, NOEC (mg/kg-bw/da)	Predicted Maximum Residue Levels		Predicted Mean Residue Levels	
		EEC (mg/kg-diet)	Chronic RQ [a]	EEC (mg/kg-diet)	Chronic RQ [a]
Pome Fruit (0.32 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and air blast equipment)					
Short grass	1000	191	0.19	68	0.36
Tall grass	1000	88	0.09	28.8	0.33
Broadleaf forage, small insects	1000	108	0.11	36	0.33
Large insects, Seeds	1000	12	0.01	5.6	0.47
Cotton (0.09 lb ai/A/App.; 3 app/yr; 7 day intervals; aerial and ground equipment)					

and Potatoes - Multiple Applications					
	Acute Toxicity Threshold, LC_{50} (mg ai /kg-diet)	Chronic Toxicity Threshold, NOEC (mg ai/kg-diet)	Predicted Maximum Residue Levels (EEC)(mg ai/kg-diet)	Acute RQ [a]	Chronic RQ [b]
Fruit, pods, seeds, large insects	>5200	962	11.97	<0.0023	1.2+
Cotton (0.09 lb ai/A/App.; 3 app/yr; 7 day intervals; ground and aerial equipment)					
Short grass	>5200	9.8	56.77	<0.01	5.8+
Tall grass	>5200	962	26.02	<0.005	2.7+
Broadleaf forage, small insects	>5200	962	31.94	<0.006	3.3+
Fruit, pods, seeds, large insects	>5200	962	3.55	<0.00068	0.36
Potato (0.078 lb ai/A/App.; 3 app/yr; 10 day intervals; ground and aerial equipment)					
Short grass	>5200	9.8	46.67	<0.01	4.8+
Tall grass	>5200	962	21.39	<0.004	2.2+
Broadleaf forage, small insects	>5200	962	26.95	<0.005	2.8+
Fruit, pods, seeds, large insects	>5200	962	2.92	<0.00056	0.30

[a] * indicates an exceedence of Endangered Species Level of Concern (LOC).
** indicates an exceedence of Acute Restricted Use LOC.
*** indicates an exceedence of Acute Risk LOC.
[b] + indicates an exceedence of Chronic LOC.

Table 8: Avian Acute and Chronic Risk Quotient Calculations for Pome Fruit, Cotton, and Potatoes - Single Applications							
	Acute Toxicity Threshold, LC_{50} (mg ai/kg-diet)	Chronic Toxicity Threshold, NOEC (mg ai/kg-diet)	Predicted Maximum Residue Levels (EEC)(mg ai/kg-diet)	Predicted Mean Residue Levels(EEC)(mg ai/kg-diet)	Acute RQ [a]	Chronic RQ [b] (Max. Residue)	Chronic RQ [b] (Mean Residue)
Pome Fruit (0.32 lb ai/A/App.)							
Short grass	>5200	9.8	76.8	27.2	<0.015	7.8+	2.3+
Tall grass	>5200	962	35	11.5	<0.0067	3.6+	1.2+
Broadleaf forage, small insects	>5200	962	43.2	14.4	<0.0083	4.4+	1.5+
Fruit, pods, seeds, large insects	>5200	962	4.8	2.2	<0.0009	0.49	0.22
Cotton (0.09 lb ai/A/App)							
Short grass	>5200	9.8	21.6	7.7	<0.0041	2.2+	0.78
Tall grass	>5200	962	9.9	3.2	<0.0019	1.0+	0.33
Broadleaf forage, small insects	>5200	962	12.5	4.1	<0.0024	1.3+	0.42

Table 8: Avian Acute and Chronic Risk Quotient Calculations for Pome Fruit, Cotton, and Potatoes - Single Applications							
	Acute Toxicity Threshold, LC_{50} (mg ai/kg-diet)	Chronic Toxicity Threshold, NOEC (mg ai/kg-diet)	Predicted Maximum Residue Levels (EEC)(mg ai/kg-diet)	Predicted Mean Residue Levels(EEC)(mg ai/kg-diet)	Acute RQ [a]	Chronic RQ [b] (Max. Residue)	Chronic RQ [b] (Mean Residue)
Cotton (0.09 lb ai/A/App)							
Short grass	>5200	9.8	21.6	7.7	<0.0041	2.2+	0.78
Tall grass	>5200	962	9.9	3.2	<0.0019	1.0+	0.33
Broadleaf forage, small insects	>5200	962	12.5	4.1	<0.0024	1.3+	0.42
Fruit, pods, seeds, large insects	>5200	962	1.35	0.6	<0.0001	0.14	0.06
Potato (0.078 lb ai/A/App.)							
Short grass	>5200	9.8	18.72	6.6	<0.0036	1.9+	0.67
Tall grass	>5200	962	8.58	2.8	<0.002	0.88	0.29
Broadleaf forage, small insects	>5200	962	10.53	3.5	<0.002	1.07+	0.36
Fruit, pods, seeds, large insects	>5200	962	1.17	0.6	<0.0001	0.12	0.06

[a] * indicates an exceedence of Endangered Species Level of Concern (LOC).
** indicates an exceedence of Acute Restricted Use LOC.
*** indicates an exceedence of Acute Risk LOC.
[b] + indicates an exceedence of Chronic LOC.

Table 9: Chronic Avian Risk Quotients From Maximum Concentration for Selected Foliar Dissipation Half-Life Values (ppm)								
Pome Fruit								
Foliar Dissipation Half-Life (Days)	**Avian and Mammalian Food Types**							
	Short Grass		**Tall Grass**		**Broadleaf/Forage Plants/Small Insects**		**Fruits, Pods, Seeds, Large Insects**	
	Max. Conc.	**Risk Quot.**	**Max. Conc.**	**Risk Quot.**	**Max. Conc.**	**Risk Quot.**	**Max. Conc.**	**Risk Quot.**
1	76.88	**7.8+**	35.23	**3.6+**	43.24	**4.4+**	4.8	0.51
5	100.8	**10.3+**	46.2	**4.7+**	56.7	**5.8+**	6.3	0.64
35	191.48	**19.5+**	87.76	**9.0+**	107.71	**11.0+**	11.97	**1.22+**
Cotton								

Table 13 : Mammalian Chronic Risk Quotient Calculations for Spray Applications					
Scenario	Chronic Toxicity Threshold, NOEC (mg/kg-bw/da)	Predicted Maximum Residue Levels		Predicted Mean Residue Levels	
		EEC (mg/kg-diet)	Chronic RQ [a]	EEC (mg/kg-diet)	Chronic RQ [a]
Large insects, Seeds	1000	3.55	0.00	1.66	0.47
Potato (0.078 lb al/A/App.; 3 app/yr; 10 day intervals; ground and aerial equipment)					
Short grass	1000	47	0.05	16.6	0.35
Tall grass	1000	21	0.02	6.9	0.33
Broadleaf forage, small insects	1000	26	0.03	8.7	0.33
Large insects, Seeds	1000	2.92	0.00	1.36	0.47

APPENDIX F: Data Requirements for Novaluron

Table 1: Environmental Fate Data Requirements for Novaluron			
Guideline #	**Data Requirement**	**Parent Novaluron**	**Study Classification**
161-1	Hydrolysis	44961008	acceptable
161-2	Photodegradation in Water	45638203	supplemental
161-3	Photodegradation on Soil	45638204	supplemental
161-4	Photodegradation in Air	N/A	
162-1	Aerobic Soil Metabolism	4496100944961010	supplemental ancillary[1]
162-2	Anaerobic Soil Metabolism	N/A	
162-3	Anaerobic Aquatic Metabolism	45638205 45638207/45789203	supplemental portion acceptable and portion unacceptable [2]
162-4	Aerobic Aquatic Metabolism	45638206	supplemental
163-1	Leaching-Adsorption/Desorption	4.49610114496e+31	supplemental supplemental supplemental[3] supplemental
163-2	Laboratory Volatility	N/A	
163-3	Field Volatility	N/A	
164-1	Terrestrial Field Dissipation	45638403 45638404 and 45789204	supplemental[4] acceptable[5]
164-2	Aquatic Field Dissipation	45785801	supplemental[6]
164-3	Forestry Dissipation	N/A	
165-4	Accumulation in Fish	4.57858024564e+23	supplemental unacceptable supplemental
165-5	Accumulation- aquatic non-target	N/A	
166-1	Ground Water- small prospective	N/A	
201-1	Droplet Size Spectrum		
202-1	Drift Field Evaluation		

[1] - a pilot study conducted prior to the final tests,
[2] - the portion of this study, conducted with [chlorophenyl-U-14C]-labeled novaluron, is classified acceptable, the portion of this study conducted with [difluorophenyl-U-14C]-labeled novaluron is classified unacceptable
[3] - an adsorption/desorption mobility study of major novaluron degradate, 275-352I,
[4] - conducted on Rimon 10EC concentration of a.i.: 9.7%,
[5] - MRID 45638404 is an interim study report and MRID 45789204 is a final report, conducted on Rimon 10EC (0.83 lb a.i./gal) and Rimon 6.7WDG (conc. of a.i.: 6.7% a.i. w/w),
[6] - conducted on Rimon 10EC concentration of a.i.: 9.5% (w/w),
[a] Member of Spray-Drift Task Force.

Table 2: Ecological Effects Data Requirements for Novaluron					
Guideline #		Data Requirement	Formulation	MRID #'s	Study Classification
71-1	850.21	Avian Oral LD_{50}	Parent	454768-01 454990-01	Core Supplemental[a]
71-2	850.22	Avian Dietary LC_{50}	Parent	454990-02 454990-03	Core Core
71-4	850.23	Avian Reproduction	Parent	456382-18 456382-19	Core Core
72-1	850.1075	Freshwater Fish LC_{50}	Parent Rimon 10EC 275352 I (degradate)	454990-04(05) 456383-14 454990-06	Supplemental[b] Supplemental[b] Core
72-2	850.101	Freshwater Invertebrate Acute LC_{50}	Parent Rimon 10 EC 275352 I (degradate)	454768-02 456383-13 454990-07	Invalid[c] Supplemental[d] Supplemental[e]
72-3(a)	850.1075	Estuarine/Marine Fish LC_{50}	Parent	456382-10	Supplemental[f]
72-3(b)	850.1025	Estuarine/Marine Mollusk EC_{50}	Parent	456382-08	Core
72-3©	850.1035 850.1045	Estuarine/Marine Shrimp EC_{50}	Parent Rimon 10EC	456382-09 460862-03	Core Core
72-4(a)	850.14	Freshwater Fish Early Life-Stage	Parent Parent Rimon 10EC	456382-16 456382-13 456384-06	Supplemental[g] Invalid[h] Supplemental[g]
72-4(b)	850.1300 850.1350	Aquatic Invertebrate Life-Cycle	Parent (freshwater) Parent (marine)	456382-11 456382-12	Core Supplemental[i]
72-5	850.15	Freshwater Fish Full Life-Cycle	Parent	457858-05	Invalid[j]
122-1(a)	850.41	Seed Germ./Seedling Emergence			
122-1(b)	850.415	Vegetative Vigor			
122-2	850.44	Aquatic Plant Growth	Parent Rimon 10EC 275382 I (dgradate)	456382-21 456384-11	Supplemental[h] Core Core
123-1(a)	850.4225	Seed Germ./Seedling Emergence (Tier 2)			N/A

Table 2: Ecological Effects Data Requirements for Novaluron					
Guideline #		Data Requirement	Formulation	MRID #'s	Study Classification
123-1(b)	850.425	Vegetative Vigor (Tier 2)			N/A
123-2	850.44	Aquatic Plant Growth (Tier 2)			N/A
141-1	850.302	Honey Bee Acute Contact LD_{50}	Parent Rimon 10EC	456382-20 456382-20	Core Core
141-2	850.303	Honey Bee Residue on Foliage			

[a] Could be up-graded to CORE if additional information is submitted.
[b] Despite several deviations from protocol, the compound was tested above the limits of solubility.
[c] Invalid due to high variability of mean measured concentrations. The test must be repeated. In addition, a sediment toxicity test performed in accordance with EPA sediment toxicity protocols must be conducted.
[d] Measured concentrations not centrifuged. However, this test does not have to be repeated.
[e] Several deviations may have impacted the water quality of this study.
[f] Stability measurements not consistent. The test must be repeated above the limits of solubility.
[g] Not performed to EPA guideline specifications.
[h] Numerous deviations from the protocol. Study should be repeated.
[i] Daily survival and mortality data were not provided. The first day of brood release was not reported, and second generation were not observed daily for at least 4 days for survival, development, and behavior. Since second generation were counted and then discarded, this study is not repairable.
[j] Raw data for survival of both generations and growth of the F_0 generation not provided. Could be up-graded to supplemental if raw data were submitted.
[k] Light intensity too high.

457858-00

MAKHTESHIM
A G A N
of
North America
Inc.

S-627382

October 16, 2002

Dr. S. Oonnithan
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Office of Pesticide Programs (7504C)
USEPA
1921 Jefferson Davis Highway
CM2, Room 266A
Arlington, VA 22202

Phone: 703-605-0368

Dear Dr. Oonnithan:

RE: RIMON (NOVALURON) END-USE PRODUCTS (EPA COMPANY NO. 66222): SUPPLEMENTAL DATA - ECOLOGICAL EFFECTS STUDIES IN SUPPORT OF POME AND COTTON USES.

Makhteshim-Agan of North America submits the enclosed reports to U.S. EPA in support of the above regulatory action.

The submission includes additional Ecological effects studies and a final report on Magnitude of the Residue in Pome Fruit. These data have been supplied to PMRA – Canada in support of the concurrent Work-Share registration review of the above use. These data are submitted in accordance with the agreement that identical sets of data would be made available to both agencies.

Enclosed are three (3) copies of each study, Formatted as per PR 86-5

I trust that these data are satisfactory but should you have any other questions or need for clarification, please do not hesitate to call.

Sincerely,
Makhteshim-Agan of North America Inc.

Robert C. Everich, Ph.D.
Senior Scientist

Cc: E. Gur, C. Iorizzo, A. Stout

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

Data matrix

MRID	Study Number	Study Title	Guideline No.
45785801 3Vol	MAK531/014023	Novaluron (Rimon 10EC) Assessment of Its Potential Biological Effects on Freshwater after Aquatic Ecosystems Based on Its Application to Outdoor Microcosms	OPPTS 850.1950
45785802	MAK775/023811	Depuration in Rainbow Trout Following Exposure to the Test Substance For 24 Hours	OPPTS 850.1730
45785803	MAK777/023873	Determination of Residue in the Carcass, Muscle and Viscera of Fathead Minnow (*Pimephales promelas*) Following Exposure for 315 Days	OPPTS 850.1730
45785804	AA010703	Magnitude of the Residue of Novaluron in Pome Fruit Raw Agricultural and Processed Commodities	OPPTS 860.1000 and 860.1500
45785805	AJ0047A	Novaluron Technical: Determination of Effects on the life Cycle of the Fathead Minnow (*Pimephales promelas*)	OPPTS 850.1500

DO NOT

457892-00

MAKHTESHIM
A G A N
of
North America
Inc.

5627383

October 16, 2002

Dr. S. Oonnithan
Document Processing Desk (APPL)
Office of Pesticide Programs (7504C)
USEPA
1921 Jefferson Davis Highway
CM2, Room 266A
Arlington, VA 22202

Phone: 703-605-0368

Dear Dr. Oonnithan:

RE: RIMON (NOVALURON) TECHNICAL (EPA REG. NO. 11678-57): FINAL REPORTS IN SUPPORT OF POME AND COTTON USES.

Makhteshim-Agan of North America, on behalf of Makhteshim Chemical Works, Ltd submits the enclosed reports to U.S. EPA in support of the above regulatory action.

The submission includes final reports in place of interim reports previously submitted.

Enclosed are three (3) copies of each study, Formatted as per PR 86-5

I trust that these data are satisfactory but should you have any other questions or need for clarification, please do not hesitate to call.

Sincerely,
Makhteshim-Agan of North America Inc.

Robert C. Everich, Ph.D.
Senior Scientist

Cc: E. Gur, C. Iorizzo, A. Stout

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

TRANSMITTAL DOCUMENT FOR NOVALURON TECHNICAL INSECTICIDE

Submitter:
Makhteshim Chemical Works Ltd. (Technical)
Beer-Sheva, ISRAEL

Regulatory action/reason for submission:
Additional Data in Support of Section 3 Registration application for Pome Fruit and Cotton
EPA Company No. 11678, File Symbol 11678-57 (Technical)

Transmittal date:
October 16, 2002

Company official:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Company name:
Makhteshim Chemical Works, Ltd.

Company contact:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Robert C. Everich, Ph.D.

Data matrix

MRID	Study Number	Study Title	Guideline No.
45789201	11626-016	Rimon-Quantification of Active Ingredient and Impurities Present at or Above 0.1% in Technical Rimon	OPPTS 830-1700, 1750 and 1800
45789202	2002-022	Multiresidue Method Testing for Novaluron	OPPTS 860.1360
45789203	PTRL 1028W-2 (UCC 2002-024)	Anaerobic Aquatic Metabolism of [^{14}C]Novaluron	162-3
45789204	AA010702	Terrestrial Field Soil Dissipation of Novaluron	164-1

TRANSMITTAL DOCUMENT FOR NOVALURON END-USE PRODUCTS 10EC AND 7.5 WDG INSECTICIDE

Submitter:
Makhteshim-Agan of North America Inc.

Regulatory action/reason for submission:
Additional Data in Support of Section 3 Registration Application for Pome Fruit and Cotton
EPA Company No. 66222

Transmittal date:
October 16, 2002

Company official:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Company name:
Makhteshim- Agan of North America Inc.

Company contact:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Robert C. Everich, Ph.D

OCT 31 2002

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

MAKHTESHIM CHEMICAL WORKS, LTD
C/O MAKHTESHIM-AGAN OF N.A.INC
551 FIFTH AVE, SUITE 1100
NEW YORK, NY 10176

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 10/25/02. 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.

MAKHTESHIM
A G A N
of
North America
Inc.

5/627 10/230

October 4, 2002

Dr. S. Oonnithan
Document Processing Desk (APPL)
Office of Pesticide Programs (7504C)
USEPA
1921 Jefferson Davis Highway
CM2, Room 266A
Arlington, VA 22202

Phone: 703-605-0368

Dear Dr. Oonnithan:

RE: RIMON (NOVALURON) TECHNICAL (EPA REG. NO. 11678-57): ADDITIONAL INFORMATION IN SUPPORT OF POME AND COTTON USES.

In response to a request from Meredith Laws, I am enclosing additional information in support of the above registration. EPA Contract reviewers in their preliminary screen identified the following data gaps:

1. **Storage Stability data for: Cotton: Magnitude of the Residue (AASI Study No. AA010704, MRID 45638412.**

The appropriate data tables from the above study and a previous study (Study No. AA990801) including summaries of storage stability are included as Attachment #1

2. **Historical control data for: Rimon Technical – Combined Carcinogenicity and Toxicity Study by Dietary Administration to CD-1 Mice for 78 Weeks. Report No. MAK 428/992033, MRID 45651507.**

Control data from the contracting laboratory, Huntingdon Life Sciences, UK,are available. Due to the substantial size of this database, HLS asks that we specify which areas are of concern. In this way they can provide historical control data specific to the concerns of the reviewer. Please contact; Dr. Elliot Gordon, Toxicologist, Makhteshim-Agan of North America, New York, NY, (212) 896-4931.

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

3. **Poultry Nature of the Residue Study.**

Enclosed are three (3) copies, Formatted as per PR 86-5

Waiver Request for: Magnitude of the Residue –Meat/Milk/Poultry/Eggs (Poultry Feeding Study) OPPTS 860.1480 and Nature of the Residue – Livestock (Poultry Metabolism Study) OPPTS 860.1300

I trust that these data are satisfactory but should you have any other questions or need for clarification, please do not hesitate to call.

Sincerely,
Makhteshim-Agan of North America Inc.

Robert C. Everich, Ph.D.
Senior Scientist

Enclosures (2) Storage Stability Data (Attachment #1)
Waiver Request – Poultry Feeding and Metabolism (3 copies)

Cc: E. Gur, E. Gordon, A. Stout

Attachment #1

Storage Stability data for: Cotton: Magnitude of the Residue (AASI Study No. AA010704, MRID 45638412.

5627110

TRANSMITTAL DOCUMENT FOR NOVALURON TECHNICAL INSECTICIDE

Submitter:
Makhteshim Chemical Works Ltd. (Technical)
Beer-Sheva, ISRAEL

Regulatory action/reason for submission:
Additional Data in Support of Section 3 Registration application for Pome Fruit and Cotton
EPA Company No. 11678, File Symbol 11678-57 (Technical)

Transmittal date:
September 30, 2002

Company official:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Company name:
Makhteshim Chemical Works, Ltd.

Company contact:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Robert C. Everich, Ph.D.

MRID	Guideline	Author	Date	Title	Data Owner
	860.1480, 860.1300	Gordon, E	2002	Waiver Request for: Magnitude of the Residue –Meat/Milk/Poultry/Eggs (Poultry Feeding Study) OPPTS 860.1480 and Nature of the Residue – Livestock (Poultry Metabolism Study) OPPTS 860.1300	MCW

569110

04
20-60-01

457718-00

MAKHTESHIM
A G A N
of
North America
Inc.

September 30, 2002

5-624036
5627087/230

Dr. S. Oonnithan
Document Processing Desk (TOR)
Office of Pesticide Programs (7504C)
USEPA, CM2, Room 266A
1921 Jefferson Davis Highway
Arlington, VA 22202-4501

Phone: 703-605-0368

Dear Dr. Oonnithan:

RE: Request for Threshold of Regulation Decision for Rimon 10 EC use on Crop Group 1D Tuberous and Corm Vegètables. Data Submitted in Support of Section 3 Registration Applications. EPA Company No. 11678, File Symbol 11678-57 (Technical) and 66222-35 (10 EC End-use product)

As per our phone conversation, I submit this request for a Threshold of Regulation Decision for the above use. In reviewing the available database generated for global registration of novaluron, and the total absence of residues in tubers, it is clear that a full MOR program in the U.S. is not warranted. I believe that this use meets the criteria for the Threshold of Regulation Policy described in the 1999 revised OPP Science Policy Document.

PMRA in Canada is also in the process of making a Threshold of Regulation determination for this use. The same dataset has been submitted to PMRA and a work-share agreement has been reached between both Agencies. For your convenience, PMRA Review Templates are included as attachments to assist in your evaluation.

Nature of the Residue

A metabolism study with 14C novaluron was performed at Huntingdon Life Sciences, UK using two applications of a field rate of 100g ai/ha at 43 and 29 days prior to harvest. Plants received two applications of either the radiolabeled difluorophenyl, or chlorophenyl novaluron formulated as "RIMON 10 EC" The majority of the radioactivity was washed off the foliage after the first application accounting for 93.8% - 95.9% TRR, decreasing to 80.5% - 83.3% TRR at harvest. Most of the remaining radioactivity was extracted from the foliage. Parent novaluron was the major radioactive residue in the foliage

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Tel: 212-661-9800 Fax: 212-661-9038 / 9043

extractions and washes. Levels of radiolabeled residues in the tubers were 0.001 ppm or less.

Magnitude of the Residue

Studies were conducted in France, Germany, Greece, Italy, Spain, Switzerland, and South Africa at up to 6 applications per season, up to 250 g ai/ha, with PHI's ranging from 0 to 37 days. In all cases, with no exceptions, residue levels were below the LOQ of 0.01ppm or the LOD of 0.002 ppm. This represents a total 28 trials including several decline curves in widely distributed geographic zones and numerous varieties.

In the U.S., we intend to label a maximum of 2 applications of the same 10 EC formulation used in the European trials. Recommended rate will be 85 g ai/ha with a 7 day PHI.

A Confined Rotational Crop study has already been submitted in support of the cotton use currently under review.

U.S. Reside Program

We are conducting (2002 season) two RAC residue trials in the U.S. at a 5x rate, 7-day and zero-day PHI, in Regions I and XI. Based on the potato metabolism study (and the existing residue database) we will analyze only RAC's - not processed fractions. This data will be submitted to U.S. EPA upon completion to supplement the enclosed MOR and NOR data.

I trust that this information and data submission is adequate to allow the Agency to make a determination on this request. However should you require additional information or a presentation of the data I would be happy to comply.

Sincerely,

Rob Everich, Ph.D.
Senior Scientist
Makhteshim-Agan

Enclosures (3) PMRA Review Templates
Transmittal Letter

Cc: E. Gur, D. Latter

TRANSMITTAL DOCUMENT FOR NOVALURON TECHNICAL AND RIMON 10 EC INSECTICIDE

Submitter:
Makhteshim Chemical Works Ltd. (Technical)
Beer-Sheva, ISRAEL

Makhteshim – Agan of North America Inc. (End-use product)
New York, NY

Regulatory action/reason for submission:
Request for Threshold of Regulation Decision for Rimon 10 EC use on Crop Group 1D Tuberous and Corm Vegetables. Data Submitted in Support of Section 3 Registration application. EPA Company No. 11678, File Symbol 11678-57 (Technical) and 66222-35 (10 EC End-use product)

Transmittal date:
September 30, 2002

Company official:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Company name:
Makhteshim Chemical Works, Ltd.
Makhteshim-Agan of North America Inc.

Company contact:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Robert C. Everich, Ph.D.

MRID	Guideline	Author	Date	Title	Data Owner
45771801	860.1500	Wilson, A	2002	Residue Decline Curve Study with "RIMON" 10EC Applied to Potatoes in Germany, Spain, and Italy. Huntingdon Life Sciences, Ltd., Study No. MAK 540/002056, Makhteshim Chemical Works Ltd. Report No. R-10927.	MCW
45771802	860.1500	Wilson, A	2002	Raw agricultural Commodity and Residue Decline Curve Study with "RIMON" 10EC Applied to Potatoes in Germany, Northern and Southern France, Spain, and Italy. Huntingdon Life Sciences, Ltd., Study No. MAK 600/004555, Makhteshim Chemical Works Ltd. Report No. R-11617.	MCW
45771803	860.1300	Crowe, A	1998	14C "Rimon" Metabolism in Potatoes. Huntingdon Life Sciences, Ltd., Study No. MAK 438/983684. Makhteshim Chemical Works Ltd. Report No. R-9003.	MCW

OCT 10 2002

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

5-627087

MAKHTESHIM CHEMICAL WORKS, LTD
C/O MAKHTESHIM-AGAN OF N.A.INC
551 FIFTH AVE, SUITE 1100
NEW YORK, NY 10176

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 10/04/02. 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.

457032-00

S614391 230

June 25, 2002

MAKHTESHIM
A G A N
of
North America
Inc.

Dr. S. Oonnithan
Document Processing Desk (APPL)
Office of Pesticide Programs (7504C)
USEPA
1921 Jefferson Davis Highway
CM2, Room 266A
Arlington, VA 22202

Phone: 703-605-0368

Dear Dr. Oonnithan:

RE: RIMON (NOVALURON) TECHNICAL (EPA REG. NO. 11678-57): ACUTE NEUROTOXICITY STUDY: ADDITIONAL INFORMATION.

Following the HIARC review of the above registration submission on Ornamentals, HED issued a Memorandum on August 15th, 2001 outlining toxicology data gaps. The review mentioned in point *c.* that the submitted acute neurotoxicity study:

(RIMON Technical: Neurotoxicity study by a single oral gavage administration to CD rats followed by a 14-day observation period. A. Broadmeadow, W.D. Harvey and M.J. Collier; Huntingdon Life Sciences, Ltd. Report No. MAK 480/983207; 2/3/99, MRID # 45082601)

was classified as Unacceptable/Guideline due to the absence of a histopathological examination on low and intermediate dosage animals and the apparent presence of neuropathology findings.

This submission consists of the results of further histopathological examination of all tissues and a peer-reviewed investigation of all of the findings.

The enclosed secondary evaluation of the above study shows that there was no statistically significant trend between Control and treated animals with respect to behavior or histopathology. In view of the relatively small number of animals affected, the incidental increase is considered fortuitous and not toxicologically significant.

It is therefore concluded that single acute oral administration of "Rimon" Technical to CD rats at dosages up to 2000 mg/kg was not neurotoxic and we request that the submitted study be upgraded to Core/Guideline.

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

Based on an absence of acute neurotoxic effects, we maintain that the requirement for an additional subchronic oral neurotoxicity study, as suggested by the HED review, is unwarranted.

In support of this submission, we enclose the following:

- EPA Application Form (8570-1)
- Three copies of data formatted to comply with PRN 86-5
- Transmittal document

Sincerely,
Makhteshim-Agan of North America Inc.

Anne Stout for

Robert C. Everich, Ph.D.
Senior Scientist

cc: E. Gur, E. Gordon

MAKHTESHIM
A G A N
of
North America
Inc.

TRANSMITTAL DOCUMENT FOR RIMON® TECHNICAL

Submitter:
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

Regulatory action/reason for submission:
Submission of additional data
EPA Reg. No. 11678-57

Transmittal date:
6-25-02

List of submitted studies:

MRID #	Title	Data Requirement
45703201	Neurotoxicity Study by a Single Oral Gavage Administration to CD Rats Followed by a 14-Day Observation Period; Response to the EPA Review of the Rimon Technical Study for MRID No. 45082601, Authors: A. Broadmeadow, W. Davies, Laboratory Study No. MAK480/983207, Makhteshim Chemical Works Project R-9817, Date: 6-25-02	Series 81-8

Company official:
Andy Eimanis
Regulatory Manager
212-896-4920

Company name:
Makhteshim-Agan of North America, Inc.

Company contact:
Anne Stout
Registration Specialist
Phone; 901-861-4400

Anne Stout

Please read instructions on reverse before completing form. Form Approved. 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 11678-57	2. EPA Product Manager S. Oonnithan	3. Proposed Classification ☑ None ☐ Restricted
4. Company/Product (Name) Rimon Technical	PM# IRB	
5. Name and Address of Applicant *(Include ZIP Code)* Makhteshim-Agan of North America, Inc. 551 Fifth Avenue, Suite 1100 New York, NY 10176 ☐ *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 _____
☐ Notification - Explain below.
☐ Final printed labels in repsonse to Agency letter dated _____
☐ "Me Too" Application.
☑ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)
Submission of additional data

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	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☐ 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)
Anne Stout	Registration Specialist	901-861-4400

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 Anne Stout	3. Title Registration Specialist
4. Typed Name Anne Stout	5. Date 6-25-02

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

JUL 0 2 2002

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

MAKHTESHIM CHEMICAL WORKS, LTD
C/O MAKHTESHIM-AGAN OF N.A.INC
551 FIFTH AVE, SUITE 1100
NEW YORK, NY 10176

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 06/27/02. 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.

457032-00

MAKHTESHIM
A G A N
of
North America
Inc.

June 25, 2002

Dr. S. Oonnithan
Document Processing Desk (APPL)
Office of Pesticide Programs (7504C)
USEPA
1921 Jefferson Davis Highway
CM2, Room 266A
Arlington, VA 22202

Phone: 703-605-0368

Dear Dr. Oonnithan:

RE: RIMON (NOVALURON) TECHNICAL (EPA REG. NO. 11678-57): ACUTE NEUROTOXICITY STUDY: ADDITIONAL INFORMATION.

Following the HIARC review of the above registration submission on Ornamentals, HED issued a Memorandum on August 15th, 2001 outlining toxicology data gaps. The review mentioned in point *c.* that the submitted acute neurotoxicity study:

(RIMON Technical: Neurotoxicity study by a single oral gavage administration to CD rats followed by a 14-day observation period. A. Broadmeadow, W.D. Harvey and M.J. Collier; Huntingdon Life Sciences, Ltd. Report No. MAK 480/983207; 2/3/99, MRID # 45082601)

was classified as Unacceptable/Guideline due to the absence of a histopathological examination on low and intermediate dosage animals and the apparent presence of neuropathology findings.

This submission consists of the results of further histopathological examination of all tissues and a peer-reviewed investigation of all of the findings.

The enclosed secondary evaluation of the above study shows that there was no statistically significant trend between Control and treated animals with respect to behavior or histopathology. In view of the relatively small number of animals affected, the incidental increase is considered fortuitous and not toxicologically significant.

It is therefore concluded that single acute oral administration of "Rimon" Technical to CD rats at dosages up to 2000 mg/kg was not neurotoxic and we request that the submitted study be upgraded to Core/Guideline.

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

Based on an absence of acute neurotoxic effects, we maintain that the requirement for an additional subchronic oral neurotoxicity study, as suggested by the HED review, is unwarranted.

In support of this submission, we enclose the following:

- EPA Application Form (8570-1)
- Three copies of data formatted to comply with PRN 86-5
- Transmittal document

Sincerely,
Makhteshim-Agan of North America Inc.

Anne Stout for

Robert C. Everich, Ph.D.
Senior Scientist

cc: E. Gur, E. Gordon

MAKHTESHIM
A G A N
of
North America
Inc.

TRANSMITTAL DOCUMENT FOR RIMON® TECHNICAL

Submitter:
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

Regulatory action/reason for submission:
Submission of additional data
EPA Reg. No. 11678-57

Transmittal date:
6-25-02

List of submitted studies:

MRID #	Title	Data Requirement
45703201	Neurotoxicity Study by a Single Oral Gavage Administration to CD Rats Followed by a 14-Day Observation Period; Response to the EPA Review of the Rimon Technical Study for MRID No. 45082601, Authors: A. Broadmeadow, W. Davies, Laboratory Study No. MAK480/983207, Makhteshim Chemical Works Project R-9817, Date: 6-25-02	Series 81-8

Company official:
Andy Eimanis
Regulatory Manager
212-896-4920

Company name:
Makhteshim-Agan of North America, Inc.

Company contact:
Anne Stout
Registration Specialist
Phone; 901-861-4400

Anne Stout

Rimon® Technical

457032-01

Study Title: Neurotoxicity Study by a Single Oral Gavage Administration to CD Rats Followed by a 14-Day Observation Period; Response to the EPA Review of the Rimon Technical Study for MRID No. 45082601.

Authors: A. Broadmeadow, W. Davies

For Makhteshim Chemical Works, Ltd.

551 Fifth Avenue, Suite 1100

New York, NY 10176

Laboratory Study No. MAK480/983207

Makhteshim Chemical Works Project R-9817

Date: 6-25-02

Pages 247-253 *Access to FIFRA health and safety data is restricted under FIFRA section 10(g)*

Please read instructions on reverse before completing form.

Form Approved. 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 11678-57	2. EPA Product Manager S. Oonnithan	3. Proposed Classification ☑ None ☐ Restricted
4. Company/Product (Name) Rimon Technical	PM# IRB	
5. Name and Address of Applicant *(Include ZIP Code)* Makhteshim-Agan of North America, Inc. 551 Fifth Avenue, Suite 1100 New York, NY 10176 ☐ *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 _____
☑ Notification - Explain below.
☑ Final printed labels in repsonse to Agency letter dated 6-18-02
☐ "Me Too" Application.
☐ Other - Explain below.

NOTIFICATION
NOTIFICATION
AUG 14 2002

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

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 submitted	If "Yes" Unit Packaging wgt. / No. per container	If "Yes" Package wgt / No. per container	

3. Location of Net Contents Information	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☐ 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)
Anne Stout	Registration Specialist	901-861-4400

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.

2. Signature A Stout	3. Title Registration Specialist	6. Date Application Received (Stamped)
4. Typed Name Anne Stout	5. Date 6-28-02	

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

RimOn®

NOTIFICATION

AUG 14 2002

TECHNICAL

(Novaluron)

For The Manufacture of Insecticides Only

	% BY WT.
ACTIVE INGREDIENT: Novaluron: 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	98.5%
INERT INGREDIENTS:	1.5%
TOTAL	100.0%

KEEP OUT OF REACH OF CHILDREN

CAUTION

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

FIRST AID

IF ON SKIN OR CLOTHING:
- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor 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.

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 eye.
- Call a poison control center or doctor 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 for further treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment.

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION. Harmful if absorbed through skin. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters except in accordance with the requirements of a 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 treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

NET CONTENTS 55 POUNDS

MAKHTESHIM AGAN NORTH AMERICA

Makhteshim Chemical Works, Ltd.
c/o Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

EPA Reg. No. 11678-57
EPA Est. No. 11678-ISR-002

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. This pesticide is for the further manufacture of formulated insecticides only. Formulators using this product are responsible for obtaining EPA registration for their formulated products.

Only for formulation into an insecticide for the following uses:

(1) Ornamentals (greenhouses, shadehouses, and outdoor nurseries)
(2) Uses for which USEPA has accepted the required data and/or citations of data that the formulator has submitted in support of registration; and
(3) Uses for experimental purposes that are in compliance with USEPA requirements.

STORAGE AND DISPOSAL

STORAGE: Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited.
PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of at an approved waste disposal facility.
CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If drum is contaminated and cannot be reused, dispose of in the same manner.

WARRANTY STATEMENT

MAKHTESHIM-AGAN OF NORTH AMERICA warrants that this product conforms to the chemical description on the label thereof and is reasonably fit for purposes stated on such label only when used in accordance with directions under normal use conditions. It is impossible to eliminate all risks inherently associated with use of this product. Crop injury, ineffectiveness, or other unintended consequences may result because of such factors as weather conditions, presence of other materials, or the manner of use or application, all of which are beyond the control of MAKHTESHIM-AGAN OF NORTH AMERICA. In no case shall MAKHTESHIM-AGAN OF NORTH AMERICA be liable for consequential, special, or indirect damages resulting from the use or handling of this product. All such risks shall be assumed by the Buyer. In addition to the foregoing, no purchaser of this product (other than an end user) shall be entitled to any reimbursement for any loss suffered as a result of any suspension or cancellation of the registration for this product by the U.S. Environmental Protection Agency. Except as expressly provided herein, MAKHTESHIM-AGAN OF NORTH AMERICA makes no warranties, guarantees, or representations of any kind, either expressed or implied, or by usage of trade, statutory or otherwise, with regard to the product sold, including, but not limited to merchantability, fitness for a particular purpose, use or eligibility of the product for any particular trade usage. The exclusive remedy of any buyer or user of this product for any and all losses, injuries, or damages resulting from or in any way arising from the use, handling, or application of this product, whether in contract, warranty, tort, negligence, strict liability, or otherwise, shall be damages not exceeding the purchase price paid for this product or, at MAKHTESHIM-AGAN OF NORTH AMERICA's election, the replacement of this product.

Rimon Technical (11678-57)(EPA app 6-18-02)

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

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

June 18, 2002

RECEIVED
JUN 25 2002

Robert Everich
Senior Scientist
Makhteshim-Agan of N. America, Inc.
551 Fifth Ave, Suite: 1100
New York, NY 10176

Subject: EPA Reg. No. 11678-57
Rimon® Technical
Label Amendment
Your Letter dated May 22, 2002

Dear Dr. Everich:

The label amendment you submitted for the product referred to above has been reviewed by the Agency. The additional uses of Rimon 10EC on ornamentals grown in shade houses and outdoor nurseries are acceptable.

A stamped copy of the label is enclosed for your records. Submit one (1) copy of your final printed labeling before you release the product for shipment. Should you have any questions, do not hesitate to contact me at 703-605-0368.

Sincerely,

S. Oonnithan
Entomologist
Insecticide Rodenticide Branch
Registration Division (7505C)

Encl:

KimOn™

ACCEPTED
JUN 18 2002
Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 11678-57

TECHNICAL

(Novaluron)

For The Manufacture of Insecticides Only

	% BY WT.
ACTIVE INGREDIENT: Novaluron: 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	98.5%
INERT INGREDIENTS:	1.5%
TOTAL	100.0%

CAUTION

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

FIRST AID

IF ON SKIN OR CLOTHING:
- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor 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.

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 eye.
- Call a poison control center or doctor 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 for further treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment.

Label

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION. Harmful if absorbed through skin. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters except in accordance with the requirements of a 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 treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

NET CONTENTS 55 POUNDS

EPA Reg. No. 11678-57
EPA Est. No. 11678-IS-1

Makhteshim Chemical Works, Ltd.
c/o Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. This pesticide is for the further manufacture of formulated insecticides only. Formulators using this product are responsible for obtaining EPA registration for their formulated products.

Only for formulation into an insecticide for the following uses:

(1) Ornamentals (greenhouse, shadehouse and outdoor nurseries)

(2) Uses for which USEPA has accepted the required data and/or citations of data that the formulator has submitted in support of registration; and

(3) Uses for experimental purposes that are in compliance with USEPA requirements.

STORAGE AND DISPOSAL

STORAGE: Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited.

PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of at an approved waste disposal facility.

CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If drum is contaminated and cannot be reused, dispose of in the same manner.

WARRANTY STATEMENT

MAKHTESHIM-AGAN OF NORTH AMERICA warrants that this product conforms to the chemical description on the label thereof and is reasonably fit for purposes stated on such label only when used in accordance with directions under normal use conditions. It is impossible to eliminate all risks inherently associated with use of this product. Crop injury, ineffectiveness, or other unintended consequences may result because of such factors as weather conditions, presence of other materials, or the manner of use or application, all of which are beyond the control of MAKHTESHIM-AGAN OF NORTH AMERICA. In no case shall MAKHTESHIM-AGAN OF NORTH AMERICA be liable for consequential, special, or indirect damages resulting from the use or handling of this product. All such risks shall be assumed by the Buyer. In addition to the foregoing, no purchaser of this product (other than an end user) shall be entitled to any reimbursement for any loss suffered as a result of any suspension or cancellation of the registration for this product by the U.S. Environmental Protection Agency. Except as expressly provided herein, MAKHTESHIM-AGAN OF NORTH AMERICA makes no warranties, guarantees, or representations of any kind, either expressed or implied, or by usage of trade, statutory or otherwise, with regard to the product sold, including, but not limited to merchantability, fitness for a particular purpose, use or eligibility of the product for any particular trade usage. The exclusive remedy of any buyer or user of this product for any and all losses, injuries, or damages resulting from or in any way arising from the use, handling, or application of this product, whether in contract, warranty, tort, negligence, strict liability, or otherwise, shall be damages not exceeding the purchase price paid for this product or, at MAKHTESHIM-AGAN OF NORTH AMERICA's election, the replacement of this product.

Rimon Technical (EPA app 9-25-01)

MAKHTESHIM
A G A N
of
North America
Inc.

June 28, 2002

Document Processing Desk (FPL)
Registration Division (7504C)
USEPA
Ariel Rios Building
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Attn: Dr. Oonni Oonnithan
Insecticide-Rodenticide Branch
Phone: 703-305-5404

Re: Final printed labeling
Rimon 10EC, EPA Reg. No. 66222-35
Rimon 10SC, EPA Reg. No. 66222-40
Rimon Technical, EPA Reg. No. 11678-57

Dear Dr. Oonnithan:

Enclosed is one copy of final printed labeling for each of the referenced products. The following administrative documents are attached:

- Application Form (EPA Form 8570-1)
- One copy of final printed labeling
- Copy of EPA approved label

Should you have additional questions, please contact me at 901-861-4400.

Sincerely,

Anne Stout

Anne Stout
Registration Specialist
For Makhteshim-Agan

Enclosures

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

To Joyce Edwards

MAKHTESHIM
A G A N
of
North America
Inc.

August 14, 2002

Document Processing Desk (FPL)
Registration Division (7504C)
USEPA
Ariel Rios Building
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Attn: Dr. Oonni Oonnithan for Ms. Joyce Edwards
Insecticide-Rodenticide Branch
Phone: 703-305-5404

Re: **Final printed labeling**
Additon of certification statement per Joyce Edward's phone call 8-14-02
Rimon 10EC, EPA Reg. No. 66222-35
Rimon 10SC, EPA Reg. No. 66222-40
Rimon Technical, EPA Reg. No. 11678-57

Dear Dr. Oonnithan:

Enclosed is one copy of final printed labeling for each of the referenced products. The following administrative documents are attached:

- Application Form (EPA Form 8570-1)
- One copy of final printed labeling
- Copy of EPA approved label

This notification is consistent with the provisions of PR Notice 98-10 and EPA regulations at 40 CFR 152.46, and no other changes have been made to the labeling or the confidential statement of formula for this product. I understand that it is a violation of 18 USC Sec. 1001 to willfully make any false statement to EPA. I further understand that if this notification is not consistent with the terms of PR Notice 98-10 and 40 CFR 152.46, this product may be in violation of FIFRA and I may be subject to enforcement action and penalties under Sections 12 and 14 of FIFRA.

Should you have additional questions, please contact me at 901-861-4400.

Sincerely,

Anne Stout

Anne Stout
Registration Specialist
For Makhteshim-Agan

Enclosures

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

TOLERANCE PETITION

5614391

PETITION PROPOSING TOLERANCES FOR RESIDUES OF NOVALURON IN OR ON RAW AGRICULTURAL PRODUCTS AND FOOD PRODUCTS

SUBMITTED BY

Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

DATE

February 28, 2002

SECTION F: PROPOSED TOLERANCE FOR THE PESTICIDE CHEMICAL IF TOLERANCES ARE PROPOSED

The petitioner, Makhteshim-Agan of North America, Inc. (EPA Company Number 66222), proposes to amend 40 CFR 180 to establish tolerances for the residues of novaluron. 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-[2,6-difluorobenzoyl] urea, in or on the following raw agricultural commodities and food products:

Commodity	Proposed Tolerance (ppm)
Pome Fruits	2.0
Apple Pomace	3.0
Cottonseed	0.6
Cotton Gin By-Products	30
Cattle, meat	0.4
Cattle, mbyp	7.0
Cattle, fat	7.0
Cattle, liver	0.5
Cattle, kidney	0.5
Milk	0.5

SECTION G: REASONABLE GROUNDS IN SUPPORT OF THIS PETITION

Makhteshim-Agan of North America, Inc. has generated and submitted data to the Agency to demonstrate that novaluron, when applied according to label directions on pome fruits and cotton, results in no residues of novaluron greater than the proposed tolerances of 2.0 ppm on pome fruits (RAC), 3.0 ppm on apple pomace, 0.6 ppm on cottonseed, 30 ppm on cotton gin by-products, 0.4 ppm in cattle meat, 7.0 ppm in cattle mbyp, 7.0 ppm in cattle fat, 0.5 ppm in cattle liver, 0.5 ppm in cattle kidney, and 0.5 ppm in milk. The use patterns of novaluron are proposed for the control of various insect pests that may include: leafminer, codling moth, and leafroller on pome fruits and tobacco budworm, cotton bollworm, beet armyworm, fall armyworm, lygus, whitefly, and thrips on cotton. The submitted data represents the maximum residues that can be expected from the intended use patterns.

It is concluded that the proposed tolerances (Section F) for novaluron in or on raw agricultural commodities and food products are adequate and appropriate and will not expose animals, man or the environment to unreasonable adverse effects.

Appendix I

Data Matrix

Appendix II

Proposed Labels

3/12/02

APPLE + PEAR

RimOn™

7.5 WDG
Novaluron Insecticide

7.5% Water Dispersible Granule Insect Growth Regulator
For Control of Insect Pests on Apple and Pear

	% BY WT.
ACTIVE INGREDIENT: novaluron: 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoro-methoxtethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	7.5%
INERT INGREDIENTS:	92.5%
Total	100%

KEEP OUT OF REACH OF CHILDREN

WARNING - AVISO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

FIRST AID

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 eye.
- Call a poison control center or doctor 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.

IF ON SKIN OR CLOTHING:
- Harmful if absorbed through skin.
- Avoid contact with skin.

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 for further treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment.
NOTE TO PHYSICIAN: This product may pose an aspiration pneumonia hazard as it contains petroleum distillate.

NET CONTENTS _____ POUNDS

EPA Reg. No. 66222-xx
EPA Est. No.

Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

WARNING. Causes substantial but temporary eye injury. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash clothing before reuse.

PERSONAL PROTECTIVE EQUIPMENT (PPE)

Some materials that are chemical-resistant to this product are listed below. If you want more options, follow the instructions for category C on an EPA chemical resistance category selection chart.

Applicators and other handlers must wear:

- Long-sleeved shirt and long pants
- Chemical resistant gloves such as barrier laminate, butyl rubber, nitrile rubber, neoprene rubber, or Viton
- Shoes plus socks
- Protective eyewear

Discard clothing and other absorbent materials that have been drenched or heavily contaminated with this product's concentrate. Do not reuse them. Follow manufacturer's instructions for cleaning/maintaining PPE. If no such instructions for washables, use detergent and hot water. Keep and wash PPE separately from other laundry.

USER SAFETY RECOMMENDATIONS

Users should:

- Wash hands before eating, drinking, chewing gum, using tobacco, or using the toilet.
- Remove clothing immediately if pesticide gets inside. Then wash thoroughly and put on clean clothing.

ENVIRONMENTAL HAZARDS

This pesticide is highly toxic to aquatic invertebrates. For terrestrial uses, do not apply directly to water, to areas where surface water is present, or to intertidal areas below the mean high water mark. Runoff from treated areas may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water by cleaning equipment or disposal of wastes.

DIRECTIONS FOR USE

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

Do not apply this product in a way that it will contact workers or other persons, either directly or through drift. Only protected handlers may be in the area during application. For any requirements specific to your State or Tribe, consult the agency responsible for pesticide regulation.

AGRICULTURAL USE REQUIREMENTS

Use this product only in accordance with the Worker Protection Standard, 40 CFR Part 170. This Standard contains requirements for the protection of agricultural workers on farms, forests, nurseries, and greenhouses, and handlers of agricultural pesticides. It contains requirements for training, decontamination, notification, and emergency assistance. It also contains specific instructions and exceptions pertaining to the statements on this label about personal protective equipment (PPE), and restricted-entry interval. The requirements in this box only apply to uses of this product that are covered by the Worker Protection Standard.

Do not enter or allow worker entry into treated areas during the restricted entry interval (REI) of 4 hours. PPE required for early entry to treated areas that is permitted under the Worker Protection Standard and that involves contact with anything that has been treated, such as plants, soil, or water is:

- Coveralls over long-sleeved shirt and long pants
- Chemical resistant gloves such as barrier laminate, butyl rubber, nitrile rubber, neoprene rubber, or Viton
- Shoes plus socks
- Protective eyewear

GENERAL INFORMATION

Novaluron is an insect growth regulator (IGR) that must be ingested by insect larvae to be fully effective. Proper application techniques help ensure through spray coverage and correct dosage necessary to obtain optimum control. Higher water volumes and increased spray pressure generally provide better coverage. Apply at the recommended rates when insect populations reach locally determined economic thresholds. Consult the cooperative extension service, professional consultants or other qualified authorities to determine appropriate threshold levels for treatment in your area.

Follow-up treatments of Novaluron should be applied as needed, to keep pest population within threshold limits. Depending on target pest, Novaluron should be applied at 7 to 14 day intervals to maintain control.

Chemigation Statement: Do not apply this product through any type of irrigation system.

NOTE: The compatibility of Novaluron with concurrent releases of insects for biocontrol of plant pests has not been established. When used as directed, Novaluron affects developing immature stages of insects by disrupting the molting process. Consequently, fully developed adult stages of pest and beneficial species are not affected.

Spray Drift: Do not allow spray to drift from the application site and contact people, structures people occupy at any time and the associated property, parks and recreation areas, nontarget crops, aquatic and wetland areas, woodlands, pastures, rangelands, or animals.

For orchard/vineyard airblast applications, do not direct spray above trees/vines and turn off outward pointing nozzles at row ends and outer rows. Apply only when wind speed is 3-10 mph at the application site as measured by an anemometer outside of the orchard/vineyard on the upwind side.

The applicator also must use all other measures necessary to control drift.

Mixing Instructions: Prepare solution concentrations in a clean, empty spray tank. Use clean spray filters. Add water to 1/3 level of tank. Add the appropriate amount of Novaluron to the tank and agitate to insure proper mixture. Continue filling tank with water until desired dilution is achieved. Shake or re-agitate sprayer before use if application is interrupted. Make up only the amount of application volume as required. Dispose of any unused spray material at the end of each day according to the instructions found in the STORAGE AND DISPOSAL section of this label.

Spray Coverage: All parts of the crop must receive uniform spray coverage or else desired result may not occur. Consult your local agricultural specialist for specific information on the best rates, timings, and spray volumes for your region.

Novaluron is an insecticide for control of certain foliar insect pests on apple and pear. Novaluron may be applied alone or in rotation with other insecticides. The primary mode of action is by disrupting cuticle formation and deposition occurring when insects change from one developmental stage to another resulting in death at molting. Due to this mode of action, Novaluron has no effect on adult stages of insects that have completed all of the successive molts through larval or nymphal stages of development.

Application

Novaluron is an insect growth regulator (IGR) that must be ingested by insect larvae to be fully effective. Proper application techniques help ensure thorough spray coverage and correct dosage necessary to obtain optimum control. Higher water volumes and increased spray pressures generally provide better coverage. Apply at the recommended rates when insect populations reach locally determined economic thresholds. Consult the cooperative extension service, professional consultants or other qualified authorities to determine appropriate threshold levels for treatment in your area.

Follow-up treatments of Novaluron should be applied as needed, to keep pest population within threshold limits. Depending on target pest, Novaluron should be applied at 10 to 14 day intervals to maintain control.

Orchard Spraying

Make applications of Novaluron by conventional ground sprayers that are calibrated to deliver a minimum of 50 gallons per acre to trellised trees or trees 10 feet tall or less. For trees over 10 feet tall, use a minimum of 100 gallons per acre. Do not exceed 400 gallons per acre.

When using an airblast sprayer, the equipment should be operated at proper ground speeds, adequate spray pressures and spray volumes to assure that the air volume within the tree canopy is completely replaced by the output from the airblast sprayer which will result in proper coverage of the target crop. Alternate row middle application patterns should be avoided since this application method may result in

less than satisfactory coverage and poor performance in conditions of high pest infestation levels, extremely large trees and/or dense foliage.

Dilute Spray Application

This application method is based on the premise that all plant parts are thoroughly wetted – to the point of runoff with spray solution. The number of gallons of dilute spray required per acre will depend on tree canopy size, tree planting density, and planting pattern. Consult the cooperative extension service, professional consultants or other qualified authorities to determine the number of gallons of dilute spray required per acre.

Concentrate Spray Application

This application method is based on the premise that all plant parts are uniformly covered with the spray solution but not to the point of runoff as with the dilute spray application method. Instead, a lower spray volume is used to deliver the same application rate per acre as used with the dilute spray application method.

FOLIAR FEEDING INSECTS CONTROLLED BY NOVALURON:

Target Pests	Application Rates Oz. Per 100 Gallons (lbai/100Gallons)	Application Rates Oz. Per Acre (lbai/Acre)	Application Timing	Target Pests
Leafminers (Spotted tentiform and Western tentiform)	8.5 – 12.8 (0.04 – 0.06)	8.5 – 51.2 (0.04 – 0.24)	Application timing for leafminers varies between species and geographic locations. Monitor the moth flights and treat at egg hatch for each generation. Do not apply more than 3 applications per season. Do not apply more than 205.2 ounces (0.96 lbs. a.i.) per season. Do not apply within 14 days of harvest.	Leafminers
Pear psylla	12.8 – 17.1 (0.06 – 0.08)	12.8 – 68.4 (0.06 – 0.32)	Apply a single spray during the Dormant or Delayed dormant period when populations are synchronized. Novaluron is most effective against 1st and 2nd instar larvae. Do not apply more than once per season for Pear Psylla control. For later season applications, use other classes of chemistry.	Pear Psylla
Codling moth,	12.8 – 17.1 (0.06 – 0.08)	12.8 – 68.4 (0.06 – 0.32)	Application timing is based on Biofix for the pest. The pest Biofix is based on the pest life cycle. Biofix is defined as the first sustained adult catch in pheromone traps – typically five moths in three traps in a seven-day period. For each codling moth generation: The 1st application should be made at 75 – 150 DD50 following the 1st Biofix, A 2nd application should be made approximately 10 – 14 days later –	Codling moth

			usually 375 – 450 DD50 following the 1st generation Biofix. A 3rd application should be made in 10 –14 days if sustained moth flight or heavy infestation is encountered. Best protection is achieved when applications are initiated at the beginning of egg oviposition but before larvae penetrate the surface of the fruit. Novaluron will provide 10 to 14 days of fruit protection depending on the application rate and speed of fruit expansion once applied. For heavy infestation or continuous moth flight and egg oviposition, use the highest labeled rate and maintain coverage of the fruit surface with timely reapplications at 10 to 14 day intervals. Novaluron may be interspersed or alternated with other insecticides targeted against the same pest as long as the application interval between applications does not exceed the period of effectiveness of the products being alternated and as long as Novaluron is applied before larvae penetrate into the fruit. Do not apply more than 3 applications per season. Do not apply more than 205.2 ounces (0.96 lbs. a.i.) per season. Do not apply within 14 days of harvest.	
Obliquebanded leafroller, Pandemis leafroller	8.5 – 17.1 (0.04 – 0.08)	8.5 – 68.4 (0.04 – 0.32)	Application timing is based on Biofix for the pest. The pest Biofix is based on the pest life cycle. Biofix is defined as the first sustained adult catch in pheromone traps – typically five moths in three traps in a seven-day period. Apply the Novaluron treatments at the following timings: Spring generation: The 1st application should be made during pink to petal fall period. A 2nd application should be made approximately 10 – 14 days later if needed. Summer generation: The 1st application should be made at 100 – 200 DD43 following the 2nd	Obliquebanded leafroller

			generation Biofix, A 2nd application should be made approximately 7 – 14 days later – usually 400 – 500 DD43 following the 2nd generation Biofix, A 3rd application should be made in 10 –14 days later – usually 700 – 800 DD43 following the 2nd generation Biofix. Best protection is achieved when applications are initiated at the beginning of egg oviposition. Novaluron will provide 10 to 14 days of protection depending on the application rate. For heavy infestations, continuous moth flight and egg oviposition, situations where it is difficult to obtain thorough coverage or for quick knockdown use the highest labeled rate and maintain coverage with timely reapplications at 10 to 14 day intervals. Do not apply more than 3 applications per season. Do not apply more than 205.2 ounces (0.96 lbs. a.i.) per season. Do not apply within 14 days of harvest.	
Redbanded leafroller, Fruittree leafroller, Variegated leafroller, Eyespotted leafroller	8.5 – 17.1 (0.04 – 0.08)	8.5 – 68.4 (0.04 – 0.32)	For control of the surface or foliar feeding leafroller larval complex, application can be made at any time larvae are feeding. However, most effective crop protection results from application made at the initiation of egg hatch. For heavy infestations, continuous moth flight and egg oviposition, situations where it is difficult to obtain thorough coverage or for quick knockdown use the highest labeled rate and maintain coverage with timely reapplications at 10 to 14 day intervals. Do not apply more than 3 applications per season. Do not apply more than 205.2 ounces (0.96 lbs. a.i.) per season. Do not apply within 14 days of harvest.	
Tufted apple budmoth	8.5 – 17.1 (0.04 – 0.08)	8.5 – 68.4 (0.04 – 0.32)	For each generation, make an application at the beginning of egg	

			hatch. A second application at 10 to 14 days later may be required. For heavy infestations, continuous moth flight and egg oviposition, situations where it is difficult to obtain thorough coverage or for quick knockdown use the highest labeled rate and maintain coverage with timely reapplications at 10 to 14 day intervals. Do not apply more than 3 applications per season. Do not apply more than 205.2 ounces (0.96 lbs. a.i.) per season. Do not apply within 14 days of harvest.	
Oriental fruit moth	12.8 – 17.1 (0.06 – 0.08)	12.8 – 68.4 (0.06 – 0.32)	For control of light to moderate infestations, begin applications before egg hatch of each generation to prevent larval penetration of the fruit Novaluron will provide 10 to 14 days of fruit protection depending on the application rate and speed of fruit expansion once applied. For heavy infestations, continuous moth flight and egg oviposition, situations where it is difficult to obtain thorough coverage or for quick knockdown use the highest labeled rate and maintain coverage with timely reapplications at 10 to 14 day intervals. Novaluron may be interspersed or alternated with other insecticides targeted against the same pest as long as the application interval between applications does not exceed the period of effectiveness of the products being alternated and as long as Novaluron is applied before larvae penetrate into the fruit. Do not apply more than 3 applications per season. Do not apply more than 205.2 ounces (0.96 lbs. a.i.) per season. Do not apply within 14 days of harvest.	

RESISTANCE MANAGEMENT: Novaluron is effective in controlling insect pests and minimizing the development of resistance when used in rotation with other insecticides in an IPM program. To reduce selection pressure for resistant pests:

- Novaluron should be used in rotation with other classes of insecticides with different modes of action. These other insecticides may include Insect Growth Regulators with dissimilar modes of action.
- For management of pests with short life cycles, do not use Novaluron more than once within each generation cycle.
- Always apply Novaluron at the recommended rates and according to label directions. Do not use less than recommended label rates alone or in tank mixtures.
- Use Novaluron as part of an insect management program that includes cultural and biological control where possible.
- Scout pest populations and begin Novaluron applications before the pest becomes established. Focus treatments on early immature stages for best results.

STORAGE AND DISPOSAL

DO NOT contaminate water, food, or feed by storage or disposal. Open dumping is prohibited.
PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of on-site or at an approved waste disposal facility.
CONTAINER DISPOSAL: Triple rinse (or equivalent). Puncture and dispose of in a sanitary landfill, or by incineration if allowed by state and local authorities. If burned, stay clear of smoke.
For minor spills, leaks, etc., follow all precautions indicated on this label and clean up immediately. Take special care to avoid contamination of equipment and facilities during cleanup and disposal of wastes.

WARRANTY STATEMENT

MAKHTESHIM-AGAN OF NORTH AMERICA warrants that this product conforms to the chemical description on the label thereof and is reasonably fit for purposes stated on such label only when used in accordance with directions under normal use conditions. It is impossible to eliminate all risks inherently associated with use of this product. Crop injury, ineffectiveness, or other unintended consequences may result because of such factors as weather conditions, presence of other materials, or the manner of use or application, all of which are beyond the control of MAKHTESHIM-AGAN OF NORTH AMERICA. In no case shall MAKHTESHIM-AGAN OF NORTH AMERICA be liable for consequential, special, or indirect damages resulting from the use or handling of this product. All such risks shall be assumed by the Buyer. In addition to the foregoing, no purchaser of this product (other than an end user) shall be entitled to any reimbursement for any loss suffered as a result of any suspension or cancellation of the registration for this product by the U.S. Environmental Protection Agency. Except as expressly provided herein, MAKHTESHIM-AGAN OF NORTH AMERICA makes no warranties, guarantees, or representations of any kind, either expressed or implied, or by usage of trade, statutory or otherwise, with regard to the product sold, including, but not limited to merchantability, fitness for a particular purpose, use or eligibility of the product for any particular trade usage. The exclusive remedy of any buyer or user of this product for any and all losses, injuries, or damages resulting from or in any way arising from the use, handling, or application of this product, whether in contract, warranty, tort, negligence, strict liability, or otherwise, shall be damages not exceeding the purchase price paid for this product or, at MAKHTESHIM-AGAN OF NORTH AMERICA's election, the replacement of this product.

Copyright 2002
Rimon™ is a registered trademark of Makhteshim Chemical Works Ltd.

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

March 8, 2002

I, Suku Oonnithan, Insecticide/Rodenticide Branch, Registration Division, Office of Pesticide Programs, Office of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency ("EPA"), certify that the pesticide product (s) listed below is, as of the date of this letter, a registered product under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, and that as such, the product(s) may be sold and marketed in the United States of America as authorized and limited by FIFRA. A true and correct copy of the product label approved by EPA is attached to accompany this letter.

Registration of this product(s) with EPA also denotes that the registrant listed below is responsible for ensuring full compliance with all the laws of the United States of America, or governing jurisdiction, regarding the sale, storage and/or disposal of the product(s). Further, the recipient of this letter is on notice that the referenced registration and/or the accompanying label may change subsequent to the date of this letter. EPA assumes no responsibility to notify the recipient of this letter of any change in the status of the registration(s) and/or the product label for the product(s) listed below.

EPA has issued registration numbers for the product(s) listed below to:

Makhteshim Chemical Works_Ltd
551 Fifth Ave Suite 1100
New York, NY 10176

EPA Registration Number:	11678-57
Name of Product:	Rimon Technical

Suku E. Oonnithan
Chemical Manager
Insecticide/Rodenticide Branch
Registration Division (7505C)

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

January 28, 2002

I, Suku Oonnithan, Insecticide/Rodenticide Branch, Registration Division, Office of Pesticide Programs, Office of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency ("EPA"), certify that the pesticide product (s) listed below is, as of the date of this letter, a registered product under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, and that as such, the product(s) may be sold and marketed in the United States of America as authorized and limited by FIFRA. A true and correct copy of the product label approved by EPA is attached to accompany this letter.

Registration of this product(s) with EPA also denotes that the registrant listed below is responsible for ensuring full compliance with all the laws of the United States of America, or governing jurisdiction, regarding the sale, storage and/or disposal of the product(s). Further, the recipient of this letter is on notice that the referenced registration and/or the accompanying label may change subsequent to the date of this letter. EPA assumes no responsibility to notify the recipient of this letter of any change in the status of the registration(s) and/or the product label for the product(s) listed below.

EPA has issued registration numbers for the product(s) listed below to:

Makhteshim Chemical Works_Ltd
551 Fifth Ave Suite 1100
New York, NY 10176

EPA Registration Number:	11678-57
Name of Product:	Rimon@ Ornamentals Technical

Suku E. Oonnithan
Chemical Manager
Insecticide/Rodenticide Branch
Registration Division (7505C)

Makhteshim - Agan of North America Inc.
551 Fifth Ave, Suite 1100, New York, NY 10176
Telephone: 212-661-9800 Fax: 212-661-9038/9043

MAKHTESHIM
A G A N
NORTH AMERICA

January 25, 2002

Ms. Deborah McCall
Branch Chief
Insecticide Rodenticide Branch
U.S. EPA (7505C)
1921 Jefferson Davis Highway.
Arlington, VA 22202

By FAX (703) 305-6596

Dear Ms. McCall:

RE: Rimon Ornamentals Registration: U.S. EPA Approved Labels

Rimon Ornamentals Technical Label	**(11678-57)**	NOVALURON - OONNI
Rimon Ornamentals 10 SC Label	**(66222-40)**	- OONNI
Rimon Ornamentals 10 EC Label	**(66222-35)**	- OONNI

Our case manager Oonni Oonnithan suggested that I contact you regarding Gold Seal Registration documents.

I have an urgent need for Gold Seal Registrations for the above labels. Please forward them to me at your earliest convenience.

If you require any additional information, please do not hesitate to call me at (212) 896-4945.

Sincerely,
Makhteshim-Agan of North America Inc.

Robert C. Everich, Ph.D.
Senior Scientist,
Rimon Product Manager

456515-00

February 28, 2002

Via FedEx

Dr. S. Oonnithan
Product Manager (7505C)
Document Processing Desk
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division
1921 Jefferson Davis Highway
Arlington, VA 22202

Re: RIMON® Technical Insecticide (EPA File Symbol: 11673-57), Rimon10 EC, Rimon 7.5 WDG Section 3 Application for Registration on Pome Fruits and Cotton

Dear Oonni:

Makhteshim Chemical Works, Ltd. c/o Makhteshim-Agan of North America Inc, its US Agent, submits the enclosed studies in support of application for registration of novaluron technical (EPA File Symbol 11673-57) and two formulations for use on Pome Fruits and Cotton..

The studies have been formatted according to PR notice 86-5 requirements. The complete application consists of the following:

- Application for FIFRA Section 3 Registration (EPA Form 8570-1)
- Certification with Respect to Data Compensation (EPA Form 8570-34)
- Study Transmittal Document
- List of Studies Submitted
- Data Matrix
- Three Copies (3) of all 86-5 formatted data
- Tolerance Petition Including Five (5) Copies of Proposed Labels
- Copy of Check for Tolerance Fees
- Notice of Filing
- Computer disc with Notice of Filing in WP Format

We trust that you will find this application complete and should you have any questions, please feel free to contact me at (212) 896-4945.

Sincerely,
Makhteshim-Agan of North America Inc.

Robert C. Everich, Ph.D.
Senior Scientist

N°RID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
1	830.7840 Pe	Comb, A. L.	1999	275-352 I: Water solubility Huntingdon Life Sciences Ltd., UK, Report No. MAK523/985188 Makhteshim Chemical Works Ltd., Report No. R-10638 GLP, Unpublished	Volume 1 of 1	MCW	45651501
2	835.1230 Fate	Aikens, P.J.	1999	^{14}C-275-352 I: Adsorption/desorption on soil Huntingdon Life Sciences Ltd., UK, Report No. MAK 528/992496 Makhteshim Chemical Works Ltd., Report No. R-10639 GLP, Unpublished	Volume 1 of 1	MCW	45638201
3	835.1240 Fate	Shaw, D.	1999	^{14}C- "RIMON": Aged residue soil column leaching Huntingdon Life Sciences Ltd., UK, Report No. MAK 496/982726 Makhteshim Chemical Works Ltd., Report No. R-10232 GLP, Unpublished	Volume 1 of 1	MCW	45638202
4	835.2240 Fate	Shaw, D.	1998	^{14}C "RIMON": Photolytic degradation in water Huntingdon Life Sciences Ltd., UK, Report No. MAK443/973390 Makhteshim Chemical Works Ltd., Report No. R-9705 GLP, Unpublished	Volume 1 of 1	MCW	45638203
5	835.2410 Fate	Shaw, D.	1998	^{14}C "RIMON": Photodegradation on soil Huntingdon Life Sciences Ltd., UK, Report No. MAK 444/973391 Makhteshim Chemical Works Ltd., Report No. R-9704 GLP, Unpublished	Volume 1 of 1	MCW	45638204
6	835.4200 Fate	Shaw, D.	1999	^{14}C-"RIMON": Anaerobic soil metabolism Huntingdon Life Sciences Ltd., UK, Report No. MAK 497/982727 Makhteshim Chemical Works Ltd., Report No. R-10231 GLP, Unpublished	Volume 1 of 1	MCW	45638205
7	835.4300 Fate	Aikens, P.J.	1999	^{14}C-"RIMON": Degradability and Fate in the Water/ Sediment System Huntingdon Life Sciences Ltd., UK, Report No. MAK 484/984634 Makhteshim Chemical Works Ltd., Report No. R-10031 GLP, Unpublished	Volume 1 of 1	MCW	45638206
8	835.4400 Fate	Shepler, K	2002	Anaerobic Aquatic Metabolism of ^{14}C ~~"RIMON"~~ Novaluron PTRL- West, Hercules, CA., Report No. 1028W Makhteshim Chemical Works Ltd., Report No. R-13880 GLP, Unpublished	Volume 1 of 1	MCW	45638207

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
9	850.1025 Eco	Cafarella, M.A.	2001	Novaluron: Acute Toxicity to Eastern Oyster (*Crassostrea virginica*) Under Flow-Through Conditions. Springborn Laboratories, Inc. Protocol No. 031301 Makhteshim Chemical Works Ltd., Report No. R-14139 GLP, In progress.	Volume 1 of 1	MCW	45638208
10	850.1035 Eco	Machado, M. W.	2001	Novaluron: Acute Toxicity to Mysids (*Americamysis bahia*) Under Flow-Through Conditions. Springborn Laboratories, Inc. Protocol No. 011901 Makhteshim Chemical Works Ltd., Report No. R-14136 GLP, In progress.	Volume 1 of 1	MCW	45638209
11	850.1075 Eco	Machado, M. W.	2001	Novaluron: Acute Toxicity to Sheepshead Minnow (*Cyprinodon variegatus*) Under Flow-Through Conditions. Springborn Laboratories, Inc. Protocol No. 020499 Makhteshim Chemical Works Ltd., Report No. R-14138 GLP, In progress.	Volume 1 of 1	MCW	45638210
12	850.1300 Eco	Jenkins, C. A.	1998	^{14}C-"RIMON": *Daphnia magna* Reproduction test Huntingdon Life Sciences Ltd., UK, Report No. MAK405/974265 Makhteshim Chemical Works Ltd., Report No. R-9341 GLP, Unpublished	Volume 1 of 1	MCW	45638211
13	850.1350 Eco	Lima, W.	2001	Novaluron: Life Cycle Toxicity Test with Mysids (*Americamysis bahia*). Springborn Laboratories, Inc. Protocol No. 040400 Makhteshim Chemical Works Ltd., Report No. R-14140 GLP, In progress.	Volume 1 of 1	MCW	45638212
14	850.1400 Eco	Barrett, K. L.	2001	^{14}C-"RIMON" Technical: Fish early life stage toxicity test for Fathead minnow (*Pimephales promelas*) Huntingdon Life Sciences Ltd., UK, Report No. MAK507/994379 Makhteshim Chemical Works Ltd., Report No. R-10281 GLP, Unpublished	Volume 1 of 1	MCW	45638213
15	850.1500 Eco	Caunter, J. E.; Williams, T. D.	2001	Novaluron: Determination of effects on the reproduction of fathead minnow (*Pimephales promelas*) Brixham Environmental Laboratory, Devon, UK, Report No. BL6993/B Makhteshim Chemical Works Ltd., Report No. R-11873	Volume 1 of 1	MCW	45638214

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
16	850.1730 Eco	Jenkins, C. A.	2000	^{14}C-"RIMON": Bioconcentration in Bluegill sunfish Huntingdon Life Sciences Ltd., UK, Report No. MAK498/985004 Makhteshim Chemical Works Ltd., Report No. R-9414 GLP, Unpublished	Volume 1 of 1	MCW	45638215
17	none Eco	Jenkins, C. A.	1998	"RIMON" Technical: Prolonged toxicity to Rainbow trout under flow-through conditions. 28 Day study Huntingdon Life Sciences Ltd., UK, Report No. MAK441/974266 Makhteshim Chemical Works Ltd., Report No. R-9840 GLP, Unpublished	Volume 1 of 1	MCW	45638216
18	None Eco	Carter, J. N.	1997	Rimon Technical: Effects on soil non-target micro-organisms Huntingdon Life Sciences Ltd., UK, Report No. MAK 400/971410 Makhteshim Chemical Works Ltd., Report No. R-9429 GLP, Unpublished	Volume 1 of 1	MCW	45638217
19	850.2300 Eco	Rodgers, M. H.	1999	"RIMON" technical: Reproduction in Bobwhite quail Huntingdon Life Sciences Ltd., UK, Report No. MAK 411/972997 Makhteshim Chemical Works Ltd., Report No. R-9417 GLP, Unpublished	Volume 1 of 3	MCW	45638218
	850.2300 Eco	Rodgers, M. H.	1999	"RIMON" technical: Reproduction in Bobwhite quail Huntingdon Life Sciences Ltd., UK, Report No. MAK 411/972997 Makhteshim Chemical Works Ltd., Report No. R-9417 GLP, Unpublished	Volume 2 of 3	MCW	
	850.2300 Eco	Rodgers, M. H.	1999	"RIMON" technical: Reproduction in Bobwhite quail Huntingdon Life Sciences Ltd., UK, Report No. MAK 411/972997 Makhteshim Chemical Works Ltd., Report No. R-9417 GLP, Unpublished	Volume 3 of 3	MCW	
20	850.2300 Eco	Rodgers, M. H.	2001	"RIMON" Technical: Reproduction in Mallard duck Huntingdon Life Sciences Ltd., UK, Report No. MAK 412/973000 Makhteshim Chemical Works Ltd., Report No. R-9418 GLP, Unpublished	Volume 1 of 2	MCW	45638219
	850.2300 Eco	Rodgers, M. H.	2001	"RIMON" Technical: Reproduction in Mallard duck Huntingdon Life Sciences Ltd., UK, Report No. MAK 412/973000 Makhteshim Chemical Works Ltd., Report No. R-9418 GLP, Unpublished	Volume 2 of 2	MCW	

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
21	850.3020 Eco	Gray, A. P.	1998	Rimon (Novaluron) Technical: Acute toxicity to honey bees (*Apis mellifera*). Huntingdon Life Sciences Ltd., UK, Report No. MAK 433/973447 + amendment, Makhteshim Chemical Works Ltd., Report No. R-9801 GLP, Unpublished	Volume 1 of 1	MCW	45638220
22	850.5400 Eco	Jenkins, C. A.	1998	"RIMON" Technical: Algal growth inhibition assay Huntingdon Life Sciences Ltd., UK, Report No. MAK449/974268 Makhteshim Chemical Works Ltd., Report No. R-9842 GLP, Unpublished	Volume 1 of 1	MCW	45638221
23	850.5400 Eco	Jenkins, C. A.	1999	275-352 I: Algal growth inhibition assay Huntingdon Life Sciences Ltd., UK, Report No. MAK527/992452 Makhteshim Chemical Works Ltd., Report No. R-10637 GLP, Unpublished	Volume 1 of 1	MCW	45638222
24	850.5400 Eco	Jenkins, C. A.	2001	"RIMON": Higher plant (*Lemna*) growth inhibition test Huntingdon Life Sciences Ltd., UK, Report No. MAK610/003705 Makhteshim Chemical Works Ltd., Report No. R-11755 GLP, Unpublished	Volume 1 of 1	MCW	45638223
25	None Eco	Rodgers, M. H.	1998	"Rimon" Technical: Acute toxicity (LC_{50}) to the earthworm (*Eisenia foetida*) Huntingdon Life Sciences Ltd., UK, Report No. MAK 413/972973 Makhteshim Chemical Works Ltd., Report No. R-9458 GLP, Unpublished	Volume 1 of 1	MCW	45638224
26	None Eco	Rodgers, M. H.	2001	Chlorophenyl urea: Acute toxicity (LC_{50}) to the earthworm (*Eisenia foetida*) Huntingdon Life Sciences Ltd., UK, Report No. MAK 619/003779 Makhteshim Chemical Works Ltd., Report No. R-11872 GLP, Unpublished	Volume 1 of 1	MCW	45638225
27	860.1300 Resid	Corden, M. T.	1998	^{14}C "RIMON": Metabolism in apples Huntingdon Life Sciences Ltd., UK, Report No. MAK429/983248 Makhteshim Chemical Works Ltd., Report No. R-9768 GLP, Unpublished	Volume 1 of 1	MCW	45638226

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
28	860.1300 Res	Crowe, A.	1998	^{14}C "RIMON": Metabolism in cabbages Huntingdon Life Sciences Ltd., UK, Report No. MAK437/982595 Makhteshim Chemical Works Ltd., Report No. R-9802 GLP, Unpublished	Volume 1 of 1	MCW	45638227
29	860.1300 Res	Crowe, A.	1998	^{14}C "RIMON": Metabolism in potatoes Huntingdon Life Sciences Ltd., UK, Report No. MAK438/983684 Makhteshim Chemical Works Ltd., Report No. R-9803 GLP, Unpublished	Volume 1 of 1	MCW	45638301
30	860.1300 Res	Aikens, P. J.	2000	^{14}C-"RIMON": Metabolism in cotton Huntingdon Life Sciences Ltd., UK, Report No. MAK549/002671 Makhteshim Chemical Works Ltd., Report No. R-11087 GLP, Unpublished	Volume 1 of 1	MCW	45638302
31	860.1300 Res	Corden, M. T.	1999	^{14}C "RIMON" Metabolism in the lactating goat Huntingdon Life Sciences Ltd., UK, Report No. MAK461/984693 Makhteshim Chemical Works Ltd., Report No. R-9846 GLP, Unpublished	Volume 1 of 1	MCW	45638303
32	860.1340 Res	Todd, M.	1998	Development and validation of an analytical method for the determination of Rimon in apples, cabbages and potatoes Huntingdon Life Sciences Ltd., UK, Report No. MAK453/972510 Makhteshim Chemical Works Ltd., Report No. R-9345 GLP, Unpublished	Volume 1 of 1	MCW	45638304
33	860.1340 Res	J. Rose	2001	Independent Validation of the Analytical Method for Novaluron (Rimon) in Apples., PTRL- West Inc., Hercules, CA Report No. 993W Makhteshim Chemical Works Ltd., Report No. R-12608 GLP, Unpublished	Volume 1 of 1	MCW	45638305
34	860.1340 Res	T. Class	2001	Independent Validation (ILV) of an HPLC/UV Based Analytical Method for the Determination Novaluron in Cotton., PTRL-Europe., GmbH Report No. P 463 G Makhteshim Chemical Works Ltd., Report No. R-13888 GLP, Unpublished	Volume 1 of 1	MCW	45638306

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
35	860.1340 Res	Todd, M.	1998	The development and validation of methodology for the determination of RIMON residues in Bovine tissues (fat, kidney, liver, muscle), milk and eggs Huntingdon Life Sciences Ltd., UK, Report No. MAK454/972535 + amendment Makhteshim Chemical Works Ltd., Report No. R-9346 GLP, Unpublished	Volume 1 of 1	MCW	45638307
36	860.1340 Res	Lindsell, S. L.	2001	Novaluron: Independent laboratory validation (ILV) of methodology for the post-registration monitoring of residues of Novaluron in milk, muscle and liver. Huntingdon Life Sciences Ltd., UK, Report No. MAK 671/012110, Makhteshim Chemical Works Ltd., Report No. R-12367 GLP, Unpublished	Volume 1 of 1	MCW	45638308
37	860.1400 Res	Todd, M.	1997	Development and validation of an analytical method for the determination of Rimon in groundwater Huntingdon Life Sciences Ltd., UK, Report No. MAK409/970198, Makhteshim Chemical Works Ltd., Report No. R-9348 GLP, Unpublished	Volume 1 of 1	MCW	45638309
38	860.1400 Res	Munro, S.	2001	Novaluron: Development and validation of methodology for the determination of residues of Novaluron and its chlorophenyl urea metabolite (275-352 I) in drinking water, ground water and surface water Huntingdon Life Sciences Ltd., UK, Report No. MAK638/004515 Makhteshim Chemical Works Ltd., Report No. R-12103 GLP, Unpublished	Volume 1 of 1	MCW	45638310
39	860.1480 Res	Redgrave, V. A.	2001	"RIMON" Technical: Residues in milk and tissues of dairy cows Huntingdon Life Sciences Ltd., UK, Report No. MAK 605/003999 Makhteshim Chemical Works Ltd., Report No. R-10993 GLP, Unpublished	Volume 1 of 1	MCW	45638311
40	860.1850 Res		2000	^{14}C-"RIMON": Accumulation in confined rotational crops Huntingdon Life Sciences Ltd., UK, Report No. MAK559/002865 Makhteshim Chemical Works Ltd., Report No. R-11236 GLP, Unpublished	Volume 1 of 1	MCW	45638312

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
41	870.3050 TOX	Hopkins, M. N., *et al*	1989	GR 572 (Technical): Toxicity to rats by dietary administration for 4 weeks Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre) Report No. AGR 48/89448, Makhteshim Chemical Works Ltd., Report No. R-8877 GLP, Unpublished	Volume 1 of 1	MCW	45638313
42	870.3100 TOX	East, P. W.	1998	"RIMON" Technical: Toxicity study by dietary administration to CD-1 Mice for 13 weeks followed by an 8 week reversibility period Huntingdon Life Sciences Ltd., UK, Report No. MAK402/973472 Makhteshim Chemical Works Ltd., Report No. R-9339 GLP, Unpublished	Volume 1 of 1	MCW	45651502
43	870.3100 TOX	Kirk, S. J., *et al*	1990	GR 572 (Technical): Toxicity to rats by dietary administration for 13 weeks Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 50/90386 Makhteshim Chemical Works Ltd., Report No. R-8878 GLP, Unpublished	Volume 1 of 1	MCW	45651503
44	870.3100 TOX	Ammannati, E.	1993	GR 572 tech.: 13-week oral toxicity study in rats RBM, Italy, Report No. RBM EXP. No. 920634 Makhteshim Chemical Works Ltd., Report No. R-8770 GLP, Unpublished	Volume 1 of 1	MCW	45651504
45	870.3700 TOX	Reynolds, S.M.	1997	"RIMON" Technical: Preliminary embryo-foetal toxicity study in the CD Rat by oral gavage administration Huntingdon Life Sciences Ltd., UK, Report No. MAK401/970269 Makhteshim Chemical Works Ltd., Report No. R-9333 GLP, Unpublished	Volume 1 of 1	MCW	45638315
46	870.3700 TOX	Reynolds, S. M.	1997	Rimon Technical: Study of tolerance in the rabbit by oral gavage administration Huntingdon Life Sciences Ltd., UK, Report No. MAK398/970016 Makhteshim Chemical Works Ltd., Report No. R-9335 GLP, Unpublished	Volume 1 of 1	MCW	45638316
47	870.3700 TOX	Reynolds, S. M.	1998	"RIMON" Technical: Preliminary embryo-foetal toxicity study in the rabbit by oral gavage administration Huntingdon Life Sciences Ltd., UK, Report No. MAK403/970336 Makhteshim Chemical Works Ltd., Report No. R-9336 GLP, Unpublished	Volume 1 of 1	MCW	45638317

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
48	870.3700 TOX	Reynolds, S. M.	1998	"RIMON" Technical: Study of embryo-fetal toxicity in the rabbit by oral gavage administration Huntingdon Life Sciences Ltd., UK, Report No. MAK423/974057 amendment Makhteshim Chemical Works Ltd., Report No. R-9337 GLP, Unpublished	Volume 1 of 1	MCW	45638318 Adverse Flag
49	870.3800 TOX	Reynolds, S. M.	1998	"RIMON" Technical: Preliminary study of effects on reproductive performance in CD rats by dietary administration Huntingdon Life Sciences Ltd., UK, Report No. MAK421/973738 Makhteshim Chemical Works Ltd., Report No. R-9409 GLP, Unpublished	Volume 1 of 1	MCW	45638319 Adverse Flag
50	870.3800 TOX	Blee, M. A. B.	1999	"RIMON" Technical: Study of reproductive performance in CD rats treated continuously through two successive generations by dietary administration Huntingdon Life Sciences Ltd., UK, Report No. MAK466/985245 Makhteshim Chemical Works Ltd., Report No. R-9410 GLP, Unpublished	Volume 1 of 3	MCW	45651505
	870.3800 TOX	Blee, M. A. B.	1999	"RIMON" Technical: Study of reproductive performance in CD rats treated continuously through two successive generations by dietary administration Huntingdon Life Sciences Ltd., UK, Report No. MAK466/985245 Makhteshim Chemical Works Ltd., Report No. R-9410 GLP, Unpublished	Volume 2 of 3	MCW	
	870.3800 TOX	Blee, M. A. B.	1999	"RIMON" Technical: Study of reproductive performance in CD rats treated continuously through two successive generations by dietary administration Huntingdon Life Sciences Ltd., UK, Report No. MAK466/985245 Makhteshim Chemical Works Ltd., Report No. R-9410 GLP, Unpublished	Volume 3 of 3	MCW	
51	870.4100 TOX	Thirlwell, P. M.	1999	"RIMON" Technical: Toxicity study by oral capsule administration to beagle dogs for 52 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK420/984737 Makhteshim Chemical Works Ltd., Report No. R-9408 GLP, Unpublished	Volume 1 of 1	MCW	45638320 Adverse Flag

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER
	870.4300 TOR	Thirlwell, P. M.	2000	"RIMON" Technical: Combined carcinogenicity and toxicity study by dietary administration to CD rats for 104 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK427/994365 + amendment Makhteshim Chemical Works Ltd., Report No. R-9412 GLP, Unpublished	Volume 1 of 7	MCW
	870.4300 TOR	Thirlwell, P. M.	2000	"RIMON" Technical: Combined carcinogenicity and toxicity study by dietary administration to CD rats for 104 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK427/994365 + amendment Makhteshim Chemical Works Ltd., Report No. R-9412 GLP, Unpublished	Volume 2 of 7	MCW
52	870.4300 TOR	Thirlwell, P. M.	2000	"RIMON" Technical: Combined carcinogenicity and toxicity study by dietary administration to CD rats for 104 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK427/994365 + amendment Makhteshim Chemical Works Ltd., Report No. R-9412 GLP, Unpublished	Volume 3 of 7	MCW
	870.4300 TOR	Thirlwell, P. M.	2000	"RIMON" Technical: Combined carcinogenicity and toxicity study by dietary administration to CD rats for 104 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK427/994365 + amendment Makhteshim Chemical Works Ltd., Report No. R-9412 GLP, Unpublished	Volume 4 of 7	MCW
	870.4300 TOR	Thirlwell, P. M.	2000	"RIMON" Technical: Combined carcinogenicity and toxicity study by dietary administration to CD rats for 104 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK427/994365 + amendment Makhteshim Chemical Works Ltd., Report No. R-9412 GLP, Unpublished	Volume 5 of 7	MCW
	870.4300 TOR	Thirlwell, P. M.	2000	"RIMON" Technical: Combined carcinogenicity and toxicity study by dietary administration to CD rats for 104 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK427/994365 + amendment Makhteshim Chemical Works Ltd., Report No. R-9412 GLP, Unpublished	Volume 6 of 7	MCW

45651506

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
52	870.4300 TR	Thirlwell, P. M.	2000	"RIMON" Technical: Combined carcinogenicity and toxicity study by dietary administration to CD rats for 104 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK427/994365 + amendment Makhteshim Chemical Works Ltd., Report No. R-9412 GLP, Unpublished	Volume 7 of 7	MCW	
	870.4200 TR	Thirlwell, P. M.	2000	"RIMON" Technical: Carcinogenicity study by dietary administration to CD-1 mice for 78 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK428/992033 Makhteshim Chemical Works Ltd., Report No. R-9413 GLP, Unpublished	Volume 1 of 4	MCW	
53	870.4200 TR	Thirlwell, P. M.	2000	"RIMON" Technical: Carcinogenicity study by dietary administration to CD-1 mice for 78 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK428/992033 Makhteshim Chemical Works Ltd., Report No. R-9413 GLP, Unpublished	Volume 2 of 4	MCW	
	870.4200 TR	Thirlwell, P. M.	2000	"RIMON" Technical: Carcinogenicity study by dietary administration to CD-1 mice for 78 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK428/992033 Makhteshim Chemical Works Ltd., Report No. R-9413 GLP, Unpublished	Volume 3 of 4	MCW	45651507
	870.4200 TR	Thirlwell, P. M.	2000	"RIMON" Technical: Carcinogenicity study by dietary administration to CD-1 mice for 78 weeks Huntingdon Life Sciences Ltd., UK, Report No. MAK428/992033 Makhteshim Chemical Works Ltd., Report No. R-9413 GLP, Unpublished	Volume 4 of 4	MCW	
54	870.5300 TR	Adams, K., Ransome, S. J., Henly, S., Lloyd, A.	1989	An assessment of the mutagenic potential of GR 572 using the mouse lymphoma TK Locus Assay Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre) Report No. AGR 58/89240, Makhteshim Chemical Works Ltd., Report No. R-8779 GLP, Unpublished	Volume 1 of 1	MCW	45638321
55	870.5395 TR	Henderson, L. M., Proudlock, R. J., Haynes, P., Meaking, K.	1989	Mouse micronucleus test on GR 572 Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre) Report No. AGR 57/881610, Makhteshim Chemical Works Ltd., Report No. R-8778 GLP, Unpublished	Volume 1 of 1	MCW	45638322

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
56	870.7485 Res	Bounds, S. V. J.	1998	^{14}C-"RIMON": Metabolism in the rat (Pilot Study) Huntingdon Life Sciences Ltd., UK, Report No. MAK442/973740 Makhteshim Chemical Works Ltd., Report No. R-9845 GLP, Unpublished	Volume 1 of 1	MCW	45638323
57	870.7485 Res	O'Connor J. F.	2000	^{14}C-"RIMON": Metabolism in the rat Huntingdon Life Sciences Ltd., UK, Report No. MAK469/980204 Makhteshim Chemical Works Ltd., Report No. R-10004 GLP, Unpublished	Volume 1 of 2	MCW	45638401 (2)
	870.7485 Res	O'Connor J. F.	2000	^{14}C-"RIMON": Metabolism in the rat Huntingdon Life Sciences Ltd., UK, Report No. MAK469/980204 Makhteshim Chemical Works Ltd., Report No. R-10004 GLP, Unpublished	Volume 2 of 2	MCW	
58	None Eco	Pugsley, R.F.	2002	Probabilistic Modeling of Novaluron Exposure to Aquatic Nontarget Organisms and Drinking Water Associated with Use on Cotton and Apples. Waterborne Environmental, Inc. Report No. 625.01 Makhteshim Chemical Works Ltd., Report No. R-14450 Non-GLP, Unpublished	Volume 1 of 1	MCW	45638402

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
59	835.6100 Fate	Wilson, [illegible]	2001	Novaluron: Terrestrial Field Dissipation Study with "Rimon" 10 EC applied to Bare Soil in Spain and Germany, 1999. Huntingdon Life Sciences Ltd., UK, Report No. MAK547/004242 Makhteshim Chemical Works Ltd., Report No. R-10971 GLP, Unpublished	Volume 1 of 1	MCW	45638403
60	835.6100 Fate	Willard, T.	2001	Terrestrial Field Soil Dissipation of Novaluron. American Agricultural Services, Inc. Cary, N.C. Report No. AA010702 Makhteshim Chemical Works Ltd., Report No. R-13885 GLP, Unpublished	Volume 1 of 2	MCW	45638404
	835.6100 Fate	Willard, T.	2001	Terrestrial Field Soil Dissipation of Novaluron. American Agricultural Services, Inc. Cary, N.C. Report No. AA010702 Makhteshim Chemical Works Ltd., Report No. R-13885 GLP, Unpublished	Volume 2 of 2	MCW	
61	850.1075 Eco	Jenkins, C. A.	1998	"RIMON" 10 EC: Acute toxicity to Rainbow trout Huntingdon Life Sciences Ltd., UK, Report No. MAK462/982146, Makhteshim Chemical Works Ltd., Report No. R-9912 GLP, Unpublished	Volume 1 of 1	MCW	45638314
62	850.1730 Eco	Jenkins, C. A.	2001	"RIMON" 10 EC: An assessment of the bioconcentration of "RIMON" in Rainbow trout in a mesocosm Huntingdon Life Sciences Ltd., UK, Report No. MAK575/003707, Makhteshim Chemical Works Ltd., Report No. R-11307 GLP, Unpublished	Volume 1 of 1	MCW	45638405
63	None Eco	Jenkins, C. A.	2000	"RIMON" 10 EC: Prolonged toxicity to Rainbow trout underflow-through conditions 28-day study Huntingdon Life Sciences Ltd., UK, Report No. MAK537/993312, Makhteshim Chemical Works Ltd., Report No. R-10933 GLP, Unpublished	Volume 1 of 1	MCW	45638406
64	850.3020 Eco	Gray, A. P.	1998	"RIMON" 10 EC: Evaluation of the effects of insect growth-regulating insecticides on honey bee (*Apis mellifera*) colony brood development Huntingdon Life Sciences Ltd., UK, Report No. MAK 435/973449 Makhteshim Chemical Works Ltd., Report No. R-9799 GLP, Unpublished	Volume 1 of 1	MCW	45638407
65	850.3020 Eco	Gray, A. P.	1997	"RIMON" 10 EC: Acute Toxicity to Honey Bees (*Apis mellifera*). Huntingdon Life Sciences Ltd., UK, Report No. MAK 434/973448 Makhteshim Chemical Works Ltd., Report No. R-9800 GLP, Unpublished	Volume 1 of 1	MCW	45638408

12

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER	
66	850.3040 Eco	Barrett, K.	2001	Novaluron: To Assess the Effect of "Rimon" 10EC to Honeybee Brood when Used in Commercial Citrus Groves. Huntingdon Life Sciences Ltd., UK, Report No. MAK542/993030 Makhteshim Chemical Works Ltd., Report No. R-10990 GLP, Unpublished	Volume 1 of 1	MCW	45638409
67	None Eco	Sharples, A.	2001	Novaluron: Evaluation of the effects of "RIMON" 10 EC on populations of non-target arthropods in citrus groves Huntingdon Life Sciences Ltd., UK, Report No. MAK543/003923, Makhteshim Chemical Works Ltd., Report No. R-10991 GLP, Unpublished	Volume 1 of 3	MCW	
	None Eco	Sharples, A.	2001	Novaluron: Evaluation of the effects of "RIMON" 10 EC on populations of non-target arthropods in citrus groves Huntingdon Life Sciences Ltd., UK, Report No. MAK543/003923, Makhteshim Chemical Works Ltd., Report No. R-10991 GLP, Unpublished	Volume 2 of 3	MCW	45638410
	None Eco	Sharples, A.	2001	Novaluron: Evaluation of the effects of "RIMON" 10 EC on populations of non-target arthropods in citrus groves Huntingdon Life Sciences Ltd., UK, Report No. MAK543/003923, Makhteshim Chemical Works Ltd., Report No. R-10991 GLP, Unpublished	Volume 3 of 3	MCW	
68	850.5400 Eco	Jenkins, C. A.	1998	"RIMON" 10 EC: Algal growth inhibition assay Huntingdon Life Sciences Ltd., UK, Report No. MAK464/982147 + amendment Makhteshim Chemical Works Ltd., Report No. R-9914 GLP, Unpublished	Volume 1 of 1	MCW	45638411
69	860.1500 Res	T. Willard	2001	Magnitude of the Residue of Novaluron in Cotton Raw Agricultural and Processed Commodities., American Agricultural Services, Inc. Cary, N.C. Report No. AA010704 Makhteshim Chemical Works Ltd., Report No. R-13887 GLP, Unpublished	Volume 1 of 1	MCW	45638412
70	870.1010 Eco	Jenkins, C. A.	1999	"RIMON" 10 EC: Acute toxicity to *Daphnia magna* Huntingdon Life Sciences Ltd., UK, Report No. MAK463/983514 Makhteshim Chemical Works Ltd., Report No. R-9913 GLP, Unpublished	Volume 1 of 1	MCW	45638413

13

MRID	GUIDELINE	AUTHOR	DATE	TITLE	VOLUME	OWNER
71	870.2400 Acceptable	Blanchard, E.	2000	"RIMON" 10EC (0.1% v/v field dilution): Eye irritation to the rabbit Huntingdon Life Sciences Ltd., UK, Report No. MAK 613/003342/SE, Makhteshim Chemical Works Ltd., Report No. R-11806 GLP, Unpublished	Volume 1 of 1	MCW 45638414
72	870.7600 Acc	Kemp, L.	2000	^{14}C-"RIMON" 10EC: *In vivo* dermal penetration study in the male rat Huntingdon Life Sciences Ltd., UK, Report No. MAK 577/002095 Makhteshim Chemical Works Ltd., Report No. R-11140 GLP, Unpublished	Volume 1 of 1	MCW 45638415
73	875.2100 Acc	Willard, T.	2001	Foliar Dislodgeable Residues of Novaluron in Cotton. American Agricultural Services, Inc. Cary, N.C. Report No. AA010705 Makhteshim Chemical Works Ltd., Report No. R-13884 GLP, Unpublished	Volume 1 of 1	MCW 45638416

14

74	830 Series Subgroup A 830.1550, 830.1600, 830.1620, 830.1650, 830.1670, 830.1700, 830.1750, 830.1800	Everich, R.	2002	Rim[illegible].5 WDG: OPPTS 830 Series Subgroup A[illegible]duct Chemistry. Makhteshim-Agan of North America Inc. Report No. MANA-02-01	Volume 1 of 1	MCW	45638417
75	830.Series 830.6302, 830.6303, 830.6304, 830.6314, 830.6315, 830.6316, 830.6319, 830.6321, 830.7000, 830.7300.	Comb, A. L.	2001	"RIMON" 7.5 WDG: Determination of the physico-chemical properties (Combined Directive 91/414/EEC Annex III and EPA/OPPTS 830 series guidelines) Huntingdon Life Sciences Ltd., UK, Report No. MAK694 Makhteshim Chemical Works Ltd., Report No. R-13048 GLP, Unpublished	Volume 1 of 1	MCW	45638418
76	830.6313	Comb, A.L.	2001	"RIMON" 7.5 WDG: Accelerated storage stability (Directive 91/414/EEC Annex III Guidelines) Huntingdon Life Sciences Ltd., UK, Report No. MAK695 Makhteshim Chemical Works Ltd., Report No. R-13047 GLP, Unpublished	Volume 1 of 1	MCW	45638419
77	860.1500 Res	T. Willard	2001	Magnitude of the Residue of Novaluron in Pome Fruit Raw Agricultural and Processed Commodities., American Agricultural Services, Inc. Cary, N.C. Report No. AA010703 Makhteshim Chemical Works Ltd., Report No. R-13886 GLP, Unpublished	Volume 1 of 1	MCW	45638420
78	870.1100 Acute ~~A-902~~	Blanchard, E	2001	"Rimon" 7.5 WDG: Acute oral toxicity to the rat Huntingdon Life Sciences Ltd., UK, Report No. MAK685/012647/AC Makhteshim Chemical Works Ltd., Report No. R-12470 GLP, Unpublished	Volume 1 of 1	MCW	45638421

15

79	870.1200 Acute	Blanchard, E	2001	"Rimon" 7.5 WDG: Acute dermal toxicity to the rat Huntingdon Life Sciences Ltd., UK, Report No. MAK 687/012648/AC, Makhteshim Chemical Works Ltd., Report No. R-12471 GLP, Unpublished	Volume 1 of 1	MCW	45638422
Admin	870.1300 Acute	Everich, R.	2002	RIMON (novaluron) 7.5 WDG – Request for Waiver of Acute Inhalation Study. Makhteshim-Agan of North America Inc. Report No. MANA-02-066.	Volume 1 of 1	MCW	
80	870.2500 Acute	Blanchard, E	2001	"Rimon" 7.5 WDG: Skin irritation to the rabbit Huntingdon Life Sciences Ltd., UK, Report No. MAK 687/012731/AC, Makhteshim Chemical Works Ltd., Report No. R-12472 GLP, Unpublished	Volume 1 of 1	MCW	45638423
81	870.2400 Acute	Dreher, D.M.	2000	"Rimon" 7.5 WDG: Acute Eye Irritation Test in the rabbit. SafePharm Laboratories Limited., UK, SRL Project Number 306/362, Makhteshim Chemical Works Ltd., Report No. R-11721 GLP, Unpublished	Volume 1 of 1	MCW	45638424
82	870.2600 Acute	Dreher, D.M.	2000	"RIMON" 7.5 WDG – Magnusson & Kligman Maximization Skin Sensitization Study in the Guinea-pig. SafePharm Laboratories Limited., UK, SRL Project Number 306/363, Makhteshim Chemical Works Ltd., Report No. R-11722 GLP, Unpublished	Volume 1 of 1	MCW	45638425
83	875.2100 ~~Acute~~ ~~TGR~~ Exp.	Willard, T	2001	Foliar Dislodgeable Residues of Novaluron in Apple. American Agricultural Services, Inc. Cary, N.C. Report ~~No. AA~~010706 Makhteshim Chemical Works Ltd., Report No. R-13883 GLP, Unpublished	Volume 1 of 1	MCW	45638426

16

U.S. ENVIRONMENTAL PROTECTION AGENCY OFFICE OF PESTICIDE PROGRAMS 1200 Pennsylvania Avenue N.W. Washington, DC 20460-0001 NOTICE OF PESTICIDE _x_ Registration ____ Reregistration (under FIFRA, as amended)	EPA Reg. Number 11678-57	Date of Issuance SEP 2 5 2001
	Term of Issuance Conditional	
	Name of Pesticide Product Rimon® Technical	

Name and Address of Registrant (include ZIP Code):
Makhteshim-Agan of North America, Inc.
551 Fifth Ave, Suite: 1100
New York, NY 10176

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

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 conditionally registered in accordance with FIFRA sec. 3(c)(7)(C) provided that you:

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

2. Replace "EPA Reg. No. 11678-LT" with "EPA Reg. No. 11678-57" on page 1 of the draft label.

3. Within two years of registration of this product, submit the following:

   a. A 90-day inhalation toxicity study in rats to further characterize the inhalation risk assessment for the greenhouse use.

continued ....

Signature of Approving Official:	Date:
Deborah McCall Deborah McCall	9-25-2001

EPA Form 8570-6

b. Two mutagenicity studies to complete the mutagenicity data requirement for a new active ingredient. The two needed studies are an *in-vitro* mammalian cell gene mutation assay and an *in-vivo* cytogenetics (i.e., micronucleus) assay.

A stamped copy of the draft label is enclosed for your records. Submit one (1) copy of your final printed labeling before you release the product for shipment. If the above conditions are not complied with, the registration will be subject to cancellation in accordance with FIFRA sec. 6(e). Your release of the product for shipment constitutes acceptance of these conditions. Should you have any questions, do not hesitate to contact the Regulatory Manager for this product, Mr. Suku Oonnithan at 703-605-0368.

Sincerely,

Deborah McCall, Acting Chief,
Insecticide Rodenticide Branch
Registration Division (7505C)

Encl.

ACCEPTED
with COMMENTS
In EPA Letter Dated:
SEP 25 2001

Under the Federal Insecticide, Fungicide, and Rodenticide Act, as amended, for the pesticide registered under EPA Reg. No. 11678-57

RIMON® TECHNICAL

(Novaluron)

For The Manufacture of Insecticides Only

	% BY WT.
ACTIVE INGREDIENT: Novaluron: 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	98.5%
INERT INGREDIENTS:	1.5%
TOTAL	100.0%

CAUTION

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

FIRST AID

IF ON SKIN OR CLOTHING:
- Take off contaminated clothing.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Call a poison control center or doctor 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.

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 eye.
- Call a poison control center or doctor 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 for further treatment advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment.

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION. Harmful if absorbed through skin. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters except in accordance with the requirements of a 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 treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. This pesticide is for the further manufacture of formulated insecticides only. Formulators using this product are responsible for obtaining EPA registration for their formulated products.

Only for formulation into an insecticide for the following uses:

(1) Ornamentals (greenhouse)
(2) Uses for which USEPA has accepted the required data and/or citations of data that the formulator has submitted in support of registration; and
(3) Uses for experimental purposes that are in compliance with USEPA requirements.

NET CONTENTS 55 POUNDS

Makhteshim Chemical Works, Ltd.
c/o Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

EPA Reg. No. 11678-xx
EPA Est. No. 11678-IS-1

STORAGE AND DISPOSAL

STORAGE: Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited.
PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of at an approved waste disposal facility.
CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If drum is contaminated and cannot be reused, dispose of in the same manner.

WARRANTY STATEMENT

MAKHTESHIM-AGAN OF NORTH AMERICA warrants that this product conforms to the chemical description on the label thereof and is reasonably fit for purposes stated on such label only when used in accordance with directions under normal use conditions. It is impossible to eliminate all risks inherently associated with use of this product. Crop injury, ineffectiveness, or other unintended consequences may result because of such factors as weather conditions, presence of other materials, or the manner of use or application, all of which are beyond the control of MAKHTESHIM-AGAN OF NORTH AMERICA. In no case shall MAKHTESHIM-AGAN OF NORTH AMERICA be liable for consequential, special, or indirect damages resulting from the use or handling of this product. All such risks shall be assumed by the Buyer. In addition to the foregoing, no purchaser of this product (other than an end user) shall be entitled to any reimbursement for any loss suffered as a result of any suspension or cancellation of the registration for this product by the U.S. Environmental Protection Agency. Except as expressly provided herein, MAKHTESHIM-AGAN OF NORTH AMERICA makes no warranties, guarantees, or representations of any kind, either expressed or implied, or by usage of trade, statutory or otherwise, with regard to the product sold, including, but not limited to merchantability, fitness for a particular purpose, use or eligibility of the product for any particular trade usage. The exclusive remedy of any buyer or user of this product for any and all losses, injuries, or damages resulting from or in any way arising from the use, handling, or application of this product, whether in contract, warranty, tort, negligence, strict liability, or otherwise, shall be damages not exceeding the purchase price paid for this product or, at MAKHTESHIM-AGAN OF NORTH AMERICA's election, the replacement of this product.

File Name and Path: C:\My Documents\MANA\MANA labels\EPA Pending Text\Rimon Technical (to EPA 9-13-01).doc

PESTICIDE
FACT SHEET

Name of Chemical:	**Novaluron**
Reason for Issuance:	Conditional Registration
Date issued:	September 24, 2001

DESCRIPTION OF CHEMICAL

Chemical Name:	1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxy-ethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea
Trade Name:	Rimon®
EPA Chemical Code:	124002
Chemical Class:	Benzoylphenyl urea
CAS Number:	116714-46-6
Year of Initial Registration:	2001
Pesticide Type:	Insecticide
Pests Controlled:	Whiteflies, thrips and leafminers
U.S. and Foreign Producers:	Makhteshim Agan of North America, Inc. 551 Fifth Avenue, Suite 1100 New York, NY 10176.

ACTIVE INGREDIENT AND FORMULATIONS

Novaluron is a new pesticide chemical belonging to the class of insecticides called insect growth regulators (IGR). IGRs slowly kill the insects over a period of few days by disrupting the normal growth and development of immature insects. Novaluron acts as an insecticide mainly by ingestion, but has some contact activity. IGR insecticides are comparatively safer to beneficial insects and environment and is compatible for use in an integrated pest management system.

Makhteshim-Agan of North America, Inc. is registering two Novaluron formulations: Rimon® Technical, a manufacturing use product (MP) and Rimon® 10 EC, an end-use product (EP) containing 98.5% and 10.0% active ingredient, respectively.

USE PATTERN

Rimon® Technical is sold for formulating other end-use-product formulations. Rimon®10 EC is an emulsifiable concentrate recommended for the control of whiteflies, thrips, leafminers and armyworms on containerized ornamentals grown in greenhouses. The Rimon®10 EC is mixed with water and applied as a foliage spray using conventional spray equipment. Depending upon the pest population pressure, 3 to 12 ozs. of product is mixed with 100 gallons of water and applied as a full coverage spray at the rate of 1 gallon per 200 sq. ft. of bench area, which is equivalent to 200 gal/acre. Two applications at the highest rate at 30 day intervals are allowed, which amounts to a maximum seasonal rate of 52 fl. ozs. of Rimon®10 EC or 0.34 lb ai/acre/season. To prevent buildup of resistance, rotation with other insecticides having dissimilar mode of action is recommended between successive applications.

PHYSICAL/CHEMICAL PROPERTIES

Adequate product specific chemistry data have been submitted for the registration of Novaluron insecticide. The manufacturing process indicate that no toxicologically significant impurities, such as chlorinated dioxins, nitrosamines and hexachlorobenzenes are formed.

HUMAN HEALTH ASSESSMENT

Summary of Toxicology Findings

Novaluron has low to moderate acute toxicity (Toxicity Category IV for oral and inhalation and III for dermal route). It is not an eye and dermal irritant and is not a skin sensitizer.

In a subchronic rat oral study, mortality, clinical signs, body weights, food consumption and efficiency, ophthalmoscopic examinations, clinical chemistry, urinalysis and gross pathology were unaffected by the test substance. At 2000 ppm, cumulative body weight gains were observed and some histopathological changes in the spleens were noted; however, these effects were not statistically significant. Based on these histopathological parameters in the spleen, the no observed adverse effect level (NOAEL) was estimated to be 8.3 mg/kg/day while the lowest observed adverse effect level (LOAEL) was 818.5 mg/kg/day. For intermediate-term incidental exposure assessment, the end points of the subchronic oral toxicity study was used.

A 28-day rat dermal toxicity study was conducted to evaluate dermal exposure, the route most directly applicable to the indoor use on ornamentals grown in containers. No systemic effects were noted up to a dose limit of 1000 mg/kg/day and no maternal or developmental toxicity was noted.

Mutagenecity of Novaluron was tested for gene mutation, chromosomal aberration and DNA damage by *in-vitro* assays. Novaluron was not cytotoxic with or without S9 activation in *Salmonella typhimurium* and did not induce a genotoxic response in any strain. In a mammalian cell chromosome aberration assay, Novaluron produced no evidence of clastogenic activity in the lymphocytes, in the presence or absence of S9 activation. In an unscheduled DNA synthesis (UDS) assay, Novaluron produced sporadic increase in gross and net nuclear grain counts; but, was considered non-mutagenic as the sporadic increases in grain counts were not reproducible. In a differential killing assay using *Bacillus subtilis* strains M45 and H17, Novaluron was equivocal for bacterial DNA damage in the absence of S9 activation; but, was negative in the presence of S9 activation. Based on the available studies, there is no concern for mutagenicity. Two additional studies are needed to confirm the negative findings observed in the five mutagenicity studies already evaluated by the Agency.

Novaluron has no anticipated dietary or residential exposures at this time; therefore, an aggregate risk assessment is not warranted. The requirement for a carcinogenicity study also is not applicable for the proposed use of Novaluron.

Occupational Exposure

The use directions are to apply Rimon® 10 EC mixed with water, as a foliage spray to containerized ornamentals grown in greenhouses using conventional high pressure hand sprayers. The application rate is to mix 12 ozs. of product in 100 gal of water and spray @ 200 gal/Acre, which is equivalent to 0.17 lb ai/Acre. The number of applications per season are 2 at a spray interval of 30 days. At this application rate, the maximum use rate is 0.34 lb ai/Acre/season. The registrant is proposing a re-entry interval (REI) of 12 hours, which is acceptable to the Agency at this time. No dermal toxicological end points were identified and no chemical specific data are available to assess potential post-application and re-entry exposures to pesticide handlers. Therefore, the occupational exposure for pesticide handlers was estimated based on short/intermediate term inhalation end points with a NOAEL of 8.3 mg/kg/day from a subchronic rat oral study. Using historical data from Pesticide Handler's Exposure Database, margins of exposure (MOEs) for occupational exposure were estimated to be >100, which do not exceed the Agency's level of concern.

Food Quality Protection Act (FQPA) considerations were not addressed this time since the current registration is for indoor non-food use only. The registered use pattern does not involve residential uses and establishing food tolerances.

ENVIRONMENTAL EXPOSURE

The current registration for Novaluron is for use on container grown ornamentals in greenhouses only. Therefore, Novaluron's mobility and persistence in soil and water and its eco-toxicity to terrestrial and aquatic life were not evaluated. Also Novaluron's

properties to contaminate ground and surface waters are not applicable due to its indoor uses.

OUTSTANDING DATA REQUIREMENTS

The following additional data are needed to fully characterize the potential risks of long term use of Rimon® insecticide.

1. *90-Day Inhalation*: A rat inhalation toxicity study is required for characterization of risks due to the potential for inhalation exposure of Rimon®10 EC when the label is expanded to include outdoor uses on ornamental plants and shade trees.

2. *Mutagenicity*: An *in-vitro* mammalian cell gene mutation and an *in-vivo* cytogenetics assay (i.e., micro nucleus assay) are the two additional studies needed to satisfy the current guideline requirements for mutagenicity.

PUBLIC INTEREST FINDING

Novaluron belong to a new class of pesticide chemicals called benzoylphenyl ureas. Some compounds of this group are broad spectrum insecticides with insect hormonal mimicking mode of action. These IGRs affect chitin synthesis of immature insects disrupting their normal growth and development. The Rimon®10 EC is being registered for the control of whiteflies,, thrips, leafminers, and other foliar feeding insect pest of ornamental plants grown in greenhouses. Novaluron is expected to reduce the reliance on organophosphates, such as acephate, diazinon, chlorpyrifos, and dimethoate, carbamates, such as (carbaryl and bendiocarb and pyrethroids, such as bifenthrin and cyfluthrin. Novaluron has low mammalian acute toxicity and has low risk to environment and non-target organisms; thus becomes an important component in any integrated pest management system. Additional uses of Novaluron for the control of insect pests on food crops is being prepared for filing by the registrant.

GOVERNMENT PERFORMANCE AND RESULTS ACT (GPRA)

Registering Novaluron will meet the objectives of GPRA (Title 3.1.1) by assuring pesticides of newer chemistry that are safer to humans and environment.

CONTACT PERSON FOR FURTHER INFORMATION

Mr. Suku Oonnithan
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Insecticide Rodenticide Branch
Registration Division (7505C)
Office of Pesticide Programs

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DISCLAIMER

The information presented in this Pesticide Fact Sheet is for informational purpose only and may not be used to fill data requirements for pesticide registration and reregistration.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460-0001

OFFICE OF
PESTICIDE PROGRAMS

September 24, 2001

DECISION MEMORANDUM

SUBJECT: Conditional Registration of Novaluron Insecticide for Use on Ornamentals Grown in Greenhouses

FROM: Peter Caulkins, Acting Director
Registration Division (7505C)

TO: Jim Jones, Deputy Director
Office of Pesticide Programs (7501C)

This memorandum recommends for concurrence on the conditional registration of a new insecticide, Novaluron for use on ornamentals grown in greenhouses only. The Science Divisions have reviewed all applicable data and the Registration Division has concluded that the criteria for conditional registration of Novaluron under FIFRA Section 3(C)(7)(C) have been met.

BACKGROUND

REGISTRANT	Makhteshim-Agan of North America, Inc., New York, NY 10176
COMMON NAME	Novaluron
CHEMICAL NAME	1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea
PRODUCTS	Rimon® Technical and Rimon® 10 EC
USES	Ornamental plants grown in greenhouses
PESTS CONTROLLED	Whiteflies, thrips, leafminers and armyworms
TYPE OF REGISTRATION	Conditional (2 Years)

Novaluron is a new active ingredient belonging to a novel class of compounds called benzoylphenyl ureas. This selective insecticide has a unique mode of action, where it disrupts the normal growth and development of insects by mimicking the action of their natural hormones. These type of insecticides are called insect growth regulators (IGRs), which are slow in their killing action, but safer to beneficial insects and environment. The IGRs work mainly as stomach and contact poisons. The registrant submitted data for a reduced risk classification for Novaluron which the Agency approved on February 18, 2000.

Makhteshim-Agan of North America, Inc. has submitted two registration applications: Rimon® Technical containing 98.5% Novaluron and Rimon®10 EC containing 10.0% Novaluron. The Rimon Technical will be registered as a manufacturing-use only product (MP) and the Rimon 10 EC will be registered as an end-use product (EP) for the control of whiteflies, thrips, leafminers and armyworms in ornamental plants grown in greenhouses. The label directions of Rimon®10 EC specify a maximum rate of 0.17 lb ai/acre/application with a maximum of 2 applications per growing season at 30-day interval. This application rate amounts to a maximum use rate of 0.34 lb ai/acre/crop season. Water is used as the diluent and the mixed product is applied using conventional spray equipment. Residual control is approximately 30 days. The label recommends rotating with other insecticides having a different mode of action between successive applications to prevent likely build up of insect resistance to Novaluron.

The Rimon®10 EC insecticide label submitted with registration application included two general use patterns for the product: indoor non-food (greenhouses) and outdoor non-food (shade houses and nurseries). The submitted data on Novaluron were found to be inadequate to assess the human and environmental risks associated with an outdoor use; therefore, only an indoor use will be approved at this time.

EXECUTIVE SUMMARY

Novaluron is a new active ingredient being registered for the control of insect pests of ornamental plants grown in greenhouses. The Agency has reviewed the generic and product specific data on the chemistry and toxicity of Novaluron formulations for indoor non-food uses. It has a low order of toxicity by the oral and inhalation routes and moderate toxicity by the dermal route. A subchronic rat oral study indicates that the

hematopoietic system is the primary target of toxicity. There is no concern for mutagenicity based on the negative findings in submitted studies.

Occupational exposure from the indoor use is only to those individuals working with plants grown in greenhouses. The margins of exposure (MOE) for occupational exposure exceed the target of 100 and therefore, are not of concern. Since Novaluron has no food or residential uses, the following do not apply at this time: (i) acute and chronic dietary end-points, (ii) aggregate exposure, (iii) Food Quality Protection Act factors and (iv) food tolerances.

Novaluron's mobility and persistence in soil and water were not applicable due to its low levels of use under indoor conditions. Also Novaluron's potential to contaminate ground and surface waters was not evaluated due to its indoor uses. Novaluron being an IGR, it is expected to have moderate to high toxicity to aquatic invertebrates (being related to insects in their growth and development); however, exposure to these species is not likely to occur due to the proposed use pattern (indoor only).

There are two sets of studies needed to better characterize the human health risks associated with the indoor non-food use of Novaluron. These include (i) a subchronic rat inhalation and (ii) two mutagenicity studies. For the inhalation study, an end point derived from a subchronic rat oral study with a 100% absorption factor was used to evaluate the potential human exposure. The two mutagenicity studies are needed to confirm the negative findings observed in the five mutagenicity studies already evaluated by the Agency.

Even though, the two sets of studies, referred to above are normally required for the registration of a product for indoor use, due to the availability of an extrapolated end point for inhalation effects and the confirmatory nature of the two mutagenicity studies, it is recommended that the Agency give the registrant two years from the date of registration to submit the required inhalation and mutagenicity studies. This approach is consistent with Rimon®10 EC's low application rate (0.17 lb ai/acre/application), method and frequency combined with the low acute inhalation toxicity of the technical material (Toxicity Category = IV). Because the current use pattern results in low levels of exposure and adequate safety end points are available to evaluate the risks to applicators when used under indoor conditions, it was concluded

that the human health risk do not exceed the Agency's level of concern. Therefore, a conditional registration of Novaluron for indoor use is recommended.

SCIENCE FINDINGS

CHEMICAL CHARACTERISTICS

Adequate chemistry data have been submitted for the registration of Rimon®Technical and Rimon®10 EC. The manufacturing process for technical Novaluron indicates that no toxicologically significant impurities like chlorinated dioxins, nitrosamines and hexachlorobenzenes are formed. The physical and chemical properties of both formulations are summarized in Table 1.

Table 1. Physical and Chemical Properties of Novaluron

Properties	TGAI	Rimon® 10 EC
Physical State	Solid	Liquid
Color	White	Salmon Pink
Odor	None	NA
Melting Point	176.5 - 178.0° C	NA
Density	1.56 g/cm^3 at 22° C	1.08
Solubility (Water)	3 μg/L	NA
Vapor Pressure	1.6 x 10^{-5} at 25° C	NA
Octanol/Water Partition Coefficient	log P_{ow} = 4.3 at 25° C	NA
pH	6.50	2.9 (1% w/v)
Flammability	NA	102° C
Explodability	NA	Not Explosive
Storage Stability	NA	Stable for 1 year
Miscibility	NA	Not Miscible with Hydrocarbon Oil

HUMAN HEALTH ASSESSMENT

ACUTE TOXICITY

Novaluron has a low order of acute oral and inhalation toxicity; but, is slightly toxic by the dermal route. The end-use product, Rimon® 10 EC is irritating to the eye and skin and is a skin

sensitizer. Appropriate precautionary statements are added on the label to reflect the irritation and sensitization properties of Rimon® 10 EC. A summary of the acute toxicity parameters of both formulations are provided in Table 2.

Table 2. Acute Toxicity of Novaluron

Type of Study	Toxicity Category and LD_{50}	
	Technical	Rimon® 10 EC
Acute Oral	IV LD_{50} >5000 mg/kg (Rat)	IV LD_{50} >5000 mg/kg (Rat)
Acute Dermal	III LD_{50} >2000 mg/kg (Rat)	III LD_{50} >2000 mg/kg (Rat)
Acute Inhalation	IV LD_{50} >5.15 mg/L (Rat)	IV Waived
Primary Eye Irritation	IV	II
Primary Dermal Irritation	IV	III
Dermal Sensitization	Not a Sensitizer	Positive
Signal Word	CAUTION	WARNING

INCIDENTAL ORAL ENDPOINTS

There are no proposed residential uses for Novaluron.

DERMAL ENDPOINTS & EXPOSURE

In a 28-day dermal study in the rat, no systemic effects were noted up to a limit dose of 1000 mg/kg/day. In addition, no maternal or developmental toxicity was noted in the rat; therefore, a dermal risk determination is not required.

INHALATION ENDPOINT

Other than an acute rat inhalation toxicity study, a subchronic or chronic inhalation study was not submitted for the registration of Novaluron. In its absence, the subchronic rat oral study was used with an inhalation absorption factor of 100%. In that study, the no observed adverse effect level (NOAEL) of 8.3 mg/kg/day was based on hematological parameters (increased methemoglobin, increased reticulocites, increased mean corpuscular

volume decreased hemoglobin, decreased erythrocytes), increased absolute/relative spleen weights and spleen histopathology (minimal to moderate extra medullary erythropoiesis, slight to moderate increased hemosiderosis) seen at the lowest observed adverse effect level (LOAEL) of 818.5 mg/kg/day. Since a 90-day inhalation toxicity in rat would give a dose and end point via the route of exposure to address the long term effects of Novaluron, this study is required to be submitted within two years from the date of registration.

MUTAGENICITY

Mutagenicity of Novaluron was tested for gene mutation, chromosomal aberration and DNA damage by *in-vitro* assays. Gene mutation was studied by four microbial mutagenicity assays. In two independent microbial mutagenicity assays, Novaluron tested up to the limit of solubility (2500 μg/plate) and the limit dose (5000 μg/plate) was not cytologic with or without S9 activation in four strains of *Salmonella typhimurium* and one strain of *Escherichia coli*, and did not induce a genotoxic response. In two other assays, Novaluron at 3333 μg/plate was not cytologic with or without S9 activation in five strains of *S. typhimurium* and did not induce a genotoxic response in any strain.

In a mammalian cell chromosome aberration assay Novaluron produced no evidence of clastogenic activity in primary human lymphocytes, in the presence or absence of S9 activation. An unscheduled DNA synthesis (UDS) and differential killing (liquid suspension) assay were used to test for DNA damage. In an UDS assay, Novaluron produced sporadic increase in gross and net nuclear grain counts. But, Novaluron was considered not to show any evidence of causing DNA damage to HeLa S3 epithelial cells, as the sporadic increases in grain counts were not reproducible between assays. In a differential killing assay, Novaluron was equivocal for bacterial DNA damage in the absence of S9 activation; but, was negative for bacterial DNA damage in the presence of S9 activation. Two additional studies, an *in-vitro* mammalian cell gene mutation assay and an *in-vivo* cytogenetics assay are required within two years from the date of registration to confirm the negative findings reported in the above mutagenicity studies.

CARCINOGENICITY

The requirement for a carcinogenicity study is not applicable for the proposed indoor non-food uses of Novaluron.

OCCUPATIONAL EXPOSURE

The use directions are to apply Rimon® 10 EC mixed with water, as a foliage spray to containerized ornamentals grown in greenhouses using conventional high pressure hand sprayers. The application rate is to mix 12 ozs. of product in 100 gal of water and spray @ 200 gal/Acre, which is equivalent to 0.17 lb ai/Acre. The number of applications per season are 2 at a spray interval of 30 days. At this application rate, the maximum use rate is 0.34 lb ai/Acre/season. The registrant is proposing a re-entry interval (REI) of 12 hours, which is acceptable to the Agency at this time. No dermal toxicological end points were identified nor were any chemical specific data available to assess potential post-application and re-entry exposures to pesticide handlers. Therefore, the occupational exposure for pesticide handlers was estimated based on short/intermediate term inhalation end points with a NOAEL of 8.3 mg/kg/day from a subchronic rat oral study. Using historical data from Pesticide Handler's Exposure Database, MOEs for occupational exposure were estimated to be >100, which do not exceed the Agency's level of concern.

AGGREGATE EXPOSURE

Novaluron has no anticipated dietary or residential exposures at this time; therefore, an aggregate risk assessment is not warranted.

FOOD QUALITY PROTECTION ACT CONSIDERATIONS

Food Quality Protection Act (FQPA) considerations were not evaluated. Since the current registration for Novaluron is only for an indoor non-food use, no tolerances are being established and there are no proposed residential uses.

ENVIRONMENTAL EXPOSURE

The proposed use pattern for Novaluron is for use on container grown ornamentals in greenhouses only. Novaluron's properties to contaminate ground and surface waters are not applicable due to its indoor uses. The ecological effects summary data provided by the registrant indicate that Novaluron is practically non-toxic orally (> 2000 mg/kg) and via dietary route (NOAEL = 5200 ppm) to mallard duck and Bobwhite quail *(Guideline 71-1 and 71-2)*. In a 96-hour fish toxicity study *(Guideline 72-1)*, the LC_{50} of Novaluron to rainbow trout and bluegill sunfish were determined to be moderately toxic (>1.0 mg/L). In a 48-hour invertebrate toxicity

study *(Guideline 72-2)* the LC_{50} of Novaluron to *Daphnia* was found to be moderately to highly toxic (0.279 mg/L); however, exposure to these species is not likely to occur from the use of Novaluron by the proposed use pattern.

OUTSTANDING DATA REQUIREMENTS

The toxicological database is adequate to support the conditional registration of Novaluron for the limited indoor use of ornamentals grown in containers. There is high confidence in the hazard end points used in the human health risk assessment. However, the following additional toxicological studies are being required to be submitted within two years time in order to fully characterize the potential risks over the long term use of this product.

1. *Guideline 82-4: 90-Day Rat Inhalation Study*: This study is required for characterization of long term risks to mixer/applicator due to the potential for inhalation exposure of Rimon® 10 EC. This study is required to be submitted within two years from the date of registration.

2. *Guideline 84-4: Mutagenicity Effects*: An *in-vitro* mammalian cell gene mutation assay and an *in-vivo* cytogenetics assay (i.e., micro nucleus assay) are the two additional studies needed to satisfy the current guideline requirements for mutagenicity. These two studies when submitted within two years from the date of registration will provide confirmation of the negative findings observed in the five mutagenicity studies submitted earlier.

RECOMMENDATION

The current indoor use pattern results in low levels of exposure and adequate safety end points are available to evaluate the risks to applicators and non-target organisms. Available data provide adequate information to support the conditional registration of Novaluron for indoor uses. Even though, there are some additional data needs to fully characterize the long term effects of Novaluron, it was concluded that the human health as well as environmental risks do not exceed the Agency's level of concern. Therefore, a conditional registration of Novaluron for indoor non-food use is recommended.

The Registration Division recommends that you concur with the conditional registration of Novaluron as a new insecticide under FIFRA Section 3(C)(7)(C).

Concur, Jim Jones, Deputy Director

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460-0001

OFFICE OF
PESTICIDE PROGRAMS

September 4, 2001

Robert C. Everich, Ph.D.
Senior Scientist
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite: 1100
New York, NY 10176

Subject: EPA File Symbol 11678-LT
Novaluron Technical
Registration of a New Active Ingredient
Your Letter October 28, 1999

Dear Dr. Everich:

The product chemistry and acute toxicity data and the label you submitted for the registration of the product referred to above, have been reviewed and the Agency's comments are as follows:

Product Chemistry

1. Address the deficiency in conclusion #3 of Product Chemistry Review dated November 3, 2000. A copy of the Agency's review was sent to you on November 27, 2000.

The confidential Statement of Formula (CSF) for the basic formulation dated 11/05/1999 is acceptable.

Label

1. Add the Signal Word, "CAUTION" in the beginning of the sentence "Harmful if absorbed .... water after handling" under HAZARDS TO HUMANS AND DOMESTIC ANIMALS.

2. Replace "Ornamentals (greenhouse and outdoor)"with "Ornamentals (greenhouse)" under DIRECTIONS FOR USE.

The Agency has reviewed all acute and short and intermediate term toxicology studies submitted on the technical novaluron for its indoor non-food use. The acute toxicity categories for novaluron technical are as follows:

Acute Oral	IV	LD_{50} >5000 mg/kg (Rat)
Acute Dermal	III	LD_{50} >2000 mg/kg (Rat)
Acute Inhalation	IV	LD_{50} >5.15 mg/L (Rat)
Primary Eye Irritation	IV	
Primary Dermal Irritation	IV	
Dermal Sensitization	Not a Sensitizer	
Signal Word	CAUTION	

The acute toxicity data requirements have been satisfied for the novaluron technical. The short and intermediate term end-points identified for exposure risk assessments are summarized in the Report of Hazard Identification Assessment Review Committee (HIARC), a copy of which is enclosed for your records. The HIARC report also identifies data gaps in the toxicology and eco-tox data requirements required for the unconditional registration of novaluron for indoor non-food uses.

Further consideration will be given to your application upon receipt of the required product chemistry data and five (5) copies of revised labeling after addressing the above comments. Should you have any questions, do not hesitate to contact me at 703-605-0368.

Sincerely,

S. Oonnithan, Entomologist
Insecticide Rodenticide Branch
Registration Division (7505C)

Encl.

11678-LT

RIMON® TECHNICAL

(Novaluron)

For The Manufacture of Insecticides Only

	% BY WT.
ACTIVE INGREDIENT: Novaluron: 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	98.5%
INERT INGREDIENTS:	1.5%
Total	100.0%

CAUTION

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

STATEMENT OF PRACTICAL TREATMENT (FIRST AID)

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.
IF SWALLOWED: Call a doctor or get medical attention. Do not induce vomiting. Do not give anything by mouth to an unconscious person. Avoid alcohol.
IF IN EYES: Flush eyes with plenty of water. Call a physician if irritation persists.

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

Harmful if absorbed through skin. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters except in accordance with the requirements of a 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 treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. This pesticide is for the further manufacture of formulated insecticides only. Formulators using this product are responsible for obtaining EPA registration for their formulated products.

Only for formulation into a insecticide for the following uses:
(1) Ornamentals (greenhouse and outdoor)
(2) Uses for which USEPA has accepted the required data and/or citations of data that the formulator has submitted in support of registration; and
(3) Uses for experimental purposes that are in compliance with USEPA requirements.

STORAGE AND DISPOSAL

STORAGE: Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited.
PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of at an approved waste disposal facility.
CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If drum is contaminated and cannot be reused, dispose of in the same manner.

WARRANTY STATEMENT

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 but 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 instruction, or under abnormal conditions, or under conditions not reasonably foreseeable to seller, and buyer assumes the risk of any such use. Buyer assumes all risks of use, storage or handling of this material not in strict accordance with directions given herewith.

NET CONTENTS _____ POUNDS

Makhteshim Chemical Works, Ltd.
c/o Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

EPA Reg. No. 11678-LT
EPA Est. No. 11678-IS-1

11678-LT

C:\MyFiles\Novaluron\riska-dow.010809

MEMORANDUM

DATE: 15 August 2001

SUBJECT: Human Exposure and Risk Assessment for the Proposed New Use of Novaluron on Containerized Ornamental Plants in Greenhouses, Shadehouses and Outdoor Nurseries. PC Code: 124002; DP Code: 272507

FROM: Mark I. Dow, Ph.D., Biologist
Registration Action Branch 1
Health Effects Division 7509C

THRU: G. Jeffrey Herndon, Acting Branch Senior Scientist
Registration Action Branch 1
Health Effects Division 7509C

TO: Suku Oonnithan, Ph.D.
Insecticide/Rodenticide Branch
Registration Division 7505C

INTRODUCTION

Makhteshim Agan, Makhteshim Chemical Works, Ltd. has applied for registration of the active ingredient Novaluron for use on containerized ornamental plants in greenhouses, shadehouses and outdoor nurseries. This document contains the Health Effects Division's (HED) assessment of handler and worker exposure and risk from the proposed use.

SUMMARY OF USE PATTERNS AND FORMULATIONS

The proposed labels forwarded to HED are for RimOn™ 10 EC and 10 SC. Both liquid formulations contain 0.83 lb active ingredient/gallon. Novaluron is an insect molting disruptant, applied as a foliar spray to control whiteflies, thrips, leafminers, armyworms "and certain other foliar feeding insects on containerized ornamentals...." The rate of application is "3-12ozs. of Rimon in 100 gals. of water ... through conventional spray equipment." For pests with short life cycles (i.e., whiteflies) do not apply more than once with each generation cycle. No maximum seasonal or amounts/acre limitations are specified. The proposed Restricted Entry Interval (REI) is 12 hours.

Table 1 Summary of Proposed New Use of Novaluron	
Formulation	10% EC, 10% SC
Sites	containerized ornamental plants in greenhouses, shadehouses and outdoor nurseries
Pests	whiteflies, thrips, leafminers, armyworms
Application Methods	high pressure hand wand, ground boom
Rates	3-12 oz product/100 gallon water; 0.0008 lb ai/gallon spray (0.17 lb a.i./A) Max
Frequency/Timing 2 Apps at Max Rate	not specified
PHI	n/a
REI	12 hr
Manufacturer	Makhteshim

Occupational Exposures

Based on the proposed use patterns, commercial and private (i.e., "grower") applicators are expected to have short-term (1-30 days) exposures. No chemical specific data are available to assess potential exposure to pesticide handlers and for possible post-application, re-entry exposure to workers. The estimates of exposure in this document are based upon study data available in the Pesticide Handler's Exposure Database (PHED) (v. 1.1, 1998). Estimates of Re-entry exposure are based upon Science Advisory Council for Exposure Policy No. 003 (7 May 98) and conventional HED methodology for assessing re-entry exposure.

Based primarily upon information in the proposed labels, HED believes that the most likely methods of delivery are by ground boom application for the outdoor uses and by high pressure hand wand (or similar equipment) inside greenhouses. For this assessment, exposure is estimated for mixer/loaders using liquid, open pour. Open cab, ground boom and high pressure hand wand applicators are also assessed.

The HED Science Advisory Council for Exposure (EXPOSAC) has directed that exposures to those who may mix, load, and apply a pesticide be estimated as combined exposures or separate exposures depending upon the equipment used. That is to say that if an individual mixes, loads and applies a pesticide using tractor drawn equipment, the estimated exposures should be presented separately. If an individual would mix, load and apply a pesticide using "hand-held" equipment such as a back pack sprayer, hand wand, or push type spreaders, then the estimated exposures should be combined (EXPOSAC Policy No. 12 (draft), 29 March 2000). Therefore, the Margins of Exposure (MOEs) for the Mixer/Loader and Applicator using high pressure hand wand equipment, are combined.

On 7 June 2001, HED's Hazard Identification Assessment Review Committee (HIARC) met to discuss the adequacy of the toxicological database relative to the compound novaluron. During that meeting, no dermal toxicological endpoints were identified. However, short-term and intermediate-term inhalation endpoints were identified (8.3 mg a.i./kg bw/day; Memo, J. Kidwell, 2 August 01, HED Doc. No. 014636). Novaluron is classified in Toxicity Category III for Acute Dermal and Toxicity Category IV for Acute Oral, Acute Inhalation, Primary Eye Irritation and Primary Skin Irritation. It is not a Dermal Sensitizer. See Appendix for summary of toxicological effects. Therefore this assessment presents HED's estimates of inhalation exposure.

Table 2 Estimated Handler Exposure and Risk from the Use of Novaluron

Activity	Unit Exposure[1] mg a.i./lb handled		Applic. Rate[2]	Units Treated[3]	Average Daily Dose[4]	MOE[5]
Mix/Load liquid Open Pour	Inhal	0.0012	0.17 lb a.i./A	40 acres/day	1.17×10^{-4}	> 70 K
Applicator Ground boom Open Cab	Inhal	0.00074			7.19×10^{-5}	> 115 K
Mix/Load liquid Open Pour	Inhal	0.0012	0.08 lb a.i. Per 100 gal	1000 gal/day (=0.17 lb a.i./A)	1.37×10^{-5}	Combined MOE > 9 K
Applicator High Pressure Hand Wand	Inhal	0.079			9.03×10^{-4}	

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Inhal. = Inhalation. Units = mg a.i./pound of active handled. Data Confidence: High for Mixer/Loader Open Pour Liquids; High for Groundboom Applicator/single layer no gloves and inhalation, Medium for single layer with gloves; Low for High Pressure Hand Wand Applicator
2. Applic. Rate. = Maximum rate of application listed on the proposed labels for RimOn™ 10 EC and SC. 0.83 lb a.i./gal +128 fl oz/gal = 0.0065 lb a.i./floz * 12 oz RimOn/100 gal water = 0.08 lb a.i./100 gal water (i.e., 0.0008 lb a.i./gal). Or, since one gallon finish spray will treat 200 ft^2 - - - 43,560 ft^2/A + 200 ft^2/gal = 218 gallons/A; ∴218gal/A * 0.0008 lb a.i./gal = 0.17 lb a.i./A
3. Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; Policy No. 9. Science Advisory Council for Exposure; Revised 5 July 2000.
4. Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated + Body Weight (70kg)
5. MOE = Margin of Exposure = NOAEL (Inhalation NOAEL = 8.3 mg a.i./kg bw/day and assumes 100% absorption) + ADD.

POST-APPLICATION - RE-ENTRY EXPOSURE

Since no dermal toxicological endpoints were identified, post-application, re-entry exposure is not estimated.

SUMMARY

HEDs level of concern is for MOEs ≤ 100. In this case, all MOEs are greater than 100 and therefore do not exceed HEDs level of concern. HED recommends that RD verify or confirm what appear to be label inconsistencies as described earlier.

APPENDIX

Acute Toxicity Profile for NOVALURON Technical

GDLN	Study Type	MRID	Results	Tox Category
870.1100	Acute Oral - rat	44961001	LD_{50} >5000 mg/kg (males and females)	IV
870.1200	Acute Dermal - rat	45003201	LD_{50} >2000 mg/kg	III
870.1300	Acute Inhalation - rat	45003202	LC_{50} >5.15 mg/L (males and females)	IV
870.2400	Primary Eye Irritation - rabbit	45003203	Not an ocular irritant	IV
870.2500	Primary Skin Irritation - rabbit	45003204	Not a dermal irritant	IV
870.2600	Dermal Sensitization - guinea pig	45084001	Not a dermal sensitizer	

Taken from Memo J. Kidwell, 2 August 01, HED Doc. No. 014636

SUMMARY OF TOXICOLOGY ENDPOINT SELECTION

The doses and toxicological endpoints selected for various exposure scenarios are summarized below.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	Not applicable	Not applicable	Not applicable
	An acute RfD was not established since the proposed registration is for a non-food use.		

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Chronic Dietary	Not applicable	Not applicable	Not applicable
	A chronic RfD was not established since the proposed registration is for a non-food use.		
Incidental Oral, Short- and Intermediate-Term	NOAEL= 8.3 mg/kg/day	Alterations in hematological parameters (increased methemoglobin, increased reticulocytes, decreased hemoglobin, decreased erythrocytes, increased mean corpuscular volume), increased absolute/relative spleen weights, and spleen histopathology (minimal to moderate extramedullary erythropoiesis, slight to moderate increased hemosiderosis) seen at the LOAEL of 818.5 mg/kg/day.	90-Day Oral Toxicity Study in the Rat
Dermal, Short- and Intermediate-Term	Not applicable	No hazard via the dermal route was identified and, therefore, risk quantification is not required. No systemic effects were noted up to the limit dose of 1000 mg/kg/day in the 28-day dermal toxicity study in the rat.	Not applicable
Dermal, Long-Term	Not applicable	The current use pattern does not indicate a long-term exposure scenario.	Not applicable
Inhalation[a], Short- and Intermediate-Term	NOAEL= 8.3 mg/kg/day MOE = 100	Alterations in hematological parameters (increased methemoglobin, increased reticulocytes, decreased hemoglobin, decreased erythrocytes, increased mean corpuscular volume), increased absolute/relative spleen weights, and spleen histopathology (minimal to moderate extramedullary erythropoiesis, slight to moderate increased hemosiderosis) seen at the LOAEL of 818.5 mg/kg/day.	90-Day Oral Toxicity Study in the Rat
Inhalation, Long-Term	Not applicable	The current use pattern does not indicate a long-term exposure scenario.	Not applicable

[a]An inhalation absorption factor of 100% should be used for route-to-route extrapolation.
Taken from Memo, J. Kidwell, 2 August 01 HED Doc. No. 014636

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

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

11678-LT

MEMORANDUM

DATE: August 15, 2001

SUBJECT: Novaluron - HED Risk Assessment Memo
PC Code: 124002; DP Barcode D276811

FROM: Jessica Kidwell, EPS
Registration Action Branch 1
Health Effects Division (7509C)

THROUGH: G. Jeffrey Herndon, Branch Senior Scientist
Registration Action Branch 1
Health Effects Division (7509C)

TO: Suku Oonnithan, PM Team 4
Insecticide/Rodenticide Branch
Registration Division (7505C)

Makhteshim Agan, Makhteshim Chemical Works, Ltd. has applied for registration of the active ingredient Novaluron for use on containerized ornamental plants in greenhouses, shadehouses and outdoor nurseries. The Health Effects Division assessed handler and worker exposure and risk from the proposed use (Memo, D272507, M. Dow, 8/15/01).

The toxicology data gaps for Novaluron are listed below:

a. *Two mutagenicity studies:* It is recommended that an *in vitro* mammalian cell gene mutation assay and an *in vivo* cytogenetics assay (i.e., micronucleus assay) be performed to satisfy the current Subdivision F guideline requirements for mutagenicity.

b. *90-Day Inhalation:* A 90-day inhalation toxicity study in the rat is required by HIARC for further characterization of inhalation risk assessments. Due to the potential for inhalation exposure, there is concern for toxicity by the inhalation route. The 90-day inhalation toxicity study would give a dose and endpoint examined via the route of exposure of concern (i.e., route specific study) and thus, would avoid using an oral study and route-to-route extrapolation).

c. *An acceptable Acute neurotoxicity study*[1]*:* The acute neurotoxicity study was classified as Unacceptable/Guideline since neuropathology was not performed on the low- and mid-dose groups. The guidelines state that if neurological alterations are observed in samples from the high dose group, samples from the intermediate and low dose groups should be examined sequentially. This is critical since neuropathology findings (sciatic and tibial nerve degeneration) at the high dose were seen in this study.

d. *Subchronic oral neurotoxicity study*[1]*:* A subchronic oral neurotoxicity study is required based on the effects seen in the acute oral neurotoxicity study. The effects in the acute neurotoxicity study included clinical signs (piloerection, fast/irregular respiration), FOB parameters (increased head swaying, abnormal gait), and neuropathology (sciatic and tibial nerve degeneration) seen at the LOAEL of 2000 mg/kg/day.

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[1]Although not required for a non-food use, any expansion of the use of novaluron should include an acceptable acute neurotoxicity study and a subchronic neurotoxicity study.

MAKHTESHIM
A G A N
of
North America
Inc.

454768-00

5602731/180

August 6, 2001

Document Processing Desk (APPL)
Office of Pesticide Programs (7504C)
USEPA
1921 Jefferson Davis Highway
CM2, Room 266A
Arlington, VA 22202

Attn: Dr. S. Oonnithan
Phone: 703-605-0368

Re: Request for Conditional Registration and Submission of Additional Eco-tox Studies in support of Novaluron Technical Insecticide: Ornamentals Use, EPA File Symbol 11678-~~LT~~ 57

Dear Oonni:

Makhteshim Chemical Works, Ltd (MCW) c/o Makhteshim-Agan of North America, Inc. (MANA) submits the enclosed ecological effects data to support the above registration.

Novaluron technical and two formulations are currently in Reduced Risk review for registration on ornamentals and scheduled for a decision within the next few weeks. The submitted labels specify "***for use in greenhouses, shadehouses and containerized ornamentals in outdoor nurseries***." This is the full use pattern that was proposed to the Agency in a pre-registration meeting, the associated Reduced Risk Petition and all subsequent communication with the Agency regarding this ornamentals registration.

It is our understanding that the Agency is hesitant to grant registration for the proposed uses and prefers to restrict the label to "*use in greenhouses only*" due to the absence of ecological effects data.

MCW is happy to supply the data for your consideration and review, however, we request that a conditional registration be issued for the full use pattern as specified in the original submission. The following points provide ample justification for approval of a conditional registration as outlined in 40 CFR § 152.114 a -e:

1. All other required test data and materials have been submitted to the Agency and have been found acceptable (40 CFR § 152.114 (b), CFR § 152.112 (a), (b), (d), (f).

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

2. The submitted studies are listed as conditionally required in 40 CFR part 158 for non-terrestrial uses on ornamentals.

3. The registrant provided a full data matrix to EPA in the Reduced Risk Petition for this use (November 19, 1999), which did not include <u>any</u> ecological effects data. The petition received a unanimous vote of approval from the committee. The designation of novaluron as a Reduced Risk Pesticide fulfills 40 CFR § 152.114 (e), "*The registration of the pesticide product and its subsequent use during the period of the conditional registration are in the public interest.*"

4. In a pre-registration meeting (October 28, 1999, minutes attached), the proposed data matrix for submission was presented and discussed. At the meeting, the Agency recommended additional studies to satisfy certain data requirements that are listed as "CR." These studies were added to the package and submitted to the Agency.

5. In the same pre-registration meeting, Branch Chief, Tina Levine stated, "*Sometime you will need to address the ecotox/environmental risk, but because of the use pattern [for greenhouse use] it would not be an issue.*"

6. A full ecological effects database is available for novaluron and has been available since our pre-registration meeting in 1999. The registrant has always been willing to answer reviewer questions and submit additional data when requested. The request for these studies was received on August 2, 2001. The registrant does not require any time to develop these data and complies with the Agency request with this submission (less than 10 days later) (40 CFR § 152.114 (a),(b)).

7. To mitigate reviewer concerns about ecological exposure, MANA proposed adding precautionary language to the end-use labels restricting the type of application equipment that could be used and directing the user to minimize off-site drift and movement to non-target areas thereby mitigating the risk of ecological effects (attached, e-mail D. Spatz, 8/2/01). The registrant maintains that the use pattern, which allows application *only to containerized ornamentals*, coupled with the risk mitigation language we propose, is sufficiently restrictive to enable the Agency to grant the use of the pesticide during the period of conditional registration without the risk of unreasonable adverse effects on the environment (CFR § 152.114 (d), CFR § 152.112 (e).

We respectfully request that the Agency grant a conditional registration as scheduled for the full labeled use and review the attached studies as soon as possible.

Included in this submission are:

- Application for Pesticide Registration (EPA 8570-1)
- List of Submitted Studies
- Transmittal document

Additionally, three (3) copies of each ecological effects study requested are enclosed. These studies have been formatted to comply with PR Notice 86-5.

Should you have questions about this application, please contact me at (212) 896-4945

Sincerely,

Robert C. Everich, Ph.D.
Senior Scientist

Enclosures:

1) Pre-application meeting notes (10/28/99)
2) e-mail, R. Everich to D. Spatz, 8/2/01

CC: E. Gur (MANA) A. Stout (MANA)
H. Lahav (MCW) J. Ball (UCC)

List of Submitted Studies:

MRID	Guideline	Author	Date	Title	Data Owner
Reject (01)	850.2100	Hakin, B., Norman, A. J., Anderson, A., Dawe, I. S.	1989a	The acute oral toxicity (LD_{50}) of GR 572 Technical to the Mallard Duck Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 68/89647 Makhteshim Chemical Works Ltd., Report No. R-8764	MCW
45476801	850.2100	Rodgers, M. H.	1998a	"Rimon" technical - Acute oral toxicity (LD_{50}) to the Bobwhite quail (*Colinus virginianus*) Huntingdon Life Sciences Ltd., UK, Report No. MAK 410/972113 Makhteshim Chemical Works Ltd., Report No. R-9416	MCW
Reject (03)	850.2200	Hakin, B., Rodgers, M., Norman, A. J., Anderson, A., Dawe, I. S.	1989c	The dietary toxicity (LC_{50}) of GR 572 to the Bobwhite quail Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 69/89126 Makhteshim Chemical Works Ltd., Report No. R-8763	MCW
Reject (04)	850.2200	Hakin, B., Rodgers, M., Norman, A. J., Anderson, A., Dawe, I. S.	1989b	The dietary toxicity (LC_{50}) of GR 572 to the Mallard Duck Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 67/89125 Makhteshim Chemical Works Ltd., Report No. R-8765	MCW
Reject (05)	850.1075	Douglas, M. T., Bell, G., MacDonald, I. A.	1989b	The acute toxicity of GR 572 Technical to Rainbow trout (*Salmo gairdneri*) Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 61(c)/891282 Makhteshim Chemical Works Ltd., Report No. R-8762	MCW

MRID	Guideline	Author	Date	Title	Data Owner
Reject (06)	850.1075	Douglas, M. T., Sewell, I. G., MacDonald, I. A.	1989a	The acute toxicity of GR 572 Technical to Bluegill sunfish (*Lepomis macrochirus)* Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 63(d)/89960 Makhteshim Chemical Works Ltd., Report No. R-8761	MCW
Reject (07)	850.1075	Jenkins, C. A.	1999a	275-352 I: Acute toxicity to Rainbow trout Huntingdon Life Sciences Ltd., UK, Report No. MAK525/992450 Makhteshim Chemical Works Ltd., Report No. R-10635	MCW
45476802	850.1010	Jenkins, C. A.	1997	"Rimon" technical: Acute toxicity to the *Daphnia magna* Huntingdon Life Sciences Ltd., UK, Report No. MAK 404/970470 Makhteshim Chemical Works Ltd., Report No. R-9340	MCW
Reject (09)	850.1010	Jenkins, C. A.	1999b	275-352 I: Acute toxicity to *Daphnia magna* Huntingdon Life Sciences Ltd., UK, Report No. MAK526/992451 Makhteshim Chemical Works Ltd., Report No. R-10636	MCW

TRANSMITTAL DOCUMENT FOR ADDITIONAL REQUESTED STUDIES
NOVALURON TECHNICAL INSECTICIDE

Submitter:
Makhteshim Chemical Works Ltd.
Beer-Sheva, ISRAEL
C/o
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

Regulatory action/reason for submission:
Additional Studies Requested by Agency
EPA Company No. 11678, File Symbol 11678-LT

Transmittal date:
August 6, 2001

Company official:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Company name:
Makhteshim Chemical Works, Ltd.

Company contact:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Robert C. Everich, Ph.D.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460-0001

OFFICE OF
PESTICIDE PROGRAMS

August 27, 2001

Robert C. Everich, Ph.D.
Senior Scientist
Makhteshim Agan of North America
551 Fifth Avenue, Suite: 1100
New York, NY 10176

Subject: EPA File Symbol 11678-LT
Novaluron Technical
Submission of Eco-tox Studies
Your Letter dated August 6, 2001

Dear Dr. Everich:

Your submission referred to above was reviewed by the Agency for formatting requirements per PR Notice 86-5. Those studies that met the requirements were assigned Master Record Identification (MRID) numbers and those that did not, were rejected. The attached letter lists the MRID numbers for the accepted studies and provides the deficiencies for the rejected studies.

The rejected studies are available for pick up if you wish. Further consideration will be given to your submission upon receipt of acceptable studies after addressing the deficiencies. Should you have any questions, do not hesitate to contact me at 703-605-0368.

Sincerely,

S. Oonnithan, Entomologist
Insecticide Rodenticide Branch
Registration Division (7505C)

Encl.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460-0001

OFFICE OF
PESTICIDE PROGRAMS

August 27, 2001

Robert C. Everich, Ph.D.
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Makhteshim Agan of North America
551 Fifth Avenue, Suite: 1100
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Sincerely,

S. Oonnithan, Entomologist
Insecticide Rodenticide Branch
Registration Division (7505C)

Encl.

List of Submitted Studies:

MRID	Guideline	Author	Date	Title	Data Owner
45499001	850.2100	Hakin, B., Norman, A. J., Anderson, A., Dawe, I. S.	1989a	The acute oral toxicity (LD_{50}) of GR 572 Technical to the Mallard Duck Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 68/89647 Makhteshim Chemical Works Ltd., Report No. R-8764	MCW
45476801	850.2100	Rodgers, M. H.	1998a	"Rimon" technical - Acute oral toxicity (LD_{50}) to the Bobwhite quail (*Colinus virginianus*) Huntingdon Life Sciences Ltd., UK, Report No. MAK 410/972113 Makhteshim Chemical Works Ltd., Report No. R-9416	MCW
45499002	850.2200	Hakin, B., Rodgers, M., Norman, A. J., Anderson, A., Dawe, I. S.	1989c	The dietary toxicity (LC_{50}) of GR 572 to the Bobwhite quail Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 69/89126 Makhteshim Chemical Works Ltd., Report No. R-8763	MCW
45499003	850.2200	Hakin, B., Rodgers, M., Norman, A. J., Anderson, A., Dawe, I. S.	1989b	The dietary toxicity (LC_{50}) of GR 572 to the Mallard Duck Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 67/89125 Makhteshim Chemical Works Ltd., Report No. R-8765	MCW
45499004	850.1075	Douglas, M. T., Bell, G., MacDonald, A.	1989b	The acute toxicity of GR 572 Technical to Rainbow trout (*Salmo gairdneri*) Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 66(c)/891282 Makhteshim Chemical Works Ltd., Report No. R-8762	MCW

MRID	Guideline	Author	Date	Title	Data Owner
45499005	850.1075	Douglas, M. T., Sewell, I. G., MacDonald, I. A.	1989a	The acute toxicity of GR 572 Technical to Bluegill sunfish (*Lepomis macrochirus)* Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 63(d)/89960 Makhteshim Chemical Works Ltd., Report No. R-8761	MCW
45499006	850.1075	Jenkins, C. A.	1999a	275-352 I: Acute toxicity to Rainbow trout Huntingdon Life Sciences Ltd., UK, Report No. MAK525/992450 Makhteshim Chemical Works Ltd., Report No. R-10635	MCW
45476802	850.1010	Jenkins, C. A.	1997	"Rimon" technical: Acute toxicity to the *Daphnia magna* Huntingdon Life Sciences Ltd., UK, Report No. MAK 404/970470 Makhteshim Chemical Works Ltd., Report No. R-9340	MCW
45499007	850.1010	Jenkins, C. A.	1999b	275-352 I: Acute toxicity to *Daphnia magna* Huntingdon Life Sciences Ltd., UK, Report No. MAK526/992451 Makhteshim Chemical Works Ltd., Report No. R-10636	MCW

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

014636

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DATE: August 2, 2001

MEMORANDUM

SUBJECT: *NOVALURON* - Report of the Hazard Identification Assessment Review Committee.

FROM: Jessica Kidwell, Toxicologist Jessica Kidwell 8/2/01
Registration Action Branch 1
Health Effects Division (7509C)

THROUGH: Jess Rowland, Co-Chair 8/6/01
and
Elizabeth Doyle, Co-Chair E.A. Doyle 8/6/01
Hazard Identification Assessment Review Committee
Health Effects Division (7509C)

TO: Mark Dow, Risk Assessor
Registration Action Branch 1
Health Effects Division (7509C)

PC Code: 124002

On June 7, 2001, the Health Effects Division (HED) Hazard Identification Assessment Review Committee (HIARC) reviewed the recommendations of the toxicology reviewer for NOVALURON with regard to the toxicological endpoint selection for use as appropriate in occupational/residential exposure risk assessments. Since this is a non-food use registration, acute and chronic dietary endpoints were not selected. Food Quality Protection Act (FQPA) considerations were NOT evaluated since this is a non-food use registration, no tolerances are being established, and there are no proposed residential uses. The conclusions drawn at this meeting are presented in this report.

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Committee Members in Attendance

Members present were: W. Burnam, E. Doyle, P. Hurley, E. Mendez, J. Rowland, Y. Yang, B. Tarplee, J. Chen, A. Assaad, P. Deschamp

Member(s) in absentia: D. Nixon (attending workshop)

Data evaluation prepared by: Jessica Kidwell, RAB1

Also in attendance were: D. Vogel, J. Herndon, and M. Dow of HED/RAB1 and O. Oonnithan of RD.

Data Evaluation / Report Presentation

Jessica Kidwell

Jessica Kidwell
Toxicologist

1. INTRODUCTION

On June 7, 2001, the Health Effects Division (HED) Hazard Identification Assessment Review Committee (HIARC) reviewed the recommendations of the toxicology reviewer for NOVALURON with regard to the toxicological endpoint selection for use as appropriate in occupational/residential exposure risk assessments. Since this is a non-food use registration, acute and chronic dietary endpoints were not selected. Food Quality Protection Act (FQPA) considerations were NOT evaluated since this is a non-food use registration, no tolerances are being established, and there are no proposed residential uses. The conclusions drawn at this meeting are presented in this report.

2. HAZARD IDENTIFICATION

2.1 Acute Reference Dose (RfD): An acute RfD was not established since the proposed registration is for a non-food use.

2.2 Chronic Reference Dose (RfD): A chronic RfD was not established since the proposed registration is for a non-food use.

2.3 Occupational/Residential Exposure

2.3.1 Short-Term (1 Day to 1 Month) Incidental Oral Exposure

Study Selected: 90-Day Oral Toxicity Study in the Rat OPPTS No. 870.3100

MRID No.: 45030001

Executive Summary: In this subchronic oral study (MRID 45030001), novaluron (99.5% a.i., Lot/batch # 031068069) was administered in the diet to 10-15 CD rats/sex/group at doses of 0, 50, 100, 10000, or 20000 ppm (equivalent to [M/F] 0/0, 4.2/4.7, 8.3/8.9, 818.5/871.0, and 1666.9/1820.6 mg/kg/day). Ten animals/sex/group were sacrificed after 13 weeks of treatment, while 5 rats/sex/group in the 0, 50, and 20000 ppm groups were maintained for a four-week recovery phase. One 100 ppm male died following routine blood sampling during week 13. Mortality, clinical signs, body weights, food consumption and efficiency, ophthalmoscopic examinations, clinical chemistry, urinalysis, and gross pathology were unaffected by the test substance. At 10000 and 20000 ppm, following the treatment phase, methemoglobin was increased ($p \leq 0.05$ or 0.001) in the males (↑93-98%) and females (↑198-245%). In addition, reticulocytes were increased ($p \leq 0.05$ or 0.001) in both sexes (↑121-175%). Other differences ($p \leq 0.01$ or 0.001) in hematological parameters observed in the 10000 and 20000 ppm females included the following: (i) decreased hemoglobin (↓9-10%); (ii)

decreased erythrocytes (↓15% each); and (iii) increased mean corpuscular volume (↑8-9%). Increased platelets (↑14%, p≤0.01) were observed in the 20000 ppm females only. Absolute spleen weights were increased (p≤0.05 or 0.01) following treatment in the 20000 males (↑21%) and in the 10000 and 20000 ppm (↑31-41%) females. In addition, increased relative (to body weight) spleen weights were increased in the 10000 and 20000 ppm females (↑33-34%, p≤0.01). The following histopathological changes (p≤0.001, 0.01, 0.05 or not statistically significant) were noted in the spleens of the 10000 and 20000 animals following the treatment phase: (i) minimal to moderate extramedullary erythropoiesis in both sexes (20/20 each vs. 8/20 controls); (ii) slightly increased hemosiderosis in the males (9/10 each vs. 1/10 controls); and (iii) slightly to moderately increased hemosiderosis in the females (10/10 each vs. 0/10 controls). Moderate focal necrosis of the spleen was observed in the 20000 ppm males only (1/10 treated vs. 0/10 controls). Minimal to slight pigment laden Kupffer cells were observed in the 10000 (5/10 treated vs. 0/10 controls) and 20000 (8/10 treated vs. 0/10 controls) ppm females following treatment and in the 20000 ppm females after recovery (1/10 treated vs. 0/10 controls). This finding is of equivocal toxicological importance. At 20000 ppm, cumulative body weight gains were increased (p≤0.05 or 0.01) throughout the treatment period in the males (↑12-19%) and females (↑10-52%). Overall (weeks 0-13) body weight gains were increased during the treatment phase in both sexes (↑10-14%, p≤0.05). In the males, slight plasmacytosis was observed in the mesenteric lymph nodes (2/10 treated vs. 0/10 controls) and a slight presence of erythrocytes and erythrophagocytosis were observed in the sinuses of the mandibular lymph nodes (1/10 treated vs. 0/10 controls) following treatment. Following the recovery phase, the following effects were noted in the 20000 ppm animals: (i) cumulative body weight gains were decreased (p≤0.01 or not statistically significant) in the females during all intervals (↓91-133%); (ii) methemoglobin remained elevated relative to concurrent controls (↑29-49%, p≤0.05 or 0.001); (iii) relative spleen weights remained higher in the 20000 ppm females relative to concurrent controls (↑19%, p≤0.05); and (iv) slightly to moderately increased hemosiderosis of the spleen was observed (p≤0.01 or not statistically significant) (6/20 treated vs. 0/20 controls). Minor toxicological effects were noted at 50 and 100 ppm and included the following: (i) increased methemoglobin in the 50 ppm females (↑27%, p≤0.05); (ii) slightly decreased (p≤0.05 or 0.001) hemoglobin (↓6%) and erythrocytes (↓4-8%) in the 50 and 100 ppm females; (iii) minimal to moderate extramedullary erythropoiesis in both sexes at 50 and 100 ppm (15/20 and 16/20, respectively vs. 8/20 controls); and (iv) slightly to moderately increased hemosiderosis in the 50 and 100 females (5/10 and 8/10, respectively vs. 0/10 controls). These minor toxicological effects were not considered to be adverse. **The LOAEL for this study is 10000 ppm (equivalent to 818.5 mg/kg/day in males and 871.0 mg/kg/day in females) based on hematological parameters (increased methemoglobin, increased reticulocytes, decreased hemoglobin, decreased erythrocytes, increased mean corpuscular**

volume), increased absolute/relative spleen weights, and spleen histopathology (minimal to moderate extramedullary erythropoiesis, slight to moderate increased hemosiderosis). The NOAEL for this study is 100 ppm (equivalent to 8.3 mg/kg/day in males and 8.9 mg/kg/day in females).

The submitted study is classified as **acceptable/guideline (§82-1[a])** and satisfies the requirements for a subchronic oral toxicity study in the rat.

Dose/Endpoint for Risk Assessment: NOAEL = 8.3 mg/kg/day, based on alterations in hematological parameters (increased methemoglobin, increased reticulocytes, decreased hemoglobin, decreased erythrocytes, increased mean corpuscular volume), increased absolute/relative spleen weights, and spleen histopathology (minimal to moderate extramedullary erythropoiesis, slight to moderate increased hemosiderosis) seen at the LOAEL of 818.5 mg/kg/day.

Comments about Study/Endpoint: The systemic toxicity seen is appropriate for the population (infants and children) of concern. Although the duration of this study does not reflect toxicity at a dose duration of less than 90 days, there are no other studies available to better represent the short-term exposure duration of interest. No maternal or developmental toxicity was noted in the developmental rat study tested up to the limit dose of 1000 mg/kg/day.

2.3.2 Intermediate-Term (1-6 Months) Incidental Oral Exposure

Study Selected: 90-Day Oral Toxicity Study in the Rat OPPTS No. 870.3100

MRID No.: 45030001

Executive Summary: See "Short-term incidental oral"

Dose/Endpoint for Risk Assessment: NOAEL = 8.3 mg/kg/day, based on alterations in hematological parameters (increased methemoglobin, increased reticulocytes, decreased hemoglobin, decreased erythrocytes, increased mean corpuscular volume), increased absolute/relative spleen weights, and spleen histopathology (minimal to moderate extramedullary erythropoiesis, slight to moderate increased hemosiderosis) seen at the LOAEL of 818.5 mg/kg/day.

Comments about Study/Endpoint: The systemic toxicity seen is appropriate for the population (infants and children) and exposure duration of concern.

2.3.3 Dermal Absorption

Dermal Absorption Factor: 82%

Comments about Dermal Absorption: There is no dermal absorption study available for review. The 28-day dermal toxicity rat study had a NOAEL of 1000 mg/kg/day with no systemic effects noted (MRID 45288501). The subchronic oral rat NOAEL/LOAEL (based on hematological parameters, spleen weights, and histopathology) is 8.3/818.5 mg/kg/day (MRID 45030001). An upper-bound estimate of dermal absorption was calculated by comparing the LOAEL from the subchronic oral rat study with the NOAEL from the dermal rat study (818.5/1000 x 100 = 82%).

2.3.4 Short-Term Dermal (1 Day to 1 Month) Exposure

Study Selected: Not applicable

MRID No.: Not applicable

Executive Summary: Not applicable

Dose and Endpoint for Risk Assessment: Not applicable

Comments about Study/Endpoint: No hazard via the dermal route was identified and, therefore, risk quantification is not required. No systemic effects were noted up to the limit dose of 1000 mg/kg/day in the 28-day dermal toxicity study in the rat (MRID 45288501), which is the study most directly applicable to this route (dermal) and exposure period of concern. In addition, no maternal or developmental toxicity was noted in the developmental rat study tested up to the limit dose of 1000 mg/kg/day.

2.3.5 Intermediate-Term Dermal (1-6 Months) Exposure

Study Selected: Not applicable

MRID No.: Not applicable

Executive Summary: Not applicable

Dose/Endpoint for Risk Assessment: Not applicable

Comments about Study/Endpoint: No hazard via the dermal route was identified and, therefore, risk quantification is not required. No systemic effects were noted

up to the limit dose of 1000 mg/kg/day in the 28-day dermal toxicity study in the rat (MRID 45288501). Although a subchronic oral rat toxicity study with a NOAEL/LOAEL of 8.3/818.5 mg/kg/day (based on alterations in hematological parameters, increased absolute/relative spleen weights and spleen histopathology) was available, it was not chosen because the toxicity of concern (hematological effects) demonstrated via the oral route was not seen via the dermal route in the same species.

2.3.6 Long-Term Dermal (>6 Months) Exposure

Study Selected: Not applicable

MRID No.: Not applicable

Executive Summary: Not applicable

Dose and Endpoint for Risk Assessment: Not applicable

Comments about Study/Endpoint:. The current use pattern does not indicate a long-term exposure scenario.

2.3.7 Short-Term (1 Day-1 Month) Inhalation Exposure

Study Selected: 90-Day Oral Toxicity Study in the Rat OPPTS No. 870.3100

MRID No.: 45030001

Executive Summary: See "Short-term incidental oral"

Dose/Endpoint for Risk Assessment: NOAEL = 8.3 mg/kg/day, based on alterations in hematological parameters (increased methemoglobin, increased reticulocytes, decreased hemoglobin, decreased erythrocytes, increased mean corpuscular volume), increased absolute/relative spleen weights, and spleen histopathology (minimal to moderate extramedullary erythropoiesis, slight to moderate increased hemosiderosis) seen at the LOAEL of 818.5 mg/kg/day.

Comments about Study/Endpoint: An oral study was selected due to lack of an inhalation study. An inhalation absorption factor of 100% should be used for risk assessment.

2.3.8 Intermediate-Term (1-6 Months) Inhalation Exposure

Study Selected: 90-Day Oral Toxicity Study in the Rat OPPTS No. 870.3100

MRID No.: 45030001

Executive Summary: See "Short-term incidental oral"

Dose/Endpoint for Risk Assessment: NOAEL = 8.3 mg/kg/day, based on alterations in hematological parameters (increased methemoglobin, increased reticulocytes, decreased hemoglobin, decreased erythrocytes, increased mean corpuscular volume), increased absolute/relative spleen weights, and spleen histopathology (minimal to moderate extramedullary erythropoiesis, slight to moderate increased hemosiderosis) seen at the LOAEL of 818.5 mg/kg/day.

Comments about Study/Endpoint: An oral study was selected due to lack of an inhalation study. An inhalation absorption factor of 100% should be used for risk assessment.

2.3.9 Long-term (>6 Months) Inhalation Exposure

Study Selected: Not applicable

MRID No.: Not applicable

Executive Summary: Not applicable

Dose and Endpoint for Risk Assessment: Not applicable

Comments about Study/Endpoint:. The current use pattern does not indicate a long-term exposure scenario. In addition, no long-term studies were submitted for this registration.

2.4.0 Margins of Exposure for Occupational/Residential Risk Assessments

The acceptable MOEs for occupational exposure is 100. The current application does not indicate potential residential exposure.

2.4.1 Recommendation for Aggregate Exposure Risk Assessments

Based on the use pattern, there is no exposure via the oral route nor any residential exposures.

3. CLASSIFICATION OF CARCINOGENIC POTENTIAL

No long-term carcinogenicity studies were submitted for this non-food use registration.

4. MUTAGENICITY

Based on the available mutagenicity studies, there is no concern for mutagenicity. The mutagenicity/genotoxicity database, however, is not adequate and does not meet the new Subdivision F Guideline requirements for mutagenicity testing. It is recommended that an *in vitro* mammalian cell gene mutation assay and an *in vivo* cytogenetics assay (i.e., micronucleus assay) be performed to satisfy the current guideline requirements for mutagenicity.

GENE MUTATION

(1) EXECUTIVE SUMMARY: In two independent microbial mutagenicity tests (MRID 44961013), *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537, and *Escherichia coli* strain WP2 *uvrA* were exposed to novaluron (99.3% a.i.Lot/Batch# 970211/4) in dimethylsulfoxide (DMSO) at concentrations of 0, 312.5, 625, 1250, 2500, or 5000 µg/plate in the presence and absence of metabolic activation (±S9). The standard plate incorporation method was performed. S9 homogenates for metabolic activation were made from Aroclor-induced rat livers. The standard strain-specific mutagens served as positive controls. Novaluron, tested up to the limit of solubility (2500 µg/plate) and the limit dose (5000 µg/plate), was not cytotoxic with or without S9 activation in four *S. typhimurium* strains and one strain of *E. coli*, and did not induce a genotoxic response in any strain. The sensitivity of the test system to detect mutagenesis was adequately demonstrated by the response obtained with the non-activated and S9-activated positive controls.

This study is classified as **acceptable (§84-2)** and does satisfy the FIFRA Test Guideline requirements for *in vitro* mutagenicity (bacterial reverse gene mutation) data.

2) EXECUTIVE SUMMARY: In two independent microbial mutagenicity tests (MRID 45030003), *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 were exposed to novaluron (93.5%, Lot/Batch # FCF/T/46) in dimethylsulfoxide (DMSO) at concentrations of 0, 10, 33, 100, 333, 1000, or 3333 µg/plate in the presence and absence of mammalian metabolic activation (±S9). The standard plate incorporation test was performed. S9 homogenates for metabolic activation were made from Aroclor-induced rat livers. The standard strain-specific mutagens served as positive controls.

Novaluron, tested up to the limit of solubility (3333 µg/plate), was not cytotoxic with or without S9 activation in five *S. typhimurium* strains, and did not induce a genotoxic response in any strain. The sensitivity of the test system to detect mutagenesis was adequately demonstrated by the response obtained with the non-activated and S9-activated positive controls.

This study is classified as **acceptable (§84-2)** and does satisfy the FIFRA Test Guideline requirements for *in vitro* mutagenicity (bacterial reverse gene mutation) data.

CHROMOSOMAL ABERRATION

(3) EXECUTIVE SUMMARY: In a mammalian cell chromosome aberration assay (MRID 44961015) primary human lymphocyte cultures were exposed to dimethylsulfoxide (DMSO) alone or to novaluron (97.5% a.i.Lot/Batch# FCF/T/81-89) in DMSO at 40, 200, and 1000 µg/mL, with and without metabolic activation (±S9). Cultures treated at 5000 µg/mL (±S9) were not scorable due to heavy precipitation. Microscope slides of metaphase-arrested lymphocytes were prepared and 300 metaphases per dose level (±S9) were examined for chromosomal aberrations. In this *in vitro* cytogenetic test, novaluron showed evidence of mitotic suppression (52% compared to solvent controls) in cultured human lymphocytes at 1000 µg/mL, with metabolic activation and no evidence of mitotic suppression at 1000 µg/mL without metabolic activation. Under both activated and non-activated conditions there were no increases in metaphases with aberrations including or excluding gaps, compared to solvent controls. The sensitivity of the test system to detect damage to chromosomes was adequately verified by the results obtained with the positive controls (chlorambucil, -S9 and cyclophosphamide, +S9). **Under the conditions of this study, novaluron produced no evidence of clastogenic activity in primary human lymphocytes, in the presence or absence of S9 activation.**

This study is **acceptable (§84-2)** and does satisfy the requirement of the FIFRA Test Guideline for *in vitro* mammalian chromosome aberrations.

DNA DAMAGE

(4) EXECUTIVE SUMMARY: In two independent unscheduled DNA synthesis (UDS) assays (MRID 45030002), HeLa S3 cultures were exposed to novaluron (94.3% a.i. Lot/Batch# FCF/T/73) in dimethylsulfoxide up to the limit of solubility at concentrations of 0.125, 0.25, 0.5, 1, 2, 4, 8, 16, 32, 64, 128, or 256 µg/mL (±S9). The criterion for a positive mutagenic response, as measured by unscheduled DNA synthesis, was a reproducible, statistically significant increase in the net nuclear grain count at any concentration as compared to concurrent vehicle control values. The positive controls [4-Nitroquinoline-1-oxide (4NQO), -S9 and 2-Aminoanthracene (2-AA), +S9] were used to assess the sensitivity of the system to detect DNA damaging agents. In the absence of S9, there were increases ($p<0.05$ or 0.01) in gross nuclear grain count at 2 and 16 µg/mL in the first assay and at 8 and 16 µg/mL in the second assay. Increases ($p<0.05$ or 0.01) in net nuclear grain count were observed at 2, 4, and 8 µg/mL in the first assay and at 0.125, 0.5, 2, 16, and 128 µg/mL in the second assay. In the presence of S9, increases ($p<0.05$ or 0.01) in gross nuclear grain count (↑38-42%) were observed at 8 and 32 µg/mL in the first assay only. No statistically significant increases in gross nuclear grain count were observed in the second assay and no statistically significant increases in net nuclear grain count were observed in either assay. The sensitivity of the system to detect DNA damaging agents was adequately shown by the response induced by the positive controls (2-AA, +S9; 4NQO, -S9). **Because the observed**

increases in gross and net nuclear grain counts were sporadic and not reproducible between assays, novaluron was considered not to show any evidence of causing DNA damage to HeLa S3 epithelioid cells in this unscheduled DNA synthesis test for mutagenic potential.

This study is classified as **acceptable (§84-2)** and does satisfy the FIFRA Test Guideline requirements for unscheduled DNA synthesis in mammalian cells in culture data.

(5) EXECUTIVE SUMMARY: In three trials of a differential killing (liquid suspension) assay, (MRID 44961014), *Bacillus subtilis* strains M45 and H17 were exposed to novaluron (Rimon technical, 99.3% a.i.Lot/Batch# 970211/4) in dimethylsulfoxide (DMSO) at concentrations of 50, 150, 500, 1,500, or 5,000 µg/plate, with and without mammalian metabolic activation (±S9). S9 homogenates for metabolic activation were made from Aroclor induced rat livers. In each trial, M45 and H17 were also exposed to kanamycin (-S9; 100, 150, 200, 250, or 300 µg/plate) or streptomycin (+S9; 450, 500, 550, 600, or 650 µg/plate) as negative controls, and AF-2 (-S9; 1.25, 2.5, 5, 10, or 20 µg/plate) or Aflatoxin B_1 (+S9; 31.25, 62.5, 125, 250, or 500 µg/plate) as positive controls. DMSO was the solvent for the test compound and the positive controls, while water was the solvent for the negative controls. Both solvents were used at 100 µL/plate (±S9). Novaluron was tested for cytotoxicity up to the limit dose (5000 µg/plate) with and without S9 using a disk diffusion (spot) test. No zones of growth inhibition were observed at any test concentration. However, in the differential killing assay, toxicity was observed in both tester strains in the absence of metabolic activation. The survival index ratio was calculated as the % survival of M45 ÷ % survival of H17. A ratio of <0.75 was considered an indication of preferential killing of the M45 (rec^-) strain. A positive response required preferential inhibition of M45 in two separate trials with evidence of dose-related toxicity. In the three trials, the survival index ratios for the high-doses (-S9) were 0.39-0.67 (1500 µg/plate) and 0.33-0.64 (5,000 µg/plate). Although there was no clear dose-response, the reproducible results obtained at the two highest dose levels (survival index ratios <0.75) suggest the potential for bacterial DNA damage in the absence of metabolic activation (-S9). Novaluron did not cause bacterial DNA damage when tested to the limit of dose (5000 µg/plate) in the presence of metabolic activation (+S9). The sensitivity of the test system to detect DNA damage was adequately demonstrated by the response obtained with AF-2 and Aflatoxin B_1 positive controls. The kanamycin and streptomycin negative controls demonstrated that a cytotoxic agent that does not cause DNA damage caused approximately equal lethality in the two tester strains. The solvent controls produced no toxicity. **Based on the results of the differential killing (liquid suspension) assay, novaluron was equivocal for bacterial DNA damage in the absence of S9 activation, and negative for bacterial DNA damage in the presence of S9 activation.**

This study is classified as **acceptable (§84-2)** and satisfies the requirements for FIFRA Test Guidelines for a rec assay with *B. subtilis*.

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

5. FQPA CONSIDERATIONS

Food Quality Protection Act (FQPA) considerations were *not* evaluated since this is a non-food use registration, no tolerances are being established, and there are no proposed residential uses.

6. HAZARD CHARACTERIZATION

Novaluron (Rimon technical) is a new insecticide proposed for use on containerized ornamental plants in greenhouses, shadehouses, and outdoor nurseries. The following guideline studies were submitted in support of this non-food use registration: 1) Acute Battery, 2) Developmental Toxicity Study in the Rat, 3) 90-Day Feeding Study in the rat, 4) Acute Neurotoxicity Study in the Rat, 5) 28-Day Dermal Toxicity Study in the Rat, and 6) Mutagenicity Studies (see Section 4). These studies were considered to be acceptable, with the exception of the acute neurotoxicity study which was considered to be unacceptable (See Data Gaps, Section 7).

The acute toxicity data for novaluron show that this chemical is not acutely toxic by the oral, dermal, or inhalation routes of exposure (Toxicity Categories III and IV). It is not irritating to the eyes or skin (Toxicity Category IV) and it is not a dermal sensitizer.

A subchronic rat study showed that the hematopoietic system is the primary target of toxicity. In the 90-day oral toxicity study in rats, the effects included increased methemoglobin, increased reticulocytes, decreased hemoglobin, decreased erythrocytes, increased mean corpuscular volume, increased absolute/relative spleen weights, and spleen histopathology (minimal to moderate extramedullary erythropoiesis, slight to moderate increased hemosiderosis). Novaluron is also neurotoxic. Acute neurotoxicity effects observed in the acute oral neurotoxicity study included clinical signs (piloerection, fast/irregular respiration), FOB parameters (increased head swaying, abnormal gait), and neuropathology (sciatic and tibial nerve degeneration).

No systemic effects were noted up to the limit dose of 1000 mg/kg/day in the 28-day dermal toxicity study in the rat. No maternal or developmental toxicity was noted in the developmental rat study tested up to the limit dose of 1000 mg/kg/day. Based on the available studies, there is no concern for mutagenicity.

7. DATA GAPS

The following data gaps have been identified for novaluron:

a. *90-Day Inhalation:* A 90-day inhalation toxicity study in the rat is required for further characterization of inhalation risk assessments. Due to the potential for inhalation exposure, there is concern for toxicity by the inhalation route. The 90-day inhalation toxicity study would give a dose and endpoint examined via the

route of exposure of concern (i.e., route specific study) and thus, would avoid using an oral study and route-to-route extrapolation).

b. *An acceptable acute neurotoxicity study*: The acute neurotoxicity study was classified as Unacceptable/Guideline since histopathology was not performed on the low- and mid-dose groups. The guidelines state that if neurological alterations are observed in samples from the high dose group, samples from the intermediate and low dose groups are examined sequentially. This is critical since neuropathology findings (sciatic and tibial nerve degeneration) at the high dose were seen in this study.

c. *A subchronic oral neurotoxicity study:* A subchronic oral neurotoxicity study is required based on the effects seen in the acute oral neurotoxicity study. The effects in the acute neurotoxicity study included clinical signs (piloerection, fast/irregular respiration), FOB parameters (increased head swaying, abnormal gait), and neuropathology (sciatic and tibial nerve degeneration) seen at the LOAEL of 2000 mg/kg/day.

d. *Two mutagenicity studies*: 1) an *in vitro* mammalian cell gene mutation assay and 2) an *in vivo* cytogenetics assay (i.e., micronucleus assay)

8. ACUTE TOXICITY

Acute Toxicity Profile for NOVALURON Technical

GDLN	Study Type	MRID	Results	Tox Category
870.1100	Acute Oral - rat	44961001	LD_{50} >5000 mg/kg (males and females)	IV
870.1200	Acute Dermal - rat	45003201	LD_{50} >2000 mg/kg	III
870.1300	Acute Inhalation - rat	45003202	LC_{50} >5.15 mg/L (males and females)	IV
870.2400	Primary Eye Irritation - rabbit	45003203	Not an ocular irritant	IV
870.2500	Primary Skin Irritation - rabbit	45003204	Not a dermal irritant	IV
870.2600	Dermal Sensitization - guinea pig	45084001	Not a dermal sensitizer	

9. SUMMARY OF TOXICOLOGY ENDPOINT SELECTION

The doses and toxicological endpoints selected for various exposure scenarios are summarized below.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	Not applicable	Not applicable	Not applicable
	An acute RfD was not established since the proposed registration is for a non-food use.		
Chronic Dietary	Not applicable	Not applicable	Not applicable
	A chronic RfD was not established since the proposed registration is for a non-food use.		
Incidental Oral, Short- and Intermediate-Term	NOAEL= 8.3 mg/kg/day	Alterations in hematological parameters (increased methemoglobin, increased reticulocytes, decreased hemoglobin, decreased erythrocytes, increased mean corpuscular volume), increased absolute/relative spleen weights, and spleen histopathology (minimal to moderate extramedullary erythropoiesis, slight to moderate increased hemosiderosis) seen at the LOAEL of 818.5 mg/kg/day.	90-Day Oral Toxicity Study in the Rat
Dermal, Short- and Intermediate-Term	Not applicable	No hazard via the dermal route was identified and, therefore, risk quantification is not required. No systemic effects were noted up to the limit dose of 1000 mg/kg/day in the 28-day dermal toxicity study in the rat.	Not applicable
Dermal, Long-Term	Not applicable	The current use pattern does not indicate a long-term exposure scenario.	Not applicable

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Inhalation[a], Short- and Intermediate-Term	NOAEL= 8.3 mg/kg/day MOE = 100	Alterations in hematological parameters (increased methemoglobin, increased reticulocytes, decreased hemoglobin, decreased erythrocytes, increased mean corpuscular volume), increased absolute/relative spleen weights, and spleen histopathology (minimal to moderate extramedullary erythropoiesis, slight to moderate increased hemosiderosis) seen at the LOAEL of 818.5 mg/kg/day.	90-Day Oral Toxicity Study in the Rat
Inhalation, Long-Term	Not applicable	The current use pattern does not indicate a long-term exposure scenario.	Not applicable

[a]An inhalation absorption factor of 100% should be used for route-to-route extrapolation.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460-0001

OFFICE OF
PESTICIDE PROGRAMS

August 27, 2001

Robert C. Everich, Ph.D.
Senior Scientist
Makhteshim Agan of North America
551 Fifth Avenue, Suite: 1100
New York, NY 10176

Subject: EPA File Symbol 11678-LT
Novaluron Technical
Submission of Eco-tox Studies
Your Letter dated August 6, 2001

Dear Dr. Everich:

Your submission referred to above was reviewed by the Agency for formatting requirements per PR Notice 86-5. Those studies that met the requirements were assigned Master Record Identification (MRID) numbers and those that did not, were rejected. The attached letter lists the MRID numbers for the accepted studies and provides the deficiencies for the rejected studies.

The rejected studies are available for pick up if you wish. Further consideration will be given to your submission upon receipt of acceptable studies after addressing the deficiencies. Should you have any questions, do not hesitate to contact me at 703-605-0368.

Sincerely,

S. Oonnithan, Entomologist
Insecticide Rodenticide Branch
Registration Division (7505C)

Encl.

AUG 21 2001

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

MAKHTESHIM CHEMICAL WORKS, LTD
C/O MAKHTESHIM-AGAN OF N.A.INC
551 FIFTH AVE, SUITE 1100
NEW YORK, NY 10176

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 08/14/01. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your data submittal was found to be partially in compliance with the standards for submission of data contained in PR Notice 86-5, with the exceptions noted below. A copy of your transmittal bibliography is enclosed, annotated with the Master Record ID's (MRIDs) assigned to each document accepted. Please use these numbers in all future references to these documents. If deficiencies were found which apply to individual accepted studies, they are listed below following the applicable MRID. Any document which has been assigned a MRID has been accepted under PR Notice 86-5. If any comments related to a MRID appear on this report, they are provided for your information and reference when preparing future submissions. Some individual documents were not acceptable, and all copies are being returned to you for correction for the reasons indicated below. These rejected studies have been assigned separate identification numbers which are annotated on both the enclosed bibliography and the rejected document labels. The rejected studies and their deficiencies are described below.

Rejected study [01] :

* Your Statement of No Data Confidentiality Claims is contradicted by the marking(s) on page(s) 31 + 43 of the study. If you do not intend to make Supplemental Claims of Data Confidentiality you can explicitly override these markings when you resubmit this study.

EPA's Good Laboratory Practice (GLP) regulation requires a 40 CFR 160.12 submission of a true and correct statement of compliance or non-compliance with the GLP requirements. An acceptable statement must address directly the study's compliance or non-compliance with the GLP regulation, without any

disclaimers, and must describe the study submitted, not the level of knowledge, understanding or belief of those who sign the statement. Qualifiers or disclaimers such as "based on someone else's signed statement," or "in the absence of any knowledge to the contrary," or "to the best of the signer's knowledge and belief" are unacceptable.

The GLP compliance statement provided in this study contains unacceptable language of the kind described above. You must eliminate the unacceptable language from the statement of GLP compliance or non-compliance before we can accept this study for further processing.

Rejected study [03] :

* Your Statement of No Data Confidentiality Claims is contradicted by the marking(s) on page(s) 31 of the study. If you do not intend to make Supplemental Claims of Data Confidentiality you can explicitly override these markings when you resubmit this study.

EPA's Good Laboratory Practice (GLP) regulation requires a 40 CFR 160.12 submission of a true and correct statement of compliance or non-compliance with the GLP requirements. An acceptable statement must address directly the study's compliance or non-compliance with the GLP regulation, without any disclaimers, and must describe the study submitted, not the level of knowledge, understanding or belief of those who sign the statement. Qualifiers or disclaimers such as "based on someone else's signed statement," or "in the absence of any knowledge to the contrary," or "to the best of the signer's knowledge and belief" are unacceptable.

The GLP compliance statement provided in this study contains unacceptable language of the kind described above. You must eliminate the unacceptable language from the statement of GLP compliance or non-compliance before we can accept this study for further processing.

Rejected study [04] :

* Your Statement of No Data Confidentiality Claims is contradicted by the marking(s) on page(s) 31 + 44 of the study. If you do not intend to make Supplemental Claims of Data Confidentiality you can explicitly override these markings when you resubmit this study.

EPA's Good Laboratory Practice (GLP) regulation

requires a 40 CFR 160.12 submission of a true and correct statement of compliance or non-compliance with the GLP requirements. An acceptable statement must address directly the study's compliance or non-compliance with the GLP regulation, without any disclaimers, and must describe the study submitted, not the level of knowledge, understanding or belief of those who sign the statement. Qualifiers or disclaimers such as "based on someone else's signed statement," or "in the absence of any knowledge to the contrary," or "to the best of the signer's knowledge and belief" are unacceptable.

The GLP compliance statement provided in this study contains unacceptable language of the kind described above. You must eliminate the unacceptable language from the statement of GLP compliance or non-compliance before we can accept this study for further processing.

Rejected study [05] :

EPA's Good Laboratory Practice (GLP) regulation requires a 40 CFR 160.12 submission of a true and correct statement of compliance or non-compliance with the GLP requirements. An acceptable statement must address directly the study's compliance or non-compliance with the GLP regulation, without any disclaimers, and must describe the study submitted, not the level of knowledge, understanding or belief of those who sign the statement. Qualifiers or disclaimers such as "based on someone else's signed statement," or "in the absence of any knowledge to the contrary," or "to the best of the signer's knowledge and belief" are unacceptable.

The GLP compliance statement provided in this study contains unacceptable language of the kind described above. You must eliminate the unacceptable language from the statement of GLP compliance or non-compliance before we can accept this study for further processing.

Rejected study [06] :

EPA's Good Laboratory Practice (GLP) regulation requires a 40 CFR 160.12 submission of a true and correct statement of compliance or non-compliance with the GLP requirements. An acceptable statement must address directly the study's compliance or non-compliance with the GLP regulation, without any disclaimers, and must describe the study submitted, not the level of knowledge, understanding or belief of those who sign the statement. Qualifiers or disclaimers such as "based on someone else's signed statement," or

"in the absence of any knowledge to the contrary," or "to the best of the signer's knowledge and belief" are unacceptable.

The GLP compliance statement provided in this study contains unacceptable language of the kind described above. You must eliminate the unacceptable language from the statement of GLP compliance or non-compliance before we can accept this study for further processing.

Rejected study [07] :

* Your Statement of No Data Confidentiality Claims is contradicted by the marking(s) on page(s) 33 of the study. If you do not intend to make Supplemental Claims of Data Confidentiality you can explicitly override these markings when you resubmit this study.

Rejected study [09] :

* Your Statement of No Data Confidentiality Claims is contradicted by the marking(s) on page(s) 31 of the study. If you do not intend to make Supplemental Claims of Data Confidentiality you can explicitly override these markings when you resubmit this study.

MAKHTESHIM
A G A N
of
North America
Inc.

454768-00

August 6, 2001

Document Processing Desk (APPL)
Office of Pesticide Programs (7504C)
USEPA
1921 Jefferson Davis Highway
CM2, Room 266A
Arlington, VA 22202

Attn: Dr. S. Oonnithan
Phone: 703-605-0368

Re: Request for Conditional Registration and Submission of Additional Eco-tox Studies in support of Novaluron Technical Insecticide: Ornamentals Use, EPA File Symbol 11678-LT

Dear Oonni:

Makhteshim Chemical Works, Ltd (MCW) c/o Makhteshim-Agan of North America, Inc. (MANA) submits the enclosed ecological effects data to support the above registration.

Novaluron technical and two formulations are currently in Reduced Risk review for registration on ornamentals and scheduled for a decision within the next few weeks. The submitted labels specify "***for use in greenhouses, shadehouses and containerized ornamentals in outdoor nurseries***." This is the full use pattern that was proposed to the Agency in a pre-registration meeting, the associated Reduced Risk Petition and all subsequent communication with the Agency regarding this ornamentals registration.

It is our understanding that the Agency is hesitant to grant registration for the proposed uses and prefers to restrict the label to "*use in greenhouses only*" due to the absence of ecological effects data.

MCW is happy to supply the data for your consideration and review, however, we request that a conditional registration be issued for the full use pattern as specified in the original submission. The following points provide ample justification for approval of a conditional registration as outlined in 40 CFR § 152.114 a -e:

1. All other required test data and materials have been submitted to the Agency and have been found acceptable (40 CFR § 152.114 (b), CFR § 152.112 (a), (b), (d), (f).

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

2. The submitted studies are listed as conditionally required in 40 CFR part 158 for non-terrestrial uses on ornamentals.

3. The registrant provided a full data matrix to EPA in the Reduced Risk Petition for this use (November 19, 1999), which did not include <u>any</u> ecological effects data. The petition received a unanimous vote of approval from the committee. The designation of novaluron as a Reduced Risk Pesticide fulfills 40 CFR § 152.114 (e), "*The registration of the pesticide product and its subsequent use during the period of the conditional registration are in the public interest.*"

4. In a pre-registration meeting (October 28, 1999, minutes attached), the proposed data matrix for submission was presented and discussed. At the meeting, the Agency recommended additional studies to satisfy certain data requirements that are listed as "CR." These studies were added to the package and submitted to the Agency.

5. In the same pre-registration meeting, Branch Chief, Tina Levine stated, "*Sometime you will need to address the ecotox/environmental risk, but because of the use pattern [for greenhouse use] it would not be an issue.*"

6. A full ecological effects database is available for novaluron and has been available since our pre-registration meeting in 1999. The registrant has always been willing to answer reviewer questions and submit additional data when requested. The request for these studies was received on August 2, 2001. The registrant does not require any time to develop these data and complies with the Agency request with this submission (less than 10 days later) (40 CFR § 152.114 (a),(b)).

7. To mitigate reviewer concerns about ecological exposure, MANA proposed adding precautionary language to the end-use labels restricting the type of application equipment that could be used and directing the user to minimize off-site drift and movement to non-target areas thereby mitigating the risk of ecological effects (attached, e-mail D. Spatz, 8/2/01). The registrant maintains that the use pattern, which allows application *only to containerized ornamentals*, coupled with the risk mitigation language we propose, is sufficiently restrictive to enable the Agency to grant the use of the pesticide during the period of conditional registration without the risk of unreasonable adverse effects on the environment (CFR § 152.114 (d), CFR § 152.112 (e).

We respectfully request that the Agency grant a conditional registration as scheduled for the full labeled use and review the attached studies as soon as possible.

Included in this submission are:

- Application for Pesticide Registration (EPA 8570-1)
- List of Submitted Studies
- Transmittal document

Additionally, three (3) copies of each ecological effects study requested are enclosed. These studies have been formatted to comply with PR Notice 86-5.

Should you have questions about this application, please contact me at (212) 896-4945

Sincerely,

Robert C. Everich, Ph.D.
Senior Scientist

Enclosures:

1) Pre-application meeting notes (10/28/99)
2) e-mail, R. Everich to D. Spatz, 8/2/01

CC: E. Gur (MANA) A. Stout (MANA)
H. Lahav (MCW) J. Ball (UCC)

TRANSMITTAL DOCUMENT FOR ADDITIONAL REQUESTED STUDIES
NOVALURON TECHNICAL INSECTICIDE

Submitter:
Makhteshim Chemical Works Ltd.
Beer-Sheva, ISRAEL
C/o
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

Regulatory action/reason for submission:
Additional Studies Requested by Agency
EPA Company No. 11678, File Symbol 11678-LT

Transmittal date:
August 6, 2001

Company official:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Company name:
Makhteshim Chemical Works, Ltd.

Company contact:
Robert C. Everich, Ph.D.
Senior Scientist
(212) 896-4945

Robert C. Everich, Ph.D.

List of Submitted Studies:

MRID	Guideline	Author	Date	Title	Data Owner
Reject(01)	850.2100	Hakin, B., Norman, A. J., Anderson, A., Dawe, I. S.	1989a	The acute oral toxicity (LD_{50}) of GR 572 Technical to the Mallard Duck Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 68/89647 Makhteshim Chemical Works Ltd., Report No. R-8764	MCW
45476801	850.2100	Rodgers, M. H.	1998a	"Rimon" technical - Acute oral toxicity (LD_{50}) to the Bobwhite quail (*Colinus virginianus*) Huntingdon Life Sciences Ltd., UK, Report No. MAK 410/972113 Makhteshim Chemical Works Ltd., Report No. R-9416	MCW
Reject(03)	850.2200	Hakin, B., Rodgers, M., Norman, A. J., Anderson, A., Dawe, I. S.	1989c	The dietary toxicity (LC_{50}) of GR 572 to the Bobwhite quail Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 69/89126 Makhteshim Chemical Works Ltd., Report No. R-8763	MCW
Reject(04)	850.2200	Hakin, B., Rodgers, M., Norman, A. J., Anderson, A., Dawe, I. S.	1989b	The dietary toxicity (LC_{50}) of GR 572 to the Mallard Duck Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 67/89125 Makhteshim Chemical Works Ltd., Report No. R-8765	MCW
Reject(05)	850.1075	Douglas, M. T., Bell, G., MacDonald, I. A.	1989b	The acute toxicity of GR 572 Technical to Rainbow trout (*Salmo gairdneri*) Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 6 1(c)/891282 Makhteshim Chemical Works Ltd., Report No. R-8762	MCW

MRID	Guideline	Author	Date	Title	Data Owner
Reject (06)	850.1075	Douglas, M. T., Sewell, I. G., MacDonald, I. A.	1989a	The acute toxicity of GR 572 Technical to Bluegill sunfish (*Lepomis macrochirus)* Huntingdon Life Sciences Ltd., UK (formerly known as Huntingdon Research Centre), Report No. AGR 63(d)/89960 Makhteshim Chemical Works Ltd., Report No. R-8761	MCW
Reject (07)	850.1075	Jenkins, C. A.	1999a	275-352 I: Acute toxicity to Rainbow trout Huntingdon Life Sciences Ltd., UK, Report No. MAK525/992450 Makhteshim Chemical Works Ltd., Report No. R-10635	MCW
45476802	850.1010	Jenkins, C. A.	1997	"Rimon" technical: Acute toxicity to the *Daphnia magna* Huntingdon Life Sciences Ltd., UK, Report No. MAK 404/970470 Makhteshim Chemical Works Ltd., Report No. R-9340	MCW
Reject (09)	850.1010	Jenkins, C. A.	1999b	275-352 I: Acute toxicity to *Daphnia magna* Huntingdon Life Sciences Ltd., UK, Report No. MAK526/992451 Makhteshim Chemical Works Ltd., Report No. R-10636	MCW

Please read instructions on reverse before completing form. Form Approved. OMB No. 2070-0060. Approval expires 2-28-95

EPA

United States
Environmental Protection Agency
Washington, DC 20460

- [x] Registration
- [ ] Amendment
- [x] Other

OPP Identifier Number

Application for Pesticide - Section I

1. Company/Product Number 11678-LT	2. EPA Product Manager Oonnithan	3. Proposed Classification ☐ None ☐ Restricted
4. Company/Product (Name) Novaluron Technical Insecticide	PM#	
5. Name and Address of Applicant *(Include ZIP Code)* Makhteshim Chemical Works Ltd. c/o Makhteshim-Agan of North America, Inc. 551 Fifth Avenue, Suite 1100, NY, NY 10176 ☐ *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.
- [x] Resubmission in response to Agency letter dated _____
- [ ] Notification - Explain below.
- [ ] Final printed labels in repsonse to Agency letter dated _____
- [ ] "Me Too" Application.
- [x] Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Requested ecological effects data

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	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☐ 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)
Robert C. Everich, Ph.D.	Senior Scientist	212 896-4945

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 knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

2. Signature	3. Title Senior Scientist	6. Date Application Received (Stamped)
4. Typed Name Robert C. Everich, Ph.D.	5. Date 8/9/01	

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

Rimon ®/novaluron Pre-application Meeting

DRAFT

A meeting was held with EPA on October 28, 1999 to introduce the Agency to novaluron.

The following people were present:
EPA: Ms Tina Levine, Rita Kumar, and S.(Oonni) Oonnithan
Makhteshim-Agan of NA(MANA): Andy Eimanis and Rob Everich
Uniroyal: Will Cummings

The meeting was well received and achieved the intended purpose. The meeting lasted approximately 1 ½ hours.

Andy and Rob presented an overview of novaluron; discussed the greenhouse non-food use application; the studies being submitted; the EPA review process; and the upcoming Reduced Risk document. The presentation closely followed the prepared handout that MANA distributed at the meeting.

Uniroyal was identified as a development partner and marketing arm for the US. The agreement will be signed in the near future.

The first issue that Tina Levine addressed was the toxicology database that is being submitted. Tina felt that to fully address the applicator exposure in a greenhouse situation, additional studies are needed. These would include a 90-day dermal and developmental study. Andy mentioned that the 40CFR158 data requirements did not list them as "R" or Required. Tina agreed that they were somewhat confusing but that you had to refer to the footnotes for each "CR" [conditionally required] . For example, the 90-day dermal *"is required if use involves purposeful dermal application to , or prolonged exposure of human skin."* We also pointed out that Allan Dixon had told us to only submit what is required for the Reduced Risk submission.

Tina mentioned that the Reduced Risk (RR) panel makes "specific" decisions for specific uses. She believes it has "good potential" for RR.
"IGR's are less toxic than conventional pesticides".
"Sometime you will need to address the ecotox/environmental risk, but because of the use pattern [for greenhouse use], it would not be an issue."

Even if it doesn't get RR if it is MANA's #1 priority (#11) then there is a good chance it might still make an 18 month review cycle. Even though there may be other RR chemicals that have the same use pattern, Tina mentioned the "essentiality' clause of FIFRA and it is to the EPA's benefit to have a lot of RR chemicals in the market place.

MANA wondered if they should meet with agency reviewers prior to the RR meeting. Tina recommended waiting because there might be different reviewers assigned to it later and it would be premature at this time.

MANA inquired whom they should call regarding future test protocols. Is it ok to contact reviewers? She recommended that e-mail be used.

MANA's Submission and Follow Up plans:
-Submit the registration application – (done on 10-28-99)
-Submit additional tox studies Tina requested.
-Complete RR package for UCC review. UCC to spend 1 wk review and supply comments to MANA.
-Schedule a joint MANA/UCC meeting and perhaps rehearse RR defense.
-Submit RR request to EPA – November 17th
-Meet with EPA for RR defense 30 days later.

MANA8

Robert Everich

From: Robert Everich
Sent: Thursday, August 02, 2001 2:35 PM
To: 'spatz.dana@epa.gov'
Cc: Judy Ball Ball (E-mail); Kevin Donovan Donovan (E-mail); Oonnithan.Suku@epamail.epa.gov Oonnithan (E-mail); Annie Stout2; James Whitehead2; Andy Eimanis
Subject: Novaluron Ornamentals Label Language.

Dear Dana:

I would like to propose the following paragraph to be added to our novaluron 10 EC and 10 SC labels for ornamentals. The objective is to minimize off-site drift and movement to non-target areas thereby mitigating the risk of ecological effects and environmental exposure. By adding this language it is my hope that the agency will grant a conditional registration for the use of novaluron on ornamentals as specified on the label:

"For Control of Insect Pests on Container Grown Ornamentals in Greenhouses, Shadehouses, and Outdoor Nurseries."

The eco-tox studies we discussed; Acute and Dietary Avian Toxicity, Acute Fish Toxicity and Acute Aquatic Invertebrate Toxicity will be submitted immediately. Following submission and Agency review of these studies, we would like to revisit this issue and delete this paragraph if it is determined to be unnecessary.

(to be added under "General Information")

Application Instructions: Apply by compressed air, hydraulic, hand-held or ground boom sprayers. Do not apply with high volume airblast sprayers or by aircraft. Minimize drift and movement to non-target areas by directing spray to foliage.

Let me know if this is satisfactory.

Best Wishes,

Rob Everich

[Federal Register: April 4, 2001 (Volume 66, Number 65)]
[Notices]
[Page 17882-17883]
From the Federal Register Online via GPO Access [wais.access.gpo.gov]
[DOCID:fr04ap01-63]

ENVIRONMENTAL PROTECTION AGENCY

[OPP-30510; FRL-6771-8]

Pesticide Products; Registration Applications

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: This notice announces receipt of applications to register pesticide products containing new active ingredients not included in any previously registered products pursuant to the provisions of section 3(c)(4) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended.

DATES: Written comments, identified by the docket control number OPP-30510, must be received on or before May 4, 2001.

ADDRESSES: Comments may be submitted by mail, electronically, or in person. Please follow the detailed instructions for each method as provided in Unit I. of the SUPPLEMENTARY INFORMATION. To ensure proper receipt by EPA, it is imperative that you identify docket control number OPP-30510 in the subject line on the first page of your response.

FOR FURTHER INFORMATION CONTACT: Suku Oonnithan, Regulatory Action Leader, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460; telephone number: (703) 605-0368; e-mail address: oonnithan.suku@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. Potentially affected categories and entities may include, but are not limited to:

Categories	NAICS codes	Examples of potentially affected entities
Industry	111	Crop production
	112	Animal production
	311	Food manufacturing
	32532	Pesticide manufacturing

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 the table could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether or not this action might apply to certain entities. If you have questions regarding the applicability of this action to a particular entity, consult the person listed under FOR FURTHER INFORMATION CONTACT.

B. How Can I Get Additional Information, Including Copies of this Document and Other Related Documents?

1. Electronically. You may obtain electronic copies of this document, and certain other related documents that might be available electronically, from the EPA Internet Home Page at http://www.epa.gov/. To access this document, on the Home Page select ``Laws and Regulations,'' ``Regulations and Proposed Rules,'' and then look up the entry for this document under the ``Federal Register--Environmental Documents.'' You can also go directly to the Federal Register listings at http://www.epa.gov/fedrgstr/.

2. In person. The Agency has established an official record for this action under docket control number OPP-30510. The official record consists of the documents specifically referenced in this action, any public comments received during an applicable comment period, and other information related to this action, including any information claimed as confidential business

[[Page 17883]]

information (CBI). This official record includes the documents that are physically located in the docket, as well as the documents that are referenced in those documents. The public version of the official record does not include any information claimed as CBI. The public version of the official record, which includes printed, paper versions of any electronic comments submitted during an applicable comment period, is available for inspection in the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Hwy., Arlington, VA, from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The PIRIB telephone number is (703) 305-5805.

C. How and to Whom Do I Submit Comments?

You may submit comments through the mail, in person, or electronically. To ensure proper receipt by EPA, it is imperative that you identify docket control number OPP-30510 in the subject line on the first page of your response.

1. By mail. Submit your comments to: Public Information and Records Integrity Branch (PIRIB), Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460.

2. In person or by courier. Deliver your comments to: Public Information and Records Integrity Branch (PIRIB), Information Resources and Services Division (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, Rm. 119, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA. The PIRIB is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The PIRIB telephone number is (703) 305-5805.

3. Electronically. You may submit your comments electronically by e-mail to: opp-docket@epa.gov, or you can submit a computer disk as described above. Do not submit any information electronically that you consider to be CBI. Avoid the use of special characters and any form of encryption. Electronic submissions will be accepted in WordPerfect 6.1/8.0 or ASCII file format. All comments in electronic form must be

identified by docket control number OPP-30510. Electronic comments may also be **filed** online at many Federal Depository Libraries.

D. How Should I Handle CBI that I Want to Submit to the Agency?

Do not submit any information electronically that you consider to be CBI. You may claim information that you submit to EPA in response to this document as CBI by marking any part or all of that information as CBI. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2. In addition to one complete version of the comment that includes any 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 version of the official record. Information not marked confidential will be included in the public version of the official record without prior notice. If you have any questions about CBI or the procedures for claiming CBI, please consult the person identified under FOR FURTHER INFORMATION CONTACT.

E. What Should I Consider as I Prepare My Comments for EPA?

You may find the following suggestions helpful for preparing your comments:

1. Explain your views as clearly as possible.
2. Describe any assumptions that you used.
3. Provide copies of any technical information and/or data you used that support your views.
4. If you estimate potential burden or costs, explain how you arrived at the estimate that you provide.
5. Provide specific examples to illustrate your concerns.
6. Offer alternative ways to improve the registration activity.
7. Make sure to submit your comments by the deadline in this notice.
8. To ensure proper receipt by EPA, be sure to identify the docket control number assigned to this action in the subject line on the first page of your response. You may also provide the name, date, and Federal Register citation.

II. Registration Applications

EPA received applications as follows to register pesticide products containing an active ingredient not included in any previously registered products pursuant to the provisions of section 3(c)(4) of FIFRA. Notice of receipt of these applications does not imply a decision by the Agency on the applications.

Products Containing an Active Ingredient Not Included in Any Previously Registered Products

1. File symbol: 11678-LT. Applicant: Makhteshim Agan of North America Inc, 551 Fifth Avenue, Suite 1100, New York, NY 10176. Product name: Rimon Technical. Type of product: Insecticide. Active ingredient: Novaluron (1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)-phenyl]-3-(2,6-difluorobenzoyl)urea). Proposed classification/Use: For manufacturing of end-use product formulations.
2. File symbol: 66222-GL. Applicant: Makhteshim Agan of North America Inc, 551 Fifth Avenue, Suite 1100, New York, NY 10176. Product name: Rimon 10 EC. Type of product: Insecticide. Active ingredient: Novaluron. Proposed classification/Use: General. For the control of insect pests on container grown ornamentals in greenhouses, shade houses, and outdoor nurseries.

List of Subjects

Environmental protection, Pesticides and pest.

Dated: March 14, 2001.
James Jones,
Director, Registration Division, Office of Pesticide Programs.
[FR Doc. **01-8141 Filed** 4-3-**01**; 8:45 am]
BILLING CODE 6560-50-S

RIMON® TECHNICAL

(Novaluron)

For The Manufacture of Insecticides Only

	% BY WT.
ACTIVE INGREDIENT: Novaluron: 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	98.5%
INERT INGREDIENTS:	1.5%
Total	100.0%

CAUTION

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

STATEMENT OF PRACTICAL TREATMENT (FIRST AID)

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.
IF SWALLOWED: Call a doctor or get medical attention. Do not induce vomiting. Do not give anything by mouth to an unconscious person. Avoid alcohol.
IF IN EYES: Flush eyes with plenty of water. Call a physician if irritation persists.

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

Harmful if absorbed through skin. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters except in accordance with the requirements of a 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 treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. This pesticide is for the further manufacture of formulated insecticides only. Formulators using this product are responsible for obtaining EPA registration for their formulated products.

Only for formulation into a insecticide for the following uses:
(1) Ornamentals (greenhouse and outdoor)
(2) Uses for which USEPA has accepted the required data and/or citations of data that the formulator has submitted in support of registration; and
(3) Uses for experimental purposes that are in compliance with USEPA requirements.

STORAGE AND DISPOSAL

STORAGE: Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited.
PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of at an approved waste disposal facility.
CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If drum is contaminated and cannot be reused, dispose of in the same manner.

WARRANTY STATEMENT

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 but 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 instruction, or under abnormal conditions, or under conditions not reasonably foreseeable to seller, and buyer assumes the risk of any such use. Buyer assumes all risks of use, storage or handling of this material not in strict accordance with directions given herewith.

NET CONTENTS _____ POUNDS

Makhteshim Chemical Works, Ltd.
c/o Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

EPA Reg. No. 11678-xx
EPA Est. No. 11678-IS-1

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460-0001

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

November 27, 2000

Andy Eimanis
Manager of Regulatory Affairs
Makhteshim-Agan of N. America, Inc.
551 Fifth Ave, Suite: 1100
New York, NY 10176

Dear Mr. Eimanis:

Subject: EPA File Symbol 11678-LT
Rimon® Technical
New Product Registration
Your Letter dated December 8, 1999

The Agency has completed review of product chemistry data submitted towards the registration of the technical formulation containing novaluron insecticide. According to the review, all the product chemistry data requirements have been satisfied except for (i) oxidation and reduction, (ii) storage stability and (iii) corrosion characteristics. A copy of the Agency's review is enclosed for your records.

Further consideration will be given to your application upon receipt of the required data to satisfy the deficiencies addressed above. Should you have any questions, do not hesitate to contact me at 703-605-0368.

Sincerely yours,

S. Oonnithan, Ph.D.
Entomologist, IRB/RD (7505C)
Office of Pesticide Programs

Encl.

MAKHTESHIM
A G A N
of
North America
Inc.

452885-00

December 18, 2000

Ms.Tina Levine for Dr. Oonni Oonnithan
Insecticide-Rodenticide Branch
Registration Division (7505C)
USEPA
1921 Jefferson Davis Highway
2nd Floor, CM-2, Room 266A
Arlington, VA 22202
Phone: 703-305-5404

5-590873

Re: Submission of additional data
Application to register a new active ingredient
Rimon Technical, EPA File Symbol 11678-LT

Dear Dr. Oonnithan:

Enclosed is an additional study submitted in support of our application to register the referenced product.

In support of this request, the following administrative documents are attached:

- Application for Pesticide Registration (EPA Form 8570-1)
- PRN 86-5 Transmittal Document
- Three copies of study formatted per PRN 86-5

Should you have additional questions, please contact me at 901-861-4400.

Sincerely,

Anne Stout

Anne Stout
Registration Specialist
For Makhteshim-Agan

Enclosures

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

MAKHTESHIM
A G A N
of
North America
Inc.

TRANSMITTAL DOCUMENT FOR APPLICATION TO REGISTER RIMON® TECHNICAL

Submitter:
Makhteshim Chemical Works, Ltd.
Care of Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

Regulatory action/reason for submission:
Application for registration of a new active ingredient
EPA Company No. 11678
EPA File Symbol 11678-LT

Transmittal date:
December 18, 2000

List of submitted studies:
See below.

Company official:
Anne Stout
901-861-4400

Company name:
Makhteshim-Agan of North America, Inc.

Company contact:
Anne Stout
901-861-4400
Anne Stout

MRID #	Study Number	MCW #	Title	Data Requirement
45288501	MAK478/982 511	R-9411	Rimon Technical Toxicity Study by Dermal Administration to CD Rats for 4 Weeks, Final Report.	82-2

551 Fifth Avenue, Suite 1100, New York, NY 10176
Tel: 212-661-9800 Fax: 212-661-9038 / 9043

DEC 28 2000

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

MAKHTESHIM CHEMICAL WORKS, LTD
C/O MAKHTESHIM-AGAN OF N.A.INC
551 FIFTH AVE, SUITE 1100
NEW YORK, NY 10176

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 12/22/00. 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.

Please read instructions on reverse before completing form. Form Approved. 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 11678-LT	2. EPA Product Manager Oonnithan	3. Proposed Classification ☑ None ☐ Restricted
4. Company/Product (Name) Rimon Technical	PM# IRB	

5. Name and Address of Applicant *(Include ZIP Code)*
Makhteshim Chemical Works c/o MANA, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

☐ *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 _____
☐ Notification - Explain below.
☐ Final printed labels in repsonse to Agency letter dated _____
☐ "Me Too" Application.
☑ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)
SUBMISSION OF ADDITIONAL DATA

S-590873

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	4. Size(s) Retail Container	5. Location of Label Directions
☐ Label ☐ 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)
Anne Stout	Registration Specialist	901-861-4400

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 Anne Stout	3. Title Registration Specialist
4. Typed Name Anne Stout	5. Date 12-18-00

03 NOV 2000

SUBJECT: Product Chemistry Review of RIMON TECHNICAL

FROM: Bruce F. Kitchens, Chemist
Product Chemistry Team
Technical Review Branch/RD (7505C)

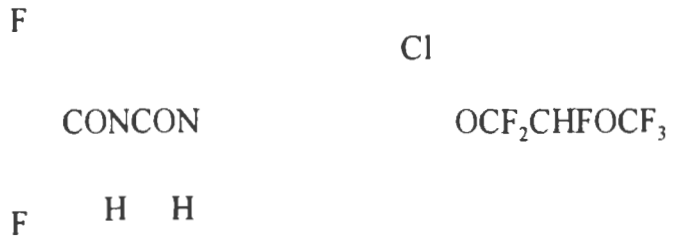
Bruce F. Kitchens
03 Nov 2000

TO: PM #04, Tina Levine/Suku Oonnithan
Insecticide-Rodenticide Branch/ RD (7505C)

DP BARCODE: D263780
EPA REG. NO.: 11678-LT
REGISTRANT: Makhteshim Chemical Works Ltd.
USE: Manufacturing Use Insecticide

INTRODUCTION:

The registrant, is requesting the registration of the technical grade of the active ingredient (TGAI), Rimon technical. The common name for this product is Novaluron. The active ingredient content of this product is 98.5%. Rimon technical is intended for the manufacture of insecticides. In support of this request, the registrant has submitted a Confidential Statement of Formula (CSF) dated 31 Aug 1999, a draft label, and product chemistry studies contained in MRID#s 449610-03 through 449610-07. The Technical Review Branch (TRB) has been asked to review this submission. Rimon has the following structure:



RIMON

SUMMARY OF FINDINGS:

1. The nominal concentration listed on the draft label and the CSF are the same.

2. The draft label contains the appropriate storage and disposal statements.

3. The certified limits as proposed on the CSF are acceptable.

CONCLUSION:

1. The basic formulation CSF dated 31 Aug 1999 is acceptable.

2. This submission meets the data requirements as specified in 40 CFR 158.155, 158.160, 158.165, 158.167, 158.175, and 158.180 with respect to product identity and composition, description of materials used to produce the product, description of formulation process, discussion of formation impurities, certified limits, and enforcement analytical method.

3. This submission also satisfies the data requirement as specified in 40 CFR 158.190 with respect to physical and chemical characteristics. The data requirements with respect to Oxidation/Reduction (830.6314), Storage Stability (830.6317), and Corrosion Characteristics (830-6320) remain outstanding.

REVIEW OF PRODUCT CHEMISTRY, OPPTS 830 SERIES

Chemical Name (IUPAC, ANSI, etc.)	1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea
Chemical Numbers (CAS; PC Code)	Reg. No.11678-LT CAS No. 116714-46-6 PC Code: 124002
Registration Symbol No.	11678-LT
Type of Product (T, FI, MP, EP)	98.5% Technical
DP Barcode	D263780
Reviewer	BKitchens

Makhteshim Chemical Works,Ltd. has submitted (1997 &1998; MRID#s 449610-03 through 449610-07) product chemistry data for evaluation.

Table 1: Manufacturing and Impurity Data for Rimon TGAI

GLN	Requirement	MRID	Status[1]	Details and/or Deficiency[2]
830.1550	Product Identity & Disclosure of Ingredients	449610-03	A	
830.1600 830.1620 830.1650	Starting Materials & Manufacturing Process	449610-03	A	
830.1670	Discussion of Impurities	449610-03	A	
830.1700	Preliminary Analysis	449610-04	A	The analysis was conducted on 3 batches. Method validation indicates that detector response is linear, the method is reproducible, and that good precision was achieved with the analytical method.
830.1750	Certification of Limits	449610-04	A	
830.1800	Analytical Methods	449610-04	A	

[1] A = Acceptable, N = Unacceptable (see Deficiency); N/A = Not Applicable
[2] Refer to CBI Appendix A for details

Table 2: Physical and Chemical Properties for the				
GLN	Requirement	MRID	Status[1]	Result[2] or Deficiency
830.6302	Color	449610-06	A	white
830.6303	Physical State	449610-05	A	solid @ 22°C
830.6304	Odor	449610-06	A	none detectable
830.6313	Stability	449610-05	A	Rimon technical is stable in contact with aluminium, iron zinc and their corresponding acetates, and at elevated temperatures when stored at 54°C for 14 days
830.6314	Oxidation/Reduction		G	None (EEC Method A.17)
830.6315	Flammability	449610-07	A	Technical is not flammable
830.6316	Explodability	449610-07	A	TGAI is not considered an explosive substance based on thermal and mechanical (shock and friction) sensitivity testing (EEC Method A.14)
830.6317	Storage Stability		G	
830.6319	Miscibility		N/A	The T is a solid at room temperature.
830.6320	Corrosion Characteristics		G	No physical changes observed in the commercial packaging (stainless steel cup and lid) following storage for 1 year at room temperature.
830.7000	pH	449610-05	A	6.5 (CIPAC MT 75)
830.7050	UV/Visible Absorption	449610-06	A	Molar absorption coefficients of PAI (99.5) at 3 maximum absorbances: 15,400 L/mol • cm at 253 µm (neutral) 9,780 L/mol • cm at 253 µm (acidic) 20,500 L/mol • cm at 263 µm (basic)
830.7100	Viscosity		N/A	The T is a solid at room temperature
830.7200	Melting Point/ Melting Range	449610-06	A	176.5 - 178.0°C (OECD Method No. 102, EEC Method A1)
830.7220	Boiling Point/ Boiling Range		N/A	TGAI is a solid at room temperature.
830.7300	Density/ Relative Density/ Bulk Density	449610-06	A	1.56 g/cm^3 at 22 C (OECD Method No. 109, EEC Method A3)
830.7370	Dissociation Constant in Water	449610-06	A	Dissociation constant of PAI not investigated due the low water solubility. (OECD Method No. 112)
830.7550 830.7560 830.7570	Partition Coefficient (Octanol/Water)	449610-06	A	log P_{ow} = 4.3 at 25 C (99.7% PAI, OECD Method No. 107, shake-flask)
830.7840 830.7860	Solubility	449610-05 449610-06	A	<u>Solubility at 25 C</u> 8.39 mg/L in n-heptane 1.88 g/L in xylene 2.85 in 1,2-dichloroethane 14.5 g/L in methanol 198 g/L in acetone 113 g/L in ethyl acetate 0.98 g/L in n-octanol 3 ug/L in water (99.5% PAI, EPA 830.7840, shake-flask)

Table 2 Physical and Chemical Properties for the				
GLN	Requirement	MRID	Status[1]	Result[2] or Deficiency
830.7950	Vapor Pressure	449610-06	A	1.6 x 10 Pa at 25 C Henry's Law Constant = 2.0 x 10 Pa • m /mol (99.5% PAI, OECD Method No. 104, EEC Method A4, vapor pressure balance method)

A = Acceptable, N = Unacceptable (see Deficiency), N/A = Not applicable, G = Data Gap.
[2] For example, "brown" for 830.6302, "155° C" for 830.7200

ATTACHMENT: CONFIDENTIAL APPENDIX

Pages 380-393 – *Manufacturing process information may be entitled to confidential treatment*

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

FEB 18 200

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Mr. Andy Eimanis
Manager Regulatory Affairs
Makhteshim-Agan of North America
551 11th Avenue, Suite 1100
New York, NY 10176

Subject: Reduced Risk Decision for Novaluron for Use on Ornamentals in Greenhouses, Shade Houses, and Nurseries.

Dear Mr. Eimanis,

Thank you for your submission for the insecticide, novaluron, for use on ornamentals in greenhouses, shade houses, and nurseries. On February 1, 2000 the Reduced Risk Committee completed its review of the information in your reduced risk rationale and granted reduced risk status to novaluron for the above use. From the information provided in your rationale, novaluron appears to have a have a better human health profile than many competing compounds.

The approval of your request for reduced risk status was due in part to the limited exposure of the indoor, non-food use pattern. Please note, however, that if your company elects to pursue reduced risk status for any outdoor or food uses, additional information will need to be provided in the accompanying reduced risk rationale.

For a food use reduced risk application, the Committee would need to see more human toxicological information, such as abstracts and data summaries of relevant studies. Agency reviewers would be particularly interested in more detail on the studies and regarding the hematological effects of the test material.

Toxicologically, the mechanism is based around the formation of methemoglobinemia. Anemia, the formation of erythrocyte inclusions such as Heinz bodies and Howell -Jolly bodies have also been reported in multiple studies in rats, mice and dogs. The effects on red blood cells lead to effects on the spleen and the liver (splenomegaly or splenic enlargement, hemosiderin deposition). These effects were considered as compensatory or secondary in nature and according to your company, reversible in adult animals within four to eight weeks. No studies were conducted that assessed the possibility of sensitivity of erythrocyte fragility in juvenile vs adult animals. Although your company has stated that there was no indication of susceptibility in reproduction studies, there are no summaries that provide information on the parameters that were evaluated to make a determination of age-based sensitivity.

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In addition, the Committee would like to see more information on ecotoxicity and environmental fate, such as abstracts and data summaries of the studies required for an outdoor use pattern. The rationale should also include a more refined risk comparison between novaluron and the alternatives based on risk quotients — not one simply based on toxicity.

The reduced risk status of any chemical is an initial assessment. Should information warrant, the Agency may re-evaluate and possibly revoke your submission's reduced risk status. Also, should the Agency determine at any time that the data base for the chemical is unacceptable or incomplete, the Agency may stop the expedited process for the chemical until adequate data are submitted.

As a result of the decision to designate these uses as reduced risk, the Agency will begin working with its science divisions to schedule the data reviews and risk assessments needed for evaluating this chemical. The Agency has a goal of completing these evaluations in an expeditious manner. Tina Levine, chief of the Insecticide-Rodenticide Branch, and her staff will now handle all regulatory issues associated with this application. Tina can be reached at (703) 308-7055. Thank you for your interest in reduced risk pesticides. If you have any questions regarding the reduced risk pesticide program please feel free to contact Alan Dixon at (703) 305-7237.

Sincerely yours,

Rick Keigwin

Rick Keigwin, Chief
Registration Support Branch
Registration Division (7505C)

cc: Tina Levine
Suku Oonnithan

FEB 8 2000

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

MAKHTESHIM CHEMICAL WORKS, LTD
C/O MAKHTESHIM-AGAN OF N.A.INC
551 FIFTH AVE, SUITE 1100
NEW YORK, NY 10176

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 02/01/00. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your data submittal was found to be partially in compliance with the standards for submission of data contained in PR Notice 86-5, with the exceptions noted below. A copy of your transmittal bibliography is enclosed, annotated with the Master Record ID's (MRIDs) assigned to each document accepted. Please use these numbers in all future references to these documents. If deficiencies were found which apply to individual accepted studies, they are listed below following the applicable MRID. Any document which has been assigned a MRID has been accepted under PR Notice 86-5. If any comments related to a MRID appear on this report, they are provided for your information and reference when preparing future submissions. Some individual documents were not acceptable, and all copies are being returned to you for correction for the reasons indicated below. These rejected studies have been assigned separate identification numbers which are annotated on both the enclosed bibliography and the rejected document labels. The rejected studies and their deficiencies are described below.

Rejected study [01] :

* Your Statement of No Data Confidentiality Claims is contradicted by the marking(s) on page(s) 306 _____ of the study. If you do not intend to make Supplemental Claims of Data Confidentiality you can explicitly override these markings when you resubmit this study.

Rejected study [02] :

* Your Statement of No Data Confidentiality Claims is contradicted by the marking(s) on page(s) 80 _____ of the study. If you do not intend to make Supplemental

Claims of Data Confidentiality you can explicitly override these markings when you resubmit this study.

Makhteshim - Agan of North America Inc.
551 Fifth Ave, Suite 1100, New York, NY 10176
Telephone: 212-661-9800 Fax: 212-661-9038/9043

450300-00

MAKHTESHIM
A G A N
of
NORTH AMERICA

January 21, 2000

Via FedEx

Dr. S. Oonnithan
Product Manager (7505C)
US Environmental Protection Agency
Office of Pesticide Programs
Registration Division
1921 Jefferson Davis Highway, CM2
Arlington, VA 22202
Phone: 703-605-0368

Re: RIMON ® Technical Insecticide
Additional Toxicology Studies - Novaluron
EPA File Symbol: 11678-LT

Dear Oonni:

Makhteshim Chemical Works, Ltd. c/o Makhteshim-Agan of North America Inc, its US agent, submits the enclosed studies in support of our application for registration of novaluron technical (EPA File Symbol 11678-LT, submitted on 12 October 1999). These files are provided in response to your request (E-mail, S. Oonnithan to R. Everich, 13 Jan, 00) for additional toxicology studies based on the preliminary assessment of HED.

The studies have been formatted according to PR Notice 86-5 requirements. The complete application consists of the following:

- Copies of the Completed Application (EPA Form 8570-1)
- A PR 86-5 Study Transmittal Document
- Three Copies (3) of all 86-5 formatted data

We trust that you will find this application complete and should you have any questions, please feel free to contact me at (212) 896-4945.

Sincerely,
Makhteshim--Agan of North America Inc.

Anne Stant for

Robert C. Everich, Ph.D.
Senior Scientist

Enclosures

Makhteshim - Agan of North America Inc.
551 Fifth Ave, Suite 1100, New York, NY 10176
Telephone: 212-661-9800 Fax: 212-661-9038/9043

MAKHTESHIM
A G A N
of
NORTH AMERICA

TRANSMITTAL DOCUMENT FOR APPLICATION TO REGISTER RIMON® TECHNICAL

Submitter:
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

Regulatory action reason for submission:
Application for registration of a new active ingredient
Submission of additional data
EPA Company No. 11678
EPA File Symbol: 11678-LT

Transmittal date:
January 21, 2000

List of submitted studies:

MRID #	Study Number	MCW #	Title	Data Requirement/ Guideline Reference No.
Reject (01)	MAK 480/983207	R-9817	Rimon Technical: Neurotoxicity Study by a Single Oral Gavage Administration to CD Rats Followed by a 14-Day Observation Period	81-8
450300Ø1	MAK399/972 319	R-9338	Rimon Technical: Toxicity Study by Dietary Administration to CD Rats for 13 Weeks Followed by a 4 Week Reversibility Period	82-1
450300Ø2	AGR 59/881801	R-8760	Assessment of Unscheduled DNA Repair Synthesis in Mammalian Cells after Exposure to GR 572	84-2
450300Ø3	4240	R-8777	GR572 (FCF/T/46): Testing for Mutagenic Activity with *Salmonella typhimurium* TA 1535, TA 1537, TA 1538, TA 98, AND TA 100	84-2
Reject (02)	MAK422/973 446	R-9334	Rimon Technical: Study of Embryo-foetal Toxicity in the CD Rat by Oral Gavage Administration	83-3

Company official:
Andy Eimanis
Regulatory Manager
212-896-4930

Company name:
Makhteshim-Agan of North America, Inc.

Company contact:
Andy Eimanis
Manager, Regulatory Affairs
212-896-4930

Makhteshim - Agan of North America Inc.
551 Fifth Ave, Suite 1100, New York, NY 10176
Telephone: 212-661-9800 Fax: 212-661-9038/9043

MAKHTESHIM
A G A N
NORTH AMERICA

December 8, 1999

11678-LT
S-572656

Dr. S. (Oonni) Oonnithan
Insecticide-Rodenticide Branch
Registration Division (7505C)
OPP, USEPA
1921 Jefferson Davis Hwy
CM2, 2nd Floor
Arlington, VA 22202

Re: Resubmission of required study pages
Your letter dated December 1, 1999

Dear Dr. Oonnithan:

Enclosed are replacement pages for the four studies referenced in your letter of December 1, 1999. Three copies of each replacement page are attached; please refer to the notes on each page to identify which pages belong to each study.

Thank you for your help with this submission. I'm looking forward to working with you on Rimon and other insecticide projects.

Sincerely,

Anne Stout

Anne Stout
Registration Specialist

Enclosures

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460-0001

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

DEC - 1 1999

Andy Eimanis
Manager, Regulatory Affairs
Makhteshim-Agan of N. America, Inc.
551 Fifth Ave, Suite: 1100
New York, NY 10176

Dear Mr. Elmanis:

Subject: EPA File Symbol 11678-LT
Rimon® Technical
New Product Application
Submission dated October 28, 1999

Your submission referred to above was reviewed for formatting requirements per Pesticide Registration Notice 86-5. Studies that did comply were assigned MRID numbers and those that did not were rejected. The accepted and rejected studies were identified in the attached letter from the Agency. The letter also explains why the studies were rejected and what action to be taken to satisfy the deficiencies.

Please resubmit the required pages/studies to me at the earliest Further consideration will be given to your application only after you satisfy the deficiencies. Should you have any questions, do not hesitate to contact me at 703-605-0368 or at oonnithan.suku@epa.gov

Sincerely yours,

S. (Oonni) Oonnithan, Ph.D.
Insecticide Rodenticide Branch
Registration Division (7505C)
Office of Pesticide Programs

Encl.

NOV 9 1999

U.S. ENVIRONMENTAL PROTECTION AGENCY
Office of Pesticide Programs

MAKHTESHIM CHEMICAL WORKS, LTD
C/O MAKHTESHIM-AGAN OF N.A.INC
551 FIFTH AVE, SUITE 1100
NEW YORK, NY 10176

Report of Analysis for Compliance with PR Notice 86-5

Thank you for your transmittal of 11/02/99. Our staff has completed a preliminary analysis of the material. The results are provided as follows:

Your data submittal was found to be partially in compliance with the standards for submission of data contained in PR Notice 86-5, with the exceptions noted below. A copy of your transmittal bibliography is enclosed, annotated with the Master Record ID's (MRIDs) assigned to each document accepted. Please use these numbers in all future references to these documents. If deficiencies were found which apply to individual accepted studies, they are listed below following the applicable MRID. Any document which has been assigned a MRID has been accepted under PR Notice 86-5. If any comments related to a MRID appear on this report, they are provided for your information and reference when preparing future submissions. Some individual documents were not acceptable, and all copies are being returned to you for correction for the reasons indicated below. These rejected studies have been assigned separate identification numbers which are annotated on both the enclosed bibliography and the rejected document labels. The rejected studies and their deficiencies are described below.

Rejected study [01] :

EPA's Good Laboratory Practice (GLP) regulation requires a 40 CFR 160.12 submission of a true and correct statement of compliance or non-compliance with the GLP requirements. An acceptable statement must address directly the study's compliance or non-compliance with the GLP regulation, without any disclaimers, and must describe the study submitted, not the level of knowledge, understanding or belief of those who sign the statement. Qualifiers or disclaimers such as "based on someone else's signed statement," or "in the absence of any knowledge to the contrary," or "to the best of the signer's knowledge and belief" are unacceptable.

The GLP compliance statement provided in this study contains unacceptable language of the kind described above. You must eliminate the unacceptable language from the statement of GLP compliance or non-compliance before we can accept this study for further processing.

Rejected study [02] :

* Your Statement of No Data Confidentiality Claims is contradicted by the marking(s) on page(s) All Pages _____ of the study. If you do not intend to make Supplemental Claims of Data Confidentiality you can explicitly override these markings when you resubmit this study.

Rejected study [03] :

EPA's Good Laboratory Practice (GLP) regulation requires a 40 CFR 160.12 submission of a true and correct statement of compliance or non-compliance with the GLP requirements. An acceptable statement must address directly the study's compliance or non-compliance with the GLP regulation, without any disclaimers, and must describe the study submitted, not the level of knowledge, understanding or belief of those who sign the statement. Qualifiers or disclaimers such as "based on someone else's signed statement," or "in the absence of any knowledge to the contrary," or "to the best of the signer's knowledge and belief" are unacceptable.

The GLP compliance statement provided in this study contains unacceptable language of the kind described above. You must eliminate the unacceptable language from the statement of GLP compliance or non-compliance before we can accept this study for further processing.

Rejected study [04] :

EPA's Good Laboratory Practice (GLP) regulation requires a 40 CFR 160.12 submission of a true and correct statement of compliance or non-compliance with the GLP requirements. An acceptable statement must address directly the study's compliance or non-compliance with the GLP regulation, without any disclaimers, and must describe the study submitted, not the level of knowledge, understanding or belief of those who sign the statement. Qualifiers or disclaimers such as "based on someone else's signed statement," or "in the absence of any knowledge to the contrary," or "to the best of the signer's knowledge and belief" are unacceptable.

The GLP compliance statement provided in this study contains unacceptable language of the kind described above. You must eliminate the unacceptable language from the statement of GLP compliance or non-compliance before we can accept this study for further processing.

LIST OF SUBMITTED STUDIES

	MRID #	Study Number	MCW #	Title	Data Requirement/Guideline Reference No.
1.	✓ 44961001	3718	R-8775	GR 572 (FCF/T46): Acute Oral Toxicity (LD_{50}) in Rats	81-1
2.	Reject 01	881399D/A GR 60/AC	R-8776	Acute Dermal Toxicity To Rats of GR 572 Tech	81-2
3.	Reject 02	9099	R-8782	GR 572 Tech: Acute Inhalation Toxicity Study in Rats (Limit Test)	81-3
4.	Reject 03	881241D/A GR 62/SE	R-8766	Irritant Effects on the Rabbit Eye of GR 572 Tech	81-4
5.	Reject 04	881239D/A GR 61/SE	R-8767	Irritant Effects on the Rabbit Skin of GR 572 Tech	81-5
6.	✓ 44961002	920636	R-8783	Skin Sensitization Test in Guinea Pigs of the Test Article GR 572 Tech	81-6
7.	✓ 44961003		R-10523	Rimon (Novaluron) Product Chemistry Data	Series 61
8.	✓ 44961004	9175.008	R-9175	Rimon-Quantification of Active Ingredient and Impurities present at or above 0.1% in technical Rimon (FIFRA Guideline – Series 62)	Series 62
9.	✓ 44961005	MAK 465/972550	R-9897	Rimon Technical: Determination of the Physico-Chemical Properties	Series 830
10.	✓ 44961006	MAK 418/970332	R-9530	Rimon (Pure): Determination of the Physico-Chemical Properties	Series 830
11.	✓ 44961007	MAK 426/972350	R-9709	Rimon Technical: Determination of the Physico-Chemical Properties	Series 830
12.	✓ 44961008	MAK 445/973392	R-9703	^{14}C"Rimon": Hydrolysis Under Laboratory Conditions	161-1
13.	✓ 44961009	MAK 483/984569	R-10030	^{14}C"Rimon": Aerobic Soil Rate of Degradation	162-1
14.	✓ 44961010	MAK 446/974308	R-9415	^{14}C"Rimon": Aerobic Soil Metabolism (Pilot Study)	162-1
	✓ 44961011	MAK 472/974399	R-10005	^{14}C"Rimon": Soil Column Leaching	163-1
16.	✓ 44961012	MAK 424/973308	R-9667	^{14}C"Rimon": Adsorption/Desorption on Soil	163-1
17.	✓ 44961013	MAK 436/973183	R-9814	Rimon Technical: Bacterial Mutation Assay	84-2
18.	✓ 44961014	MAK 425/982353	R-9666	Rimon Technical: Bacterial DNA Repair (*REC*) Assay	84-2
19.	✓ 44961015	91/AMN001/0906	R-8780	In Vitro Assessment of the Clastogenic Activity of GR 572 in Cultured Human Lymphocytes	84-2

Makhteshim - Agan of North America Inc.
551 Fifth Ave. Suite 1100, New York, NY 10176
Telephone: 212-661-9800 Fax: 212-661-9038/9043

450032-00

MAKHTESHIM
A G A N
NORTH AMERICA

HAND DELIVERED

October 28, 1999

Ms. Tina Levine
Insecticide-Rodenticide Branch Chief
Registration Division (H7505) – (APPL)
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Re: RIMON ® Technical Insecticide
Application to Register a New Active Ingredient – Novaluron
Application No. 11678-

Dear Ms. Levine:

Makhteshim Chemical Works, Ltd. c o Makhteshim-Agan of North America Inc. its US Agent, "Makhteshim" is applying to register a new active ingredient- Novaluron. This active is a novel benzoyl-urea insect growth regulator for the control of whiteflies and thrips on ornamentals in commercial greenhouses.

The product is proprietary and all rights in this submission have been licensed to the Makhteshim organization. All data in support of this application are fully owned by Makhteshim or Isagro, Sp.A, Italy property for which a permission letter is enclosed. All data should be treated in the traditional Agency proprietary fashion.

As a generic supplier, this is the first application that Makhteshim has submitted to Registration Division seeking approval for a new active ingredient and requiring FY scheduling. The company has apprised the Agency of the need for EPA resources to process this application as early as 1995. This is the first active ingredient submitted to RD requiring HED and other scientific reviews in the history of our company. We therefore, are exercising our first full priority of the original five granted to participating registrants. We have been informed by EPA that this program was instituted to permit EPA efficient utilization of its resources. Makhteshim Chemical Works, LTD. (MCW) has scheduled annual meetings since 1995 to update the Agency of its registration priorities and we plan to continue this practice in the future.
We contend that Novaluron chemistry is a Safer Pesticide. A reduced risk petition is in final preparation and will be provided to the Agency's review committee within the next 30 – 60 days for their consideration. The Agency has been informed of our progress to make this submission and we continue to seek our slot within ongoing FY 2000 review

process. The approval of the Novaluron application will eliminate some greenhouse uses of organophosphates and oncogens. We are reserving this discussion for the reduced risk petition hearing where we plan to fully review the competitive products this active will displace. Under the standards imposed by FQPA, Novaluron is not known to be an endocrine disrupter and since no dietary exposure is likely from the proposed use, acute dietary and dietary assessments are not required. This product is not intended for use in residential settings. Since no food or food additive tolerance is required for this use pattern, no accompanying tolerance petition or waiver request is planned.

This active ingredient has low mammalian toxicity. It is not a genotoxin, oncogen nor does it influence human reproductive or developmental effects. It also is practically non-toxic to birds and does not affect adult beneficial insects. Our test results indicate it is ten times (10X) more active on whiteflies than currently registered products. This pest causes extensive damage to greenhouse ornamentals.

This application is for the control of whiteflies, thrips, leafminers, and other foliar feeding insects under the EPA defined use pattern know as "Greenhouse – Non-food." Section 158 of the 40 CFR lists the following data requirements for this use. :

GREENHOUSE NON-FOOD USE PATTERN SECTION 158 DATA REQUIREMENTS		
PRODUCT CHEMISTRY	Series 61 Series 62 Series 850	Product Composition Preliminary Analysis Physical Chemical Properties
TOXICOLOGY ACUTES	81-1 81-2 81-3 81-4 81-5 81-6	Acute oral toxicity rat Acute dermal toxicity Acute inhalation rat- waiver request Primary eye irritation Primary dermal irritation Dermal Sensitization
TOXICOLOGY MUTAGENICITY	84-2 84-2 84-4	Gene Mutation Structural Chromosomal Aberration Other genotoxic effects
ENVIRONMENTAL FATE	161-1 162-1 163-1	Hydrolysis Aerobic Soil Metabolism Leaching and adsorption desorption
DIRECTIONS FOR USE		Rimon 10EC End-use Product Draft Label

TRANSMITTAL DOCUMENT FOR
APPLICATION TO REGISTER RIMON® TECHNICAL

Submitter:
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

Regulatory action/reason for submission:
Application for registration of a new active ingredient
EPA Company No. 11678

Transmittal date:
October 12, 1999

List of submitted studies:
See page 2 of this transmittal document

Company official:
Andy Eimanis
Regulatory Manager
212-896-4920

Company name:
Makhteshim-Agan of North America, Inc.

Company contact:
Andy Eimanis
Manager, Regulatory Affairs
212-896-4930

Andy Elmanis

LIST OF SUBMITTED STUDIES

	MRID #	Study Number	MCW #	Title	Data Requirement/Guideline Reference No.
1.	44961001	3718	R-8775	GR 572 (FCF/T46): Acute Oral Toxicity (LD_{50}) in Rats	81-1
2.	45003201	881399D/A GR 50/AC	R-8776	Acute Dermal Toxicity To Rats of GR 572 Tech	81-2
3.	45003202	9099	R-8782	GR 572 Tech: Acute Inhalation Toxicity Study in Rats (Limit Test)	81-3
4.	45003203	881241D/A GR 62/SE	R-8766	Irritant Effects on the Rabbit Eye of GR 572 Tech	81-4
5.	45003204	881239D/A GR 61/SE	R-8767	Irritant Effects on the Rabbit Skin of GR 572 Tech	81-5
6.	44961002	920636	R-8783	Skin Sensitization Test in Guinea Pigs of the Test Article GR 572 Tech	81-6
7.	44961003		R-10523	Rimon (Novaluron) Product Chemistry Data	Series 61
8.	44961004	9175 008	R-9175	Rimon-Quantification of Active Ingredient and Impurities present at or above 0.1% in technical Rimon (FIFRA Guideline – Series 62)	Series 62
9.	44961005	MAK 465/972550	R-9697	Rimon Technical: Determination of the Physico-Chemical Properties	Series 830
10.	44961006	MAK 418/970332	R-9530	Rimon (Pure): Determination of the Physico-Chemical Properties	Series 830
11.	44961007	MAK 426/972350	R-9709	Rimon Technical: Determination of the Physico-Chemical Properties	Series 830
12.	44961008	MAK 445/973392	R-9703	"C"Rimon": Hydrolysis Under Laboratory Conditions	161-1
13.	44961009	MAK 483/984589	R-10030	"C"Rimon": Aerobic Soil Rate of Degradation	162-1
14.	44961010	MAK 448/974308	R-9415	"C"Rimon": Aerobic Soil Metabolism Pilot Study	162-1
15.	44961011	MAK 472/974399	R-10005	"C"Rimon": Soil Column Leaching	163-1
16.	44961012	MAK 424/973308	R-9697	"C"Rimon": Adsorption/Desorption on Soil	163-1
17.	44961013	MAK 436/973153	R-9814	Rimon Technical: Bacterial Mutation Assay	84-2
18.	44961014	MAK 425/973353	R-9656	Rimon Technical: Bacterial DNA Repair (REC) Assay	84-2
19.	44961015	91/AMN001/0905	R-8760	In Vitro Assessment of the Clastogenic Activity of GR 572 in Cultured Human Lymphocytes	84-2

Makhteshim - Agan of North America Inc.
551 Fifth Ave, Suite 1100, New York, NY 10176
Telephone: 212-661-9800 Fax: 212-661-9038/9043

449610-00

MAKHTESHIM
A G A N
of
NORTH AMERICA

HAND DELIVERED

5-571239

October 28, 1999

Ms. Tina Levine
Insecticide-Rodenticide Branch Chief
Registration Division (H7505) – (APPL)
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Re: RIMON ® Technical Insecticide
Application to Register a New Active Ingredient – Novaluron
Application No. 11678- LT

Dear Ms. Levine:

Makhteshim Chemical Works, Ltd. c/o Makhteshim-Agan of North America Inc, its US Agent, "Makhteshim" is applying to register a new active ingredient- Novaluron. This active is a novel benzoyl-urea insect growth regulator for the control of whiteflies and thrips on ornamentals in commercial greenhouses.

The product is proprietary and all rights in this submission have been licensed to the Makhteshim organization. All data in support of this application are fully owned by Makhteshim or Isagro, Sp.A, Italy property for which a permission letter is enclosed. All data should be treated in the traditional Agency proprietary fashion.

As a generic supplier, this is the first application that Makhteshim has submitted to Registration Division seeking approval for a new active ingredient and requiring FY scheduling. The company has apprised the Agency of the need for EPA resources to process this application as early as 1995. This is the first active ingredient submitted to RD requiring HED and other scientific reviews in the history of our company. We therefore, are exercising our first full priority of the original five granted to participating registrants. We have been informed by EPA that this program was instituted to permit EPA efficient utilization of its resources. Makhteshim Chemical Works, LTD. (MCW) has scheduled annual meetings since 1995 to update the Agency of its registration priorities and we plan to continue this practice in the future.
We contend that Novaluron chemistry is a Safer Pesticide. A reduced risk petition is in final preparation and will be provided to the Agency's review committee within the next 30 – 60 days for their consideration. The Agency has been informed of our progress to make this submission and we continue to seek our slot within ongoing FY 2000 review

process. The approval of the Novaluron application will eliminate some greenhouse uses of organophosphates and oncogens. We are reserving this discussion for the reduced risk petition hearing where we plan to fully review the competitive products this active will displace. Under the standards imposed by FQPA, Novaluron is not known to be an endocrine disrupter and since no dietary exposure is likely from the proposed use, acute dietary and dietary assessments are not required. This product is not intended for use in residential settings. Since no food or food additive tolerance is required for this use pattern, no accompanying tolerance petition or waiver request is planned.

This active ingredient has low mammalian toxicity. It is **not** a genotoxin, oncogen nor does it influence human reproductive or developmental effects. It also is practically non-toxic to birds and does not affect adult beneficial insects. Our test results indicate it is ten times (10X) more active on whiteflies than currently registered products. This pest causes extensive damage to greenhouse ornamentals.

This application is for the control of whiteflies, thrips, leafminers, and other foliar feeding insects under the EPA defined use pattern know as "Greenhouse – Non-food." Section 158 of the 40 CFR lists the following data requirements for this use. :

GREENHOUSE NON-FOOD USE PATTERN SECTION 158 DATA REQUIREMENTS		
PRODUCT CHEMISTRY	Series 61 Series 62 Series 850	Product Composition Preliminary Analysis Physical Chemical Properties
TOXICOLOGY ACUTES	81-1 81-2 81-3 81-4 81-5 81-6	Acute oral toxicity rat Acute dermal toxicity Acute inhalation rat- waiver request Primary eye irritation Primary dermal irritation Dermal Sensitization
TOXICOLOGY MUTAGENICITY	84-2 84-2 84-4	Gene Mutation Structural Chromosomal Aberration Other genotoxic effects
ENVIRONMENTAL FATE	161-1 162-1 163-1	Hydrolysis Aerobic Soil Metabolism Leaching and adsorption/desorption
DIRECTIONS FOR USE		Rimon 10EC End-use Product Draft Label

TRANSMITTAL DOCUMENT FOR
APPLICATION TO REGISTER RIMON® TECHNICAL

Submitter:
Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

Regulatory action/reason for submission:
Application for registration of a new active ingredient
EPA Company No. 11678

Transmittal date:
October 12, 1999

List of submitted studies:
See page 2 of this transmittal document

Company official:
Andy Eimanis
Regulatory Manager
212-896-4920

Company name:
Makhteshim-Agan of North America, Inc.

Company contact:
Andy Eimanis
Manager, Regulatory Affairs
212-896-4930

Andy Eimanis

LIST OF SUBMITTED STUDIES

	MRID #	Study Number	MCW #	Title	Data Requirement/Guideline Reference No.
1.	44961001	3718	R-8775	GR 572 (FCF/T46): Acute Oral Toxicity (LD_{50}) in Rats	81-1
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6.	44961002	920636	R-8783	Skin Sensitization Test in Guinea Pigs of the Test Article GR 572 Tech	81-6
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11.	44961007	MAK 426/972350	R-9709	Rimon Technical: Determination of the Physico-Chemical Properties	Series 830
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All Technical

Makhteshim - Agan of North America Inc.
551 Fifth Ave, Suite 1100, New York, NY 10176
Telephone: 212-661-9800 Fax: 212-661-9038/9043

EPA
10-28-99

MAKHTESHIM
A G A N
of
NORTH AMERICA

HAND DELIVERED

#124002

5-571239

D263747

October 28, 1999

Ms. Tina Levine
Insecticide-Rodenticide Branch Chief
Registration Division (H7505)
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

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ENVIRONMENTAL FATE	161-1 162-1 163-1	Hydrolysis Aerobic Soil Metabolism Leaching and adsorption/desorption
DIRECTIONS FOR USE		Rimon 10EC End-use Product Draft Label

The studies have been formatted according to PR notice 86-5 requirements.
The complete application consists of the following:

- Copies of the Completed Application (EPA Form 8570-1)
- Completed Confidential Statement of Formula (EPA Form 8570-4)
- Completed Copy of Certification with Respect to Citation of Data (EPA Form 8570-34)
- Five (5) Copies of Draft Technical Product Labeling.
- A PR 86-5 Study Transmittal Document
- Three Copies (3) of all 86-5 formatted data
- A courtesy copy of the Rimon 10 EC Draft labeling describing the "Directions For Use" is enclosed
- One copy of data summaries
- Data Matrix (EPA Form 8570-35)

Makhteshim will separately make an application for the end-use product, RIMON® 10EC. In addition to the remaining patent life of this product, we intend to assert exclusive use rights upon the granting of this registration. Should you have any questions, please feel free to contact me at (212) 896-4930.

Sincerely,
Makhteshim-Agan of North America Inc.

A. Eimanis
Manager of Regulatory Affairs

AE/cs

Enclosures

LIST OF SUBMITTED STUDIES

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14.	44961010	MAK 446/974308	R-9415	^{14}C"Rimon" Aerobic Soil Metabolism (Pilot Study)	162-1
15.	44961011	MAK 472/974399	R-10005	^{14}C"Rimon" Soil Column Leaching	163-1
16.	44961012	MAK 424/973308	R-9667	^{14}C"Rimon" Adsorption/Desorption on Soil	163-1
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18.	44961014	MAK 425/982353	R-9666	Rimon Technical: Bacterial DNA Repair (*REC*) Assay	84-2
19.	44961015	91/AMN001/0906	R-8780	In Vitro Assessment of the Clastogenic Activity of GR 572 in Cultured Human Lymphocytes	84-2

All Technical

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 activities 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 the 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 form to this address.

DATA MATRIX

Date 10-13-99

EPA Reg No./File Symbol 11678-~~xxx~~ L 7

Page 1 of 1

Applicant's/Registrant's Name & Address
Makhteshim Chemical Works c/o MANA Inc, 551 Fifth Avenue, Suite 1100, New York, NY 10176

Product
Rimon Technical

Ingredient novaluron

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
81-1	GR 572 (FCF/T46): Acute Oral Toxicity (LD_{50}) in Rats		Makhteshim-Agan of North America, Inc.	PER	
81-2	Acute Dermal Toxicity To Rats of GR 572 Tech		Makhteshim-Agan of North America, Inc.	PER	
81-3	GR 572 Tech: Acute Inhalation Toxicity Study in Rats (Limit Test)		Makhteshim-Agan of North America, Inc.	PER	
81-4	Irritant Effects on the Rabbit Eye of GR 572 Tech		Makhteshim-Agan of North America, Inc.	PER	
81-5	Irritant Effects on the Rabbit Skin of GR 572 Tech		Makhteshim-Agan of North America, Inc.	PER	
81-6	Skin Sensitization Test in Guinea Pigs of the Test Article GR 572 Tech		Makhteshim-Agan of North America, Inc.	PER	
Series 61	Rimon (Novaluron) Product Chemistry Data		Makhteshim-Agan of North America, Inc.	OWN	
Series 62	Rimon-Quantification of Active Ingredient and Impurities present at or above 0.1% in technical Rimon (FIFRA Guideline – Series 62)		Makhteshim-Agan of North America, Inc.	OWN	
Series 830	Rimon Technical: Determination of the Physico-Chemical Properties		Makhteshim-Agan of North America, Inc.	OWN	
Series 830	Rimon (Pure): Determination of the Physico-Chemical Properties		Makhteshim-Agan of North America, Inc.	OWN	
Series 830	Rimon Technical: Determination of the Physico-Chemical Properties		Makhteshim-Agan of North America, Inc.	OWN	
161-1	^{14}C"Rimon": Hydrolysis Under Laboratory Conditions		Makhteshim-Agan of North America, Inc.	OWN	
162-1	^{14}C"Rimon": Aerobic Soil Rate of Degradation		Makhteshim-Agan of North America, Inc.	OWN	
162-1	^{14}C"Rimon": Aerobic Soil Metabolism (Pilot Study)		Makhteshim-Agan of North America, Inc.	OWN	
163-1	^{14}C"Rimon": Soil Column Leaching		Makhteshim-Agan of North America, Inc.	OWN	
163-1	^{14}C"Rimon": Adsorption/Desorption on Soil		Makhteshim-Agan of North America, Inc.	OWN	
84-2	Rimon Technical: Bacterial Mutation Assay		Makhteshim-Agan of North America, Inc.	OWN	
84-2	Rimon Technical: Bacterial DNA Repair (*REC*) Assay		Makhteshim-Agan of North America, Inc.	OWN	
84-2	*In Vitro* Assessment of the Clastogenic Activity of GR 572 in Cultured Human Lymphocytes		Makhteshim-Agan of North America, Inc.	PER	

Signature

Name and Title
Andy Eimanis, Manager, Regulatory Affairs

Date
10-13-99

EPA Form 8570-35 (9-97) Electronic and Paper versions available. Submit only Paper version.

Agency Internal Use Copy

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
WASHINGTON, D.C. 20460

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Do not send the completed form to this address.

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number Makhteshim Chemical Works c/o MANA, Inc., 551 Fifth Ave, Ste 1100, New York, NY 10176 (212)89[illegible]	EPA Registration Number/File Symbol 11678-~~[illegible]~~ LT
Active Ingredient(s) and/or representative test compound(s) novaluron 493c	Date 10-13-99
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) greenhouse nonfood	Product Name Rimon Technical

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
A. Eimanis	10-13-99	Andy Eimanis, Manager, Regulatory Affairs

EPA Form 8570-34 (9-97) Electronic and Paper versions available. Submit only Paper version.

Please read instructions on reverse before completing form.

Form Approved. OMB No. 2070-0060. Approval expires 2-28-95

EPA

United States
Environmental Protection Agency
Washington, DC 20460

- [x] Registration
- [ ] Amendment
- [ ] Other

OPP Identifier Number: 267169

Application for Pesticide - Section I

1. Company/Product Number: 11678-~~xxx~~ LT	2. EPA Product Manager: ~~Marion Johnson~~ Tina Levine	3. Proposed Classification: [x] None [ ] Restricted
4. Company/Product (Name): Rimon (R) Technical	PM#: ~~10~~ 04	

5. Name and Address of Applicant *(Include ZIP Code)*
Makhteshim Chemical Works c/o MANA, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

[ ] *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 _____
- [ ] Notification - Explain below.
- [ ] Final printed labels in repsonse to Agency letter dated _____
- [ ] "Me Too" Application.
- [ ] Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)
Application for Registration of a New Active Ingredient

Section - III

1. Material This Product Will Be Packaged In:

Child-Resistant Packaging	Unit Packaging	Water Soluble Packaging	2. Type of Container
[ ] Yes	[ ] Yes	[ ] Yes	[ ] Metal
[x] No	[x] No	[x] No	[ ] Plastic
			[ ] Glass
			[ ] Paper
			[x] Other (Specify) poly-lined fiber
* *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: [x] Label [ ] Container
4. Size(s) Retail Container: No retail container-only drum
5. Location of Label Directions: [ ]
6. Manner in Which Label is Affixed to Product: [x] 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)
Andy Eimanis	Manager, Regulatory Affairs	212-896-4930

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 knowingly false or misleading statement may be punishable by fine or imprisonment or both under applicable law.

6. Date Application Received (Stamped)

2. Signature	3. Title: Manager, Regulatory Affairs	
4. Typed Name: Andy Eimanis	5. Date: 10-13-99	

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

11/03/99

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Makhteshim Chemical Works
c/o MANA, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

PRODUCT NAME: Rimon Technical
OPP IDENTIFICATION NUMBER: 267169
EPA FILE SYMBOL: 11678-LT
EPA RECEIPT DATE: 10/13/99

SUBJECT: RECEIPT OF APPLICATION FOR A NEW REGISTRATION

DEAR REGISTRANT:

The Office of Pesticides Programs has received your application for a new registration and it has passed an administrative screen for completeness.

Please note that this is only a notification of receipt of your application. This is only the first step in the application process, and does NOT constitute approval.

If you have any questions, please contact the Insecticide /Rodenticide Branch, at (703)-305-5404.

Sincerely,

Front End Processing Staff
Information Resources & Services Division
Information Services Branch

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 activities 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 the 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 form to this address.

DATA MATRIX

Date 10-13-99	EPA Reg No./File Symbol 11678-~~xxx~~ L T	Page 1 of 1
Applicant's/Registrant's Name & Address Makhteshim Chemical Works c/o MANA Inc, 551 Fifth Avenue, Suite 1100, New York, NY 10176	Product Rimon Technical	
Ingredient novaluron		

Guideline Reference Number	Guideline Study Name	MRID Number	Submitter	Status	Note
81-1	GR 572 (FCF/T46): Acute Oral Toxicity (LD_{50}) in Rats		Makhteshim-Agan of North America, Inc.	PER	
81-2	Acute Dermal Toxicity To Rats of GR 572 Tech		Makhteshim-Agan of North America, Inc.	PER	
81-3	GR 572 Tech: Acute Inhalation Toxicity Study in Rats (Limit Test)		Makhteshim-Agan of North America, Inc.	PER	
81-4	Irritant Effects on the Rabbit Eye of GR 572 Tech		Makhteshim-Agan of North America, Inc.	PER	
81-5	Irritant Effects on the Rabbit Skin of GR 572 Tech		Makhteshim-Agan of North America, Inc.	PER	
81-6	Skin Sensitization Test in Guinea Pigs of the Test Article GR 572 Tech		Makhteshim-Agan of North America, Inc.	PER	
Series 61	Rimon (Novaluron) Product Chemistry Data		Makhteshim-Agan of North America, Inc.	OWN	
Series 62	Rimon-Quantification of Active Ingredient and Impurities present at or above 0.1% in technical Rimon (FIFRA Guideline – Series 62)		Makhteshim-Agan of North America, Inc.	OWN	
Series 830	Rimon Technical: Determination of the Physico-Chemical Properties		Makhteshim-Agan of North America, Inc.	OWN	
Series 830	Rimon (Pure): Determination of the Physico-Chemical Properties		Makhteshim-Agan of North America, Inc.	OWN	
Series 830	Rimon Technical: Determination of the Physico-Chemical Properties		Makhteshim-Agan of North America, Inc.	OWN	
161-1	^{14}C"Rimon": Hydrolysis Under Laboratory Conditions		Makhteshim-Agan of North America, Inc.	OWN	
162-1	^{14}C"Rimon": Aerobic Soil Rate of Degradation		Makhteshim-Agan of North America, Inc.	OWN	
162-1	^{14}C"Rimon": Aerobic Soil Metabolism (Pilot Study)		Makhteshim-Agan of North America, Inc.	OWN	
163-1	^{14}C"Rimon": Soil Column Leaching		Makhteshim-Agan of North America, Inc.	OWN	
163-1	^{14}C"Rimon": Adsorption/Desorption on Soil		Makhteshim-Agan of North America, Inc.	OWN	
84-2	Rimon Technical: Bacterial Mutation Assay		Makhteshim-Agan of North America, Inc.	OWN	
84-2	Rimon Technical: Bacterial DNA Repair (*REC*) Assay		Makhteshim-Agan of North America, Inc.	OWN	
84-2	In Vitro Assessment of the Clastogenic Activity of GR 572 in Cultured Human Lymphocytes		Makhteshim-Agan of North America, Inc.	PER	

Signature	Name and Title Andy Eimanis, Manager, Regulatory Affairs	Date 10-13-99

EPA Form 8570-35 (9-97) Electronic and Paper versions available. Submit only Paper version.

Agency Internal Use Copy

NFT

Please read instructions on reverse before completing form.

Form Approved. OMB No. 2070-0060. Approval expires 2-28-95

EPA

United States
Environmental Protection Agency
Washington, DC 20460

☑ Registration
☐ Amendment
☐ Other

OPP Identifier Number
267169

Application for Pesticide - Section I

1. Company/Product Number 11678-~~xxx~~ LT	2. EPA Product Manager ~~Marion Johnson~~ Tina Levine	3. Proposed Classification ☑ None ☐ Restricted
4. Company/Product (Name) Rimon (R) Technical	PM# ~~10~~ 04	
5. Name and Address of Applicant *(Include ZIP Code)* Makhteshim Chemical Works c/o MANA, Inc. 551 Fifth Avenue, Suite 1100 New York, NY 10176 ☐ *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 _____
● Notification - Explain below.
☐ Final printed labels in repsonse to Agency letter dated _____
☐ "Me Too" Application.
☐ Other - Explain below.

Explanation: Use additional page(s) if necessary. (For section I and Section II.)

Application for Registration of a New Active Ingredient

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) poly-lined fiber
* *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	4. Size(s) Retail Container	5. Location of Label Directions
☑ Label ☐ Container	No retail container-only drum	☐

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)
Andy Eimanis	Manager, Regulatory Affairs	212-896-4930

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	3. Title	5. Date
	Manager, Regulatory Affairs	10-13-99
4. Typed Name Andy Eimanis		

EPA Form 8570-1 (Rev. 3-94) Previous editions are obsolete. White - EPA File Copy (original) Yellow - Applicant Copy

Form Approved OMB No. 2070-0060

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
401 M Street, S.W.
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Do not send the completed form to this address.

Certification with Respect to Citation of Data

Applicant's/Registrant's Name, Address, and Telephone Number Makhteshim Chemical Works c/o MANA, Inc., 551 Fifth Ave, Ste 1100, New York, NY 10176 (212)896-4930	EPA Registration Number/File Symbol 11678-~~xxx~~ LT
Active Ingredient(s) and/or representative test compound(s) novaluron	Date 10-13-99
General Use Pattern(s) (list all those claimed for this product using 40 CFR Part 158) greenhouse nonfood	Product Name Rimon Technical

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 A. Eimanis	Date 10-13-99	Typed or Printed Name and Title Andy Eimanis, Manager, Regulatory Affairs

EPA Form 8570-34 (9-97) Electronic and Paper versions available. Submit only Paper version.

1. IDENTITY OF THE ACTIVE INGREDIENT

Manufacturer's name
Makhteshim Chemical Works Ltd.
P.O. Box 60, Beer Sheva, 84100
Israel

Trade name:
"RIMON"

ISO chemical name
Novaluron

IUPAC chemical Name
Novaluron

Chemical name
1-[3- chloro-4- (1,1,2- trifluoro- 2- trifluoro- methoxyethoxy) phenyl]-3-(2,6-difluorobenzoyl) urea

Code numbers
GR 572 or MCW 275

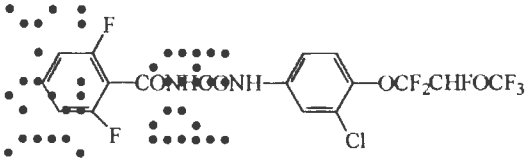
CAS number
[116714-46-6]

UN number
Not classified

Empirical formula, structural formula, molecular weight

Empirical formula
$C_{17}H_9ClF_8N_2O_4$

Structural Formula



Molecular weight
492.77

2. CHEMICAL AND PHYSICAL PROPERTIES

Melting point: 176.5 – 178^{0}C
Boiling point: Not applicable (solid)
Relative density (D^{22}_4): 1.56
Vapour pressure: 1.6 x 10^{-5} Pascals
Volatility: Henry's Law Constant = 2.0 Pa. m^3. mol^{-1}
Physical state: Solid
Colour: White
Odour: Non-detectable

Solubility in water under various pH and temperature
3 µg/l at 20^{0}C.

Solubility in organic solvents at various temperatures

N-heptane:	8.39 mg/l
M-octanol:	0.98 g/l
Xylene:	1.88 g/l
1.2 dichloroethane:	2.85 g/l
Methanol:	14.5 g/l
Acetone:	198 g/l
Ethyl acetate:	113 g/l

Ref. (R – 9897)

Stability in organic solvents:
Stable in organic solvents.

Thermal stability:
Relative self-ignition temperature – none below melting range.

Flammability:
Non flammable, melted but did not sustain a flame.

Flash point:
Not applicable.

Surface tension:
Not determined due to low water solubility.

Explosive properties:
Not explosive.

Ref. (R – 9709)

Oxidative properties:
Novaluron has no oxidizing/reducing action.

Chemical reactions with the packaging:
There is not reactivity of the technical material with the packaging.

3. TOXICOLOGICAL PROPERTIES

Acute toxicity tests

Acute Oral – LD_{50}

The acute oral toxicity to rat was investigated in groups of 5 male and 5 female Sprague-Dawley rats using dose levels of 100, 500, 1000, 3000 and 5000 mg/kg. There were no deaths and no clinical signs were noted in the dose ranging test and therefore a single dose level of 5000 mg/kg was investigated in the main study. No animals died and no clinical signs were noted.

Under the conditions of the study, the acute median lethal dose was: $LD_{50} > 5000$ mg/kg.

Ref. (R – 8775)

Acute Dermal (dermal LD_{50})

The acute dermal toxicity of Novaluron was investigated in 5 male and 5 female rats at a dose level of 2000 mg/ kg.

Under the conditions of the study, the acute dermal median lethal dose (LD_{50}) was found to be greater than 2000 mg/ kg.

Ref. (R – 8776)

Acute Inhalation

The acute inhalation toxicity was investigated in one group of 5 males and 5 females of rats for a single period of 4-hr exposure.
No mortality occurred during the exposure period. Slow, laboured breathing was noted for all animals during exposure. All animals appeared normal 1-2 hrs. after dosing, and throughout the 14 days observation period.
No significant abnormalities were observed at the end of the 14 days observation period.

Under the conditions of the study, the LC_{50} was greater than 5.15 mg/l.

Ref. (R – 8782)

Primary Skin Irritation

The potential of Novaluron to cause skin irritation was tested using a single dose of 0.5 g of Novaluron for a period of four hours, to the skin of the rabbits under occluded conditions.
None of the animals showed any response to treatment.

Under the conditions of the study, Novaluron was found non-irritant to rabbit skin.

Ref. (R – 8767)

Primary Eye Irritation

The acute irritation was assessed using a single application of the test material to the eye of six rabbits.
Instillation of the product into the rabbit eye did not elicit a positive response in any of the six treated animals. Novaluron was minimally irritant to the rabbit eye.

Ref. (R – 8776)

Skin Sensitization

The potential of Novaluron to cause delayed contact sensitivity in Guinea pigs was investigated using a topical exposure by occlusive patch.
The concentration of 10% (W/V) was used in the test and the dose administered was 50 mg/animal for each application.
In the group treated with the test article no animals showed positive reaction at the challenge. Under the experimental conditions of the study the test material is not considered to be a contact sensitizer.

Ref. (R – 8783)

Special toxicity tests

1. **Mutagenicity** – series of tests assesing DNA perturbation, chromosomal aberration and gene mutation.

Ames Test

The study was performed according to EPA FIFRA series 152-17 and J MAFF requirements.
The mutagenic potential of "RIMON" Technical was assessed in an in-vitro test, using four strains of *Salmonella typhimurium* (strains TA 1535, TA 1537, TA 98 and T. 100), and an additional mutant, *Escherichia coli* (wp 2 uvr A).

The mutants were exposed to the test substance, diluted in dimethyl sulphoxide, which was also used as a negative control.
The dose levels were 312.5, 625, 1250, 2500 and 5000 µg/plate. Two independent mutation tests were performed, in the presence and absence of liver preparations from Aroclor 1254-induced rats.
Under the conditions of the test, "RIMON" Technical shows no evidence to mutagenic activity.

Ref. (R – 9814)

Unscheduled DNA repair synthesis in mammalian cells – in vitro

Novaluron was tested for potential mutagenic activity measuring its ability to induce DNA repair in cultured human epitheloid cells.
Twelve concentrations in two separate occasions in both the presence and absence of metabolic activation by S9 mix were used.
It is concluded that Novaluron has not shown any evidence of causing DNA damage in this *in vitro* test for mutagenic potential.

Ref. (R – 8760)

Clastogenic activity in cultured human lymphocytes – *in vitro*

The effects on chromosomal structure of exposure to Novaluron were investigated in cultured human lymphocytes. Tests were conducted with and without the inclusion of a rat liver-derived metabolic activation system (S-9 mix); without S-9 mix cells were exposed for 24 hours with S-9 mix exposure was limited to three hours and cells were harvested 21 hours later. Treatments were established by the addition of test solutions in dimethyl sulphoxide (DMSO) to 48-hour cultures established from whole, human blood. Cell division was arrested by the addition of the spindle poison, Colcemid (to a final concentration of 0.4 μg/ml), three hours before the cells were harvested; slides were than prepared for microscopic analysis.
No statistically significant increases in the frequency of aberrant metaphases, compared to solvent control values were recorded at any concentration of Novaluron tested either in the absence or presence of S-9 mix ($p > 0.06$); this was true whether gap-type aberrations were included in or excluded from analysis.
It is concluded that Novaluron, under the conditions of the test, showed no evidence of clastogenic activity either in the absence or presence on S-9 mix. The sensitivity of the test procedure, and the metabolic responses activity of the S-9 mix employed, were demonstrated by the clear response to the positive control agents.

Ref. (R – 8780)

4. BEHAVIOR OF THE MATERIAL IN THE ENVIRONMENT

Hydrolysis

The study was performed according to European Community Council Directive 91/414/EEC.The hydrolytic stability of ^{14}-C "RIMON" has been studied in buffered aqueous solution at pH 5, 7 and 9. The solutions were incubated in darkness at ca. 25°C (pH 5, 7 and 9), ca. 50°C (pH 9) and ca. 70°C (pH 9) under

aseptic conditions. Two different radiolabelled forms of ^{14}-C "RIMON" were used, labeled with carbon-14 in either the chlorophenyl or the difluorophenyl ring, each at initial concentration in solution of ca. 1.5 µg/litre.
The solutions were analyzed at zero time and at a number of further intervals up to maximum 30 days. Total recoveries of radioactivity were in the range 87-118% of the initial amounts.

The rate of hydrolysis of "RIMON" was dependent upon solution pH and temperature.

The stability of "RIMON" is summarized in the following table:

pH / Temp	5 25°C	7 25°C	9 25°C	9 50°C	9 70°C	9 20°C
Stability /Half-life	stable	stable	101 d	1.2 d	0.09 d	217 d (by extrapolation)

At least eight hydrolysis products were formed in pH buffered solution. Only one of these contained both phenyl rings. The remaining products resulted from cleavage of the "RIMON" molecule to products that contained either the difluorophenyl ring only or the chlorophenyl ring only.

Aerobic Soil Metabolism and Rate of Degradation

Three test soils covering a range of textural classes (clay, sandy loam and silty clay loam), organic carbon content (0.8 – 3.7%) and pH (5.8 – 8.8) were treated separately with [chlorophenyl-^{14}C(U)] "RIMON" at an application rate of 0.130 ppm; equivalent to an agricultural use of rate of approximately 100g a.i./ha. Soils were incubated at either 10 or 20^{0}C under aerobic conditions at 40% maximum water holding capacity for up to 120 days after test substance application.

At zero time, 1, 3, 7, 14, 30, 59, 90 and 120 days duplicate soil samples of each soil type and incubation temperature were sampled. At each sampling time a single sample was taken for analysis whilst the remaining replicate was stored frozen for later analysis if required. The samples were extracted and radioactivity in the solvent extracts and the soil residues after extraction were measured. Volatile radioactivity was not collected as it had been previously demonstrated that the aerobic soil metabolism of its radiolabelled form of "RIMON" did not produce significant (*i.e.* greater than 20% applied radioactivity) proportions of volatile radioactivity. The proportion and identity of degradation products in extracts was investigated by high performance liquid chromatography (HPLC).

The decline of "RIMON" in all soils was biphasic in nature. DT_{50} values were calculated using a biexponential equation.

The initial degradation of "RIMON" was rapid with a DT_{50} for all soil types at 20^{0}C in a range of 5 – 13 days. Degradation of "RIMON" then continued at a reduced rate, greater than 80% degradation was observed by 59 days in all soil

types at 20^0C. However, very little further degradation was observed after this time resulting in DT_{90} values of greater than 120 days.

DT_{50} for the degradation of "RIMON" at 10^0C was 20 days, approximately double that observed at 20^0C.

One major metabolite of [chlorophenyl-^{14}C(U)] "RIMON" was detected which exceeded 10% AR. (Applied Radioactivity). This metabolite was characterized as 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl] urea (code name 275-352 I). This metabolite was formed rapidly and peaked at 20 – 27% AR generally after 7 days incubation at 20^0C. DT_{50} values for this metabolite were in the range 46 – 55 days for the 20^0C incubation and 110 days for the 10^0C incubation. No other radioactive metabolites of "RIMON" exceeded 10% AR.

Ref. (R – 10030)

Adsorption/desorption on Soil

The soil leaching potential of the insecticide Novaluron was studied using the absorption/desorption batch equilibration method. Novaluron was labeled with carbon^{-14} uniformly in the phenyl rings.
Four test soils, which covered a wide range of agricultural soil types, were used namely:

Wick sandy loam (UK)
Speyer 2.2 loamy sand (Germany)
Evesham 3 clay loam (UK)
Arrow sandy loam (UK)

An initial solution concentration of 1.5 µg/L ^{14}C-Novaluron in 0.01 M aqueous calcium chloride was studied. It was not possible to produce Freundlich adsorption/desorption isotherms due to the low water solubility of the test compound. Simple adsorption and desorption constants were calculated with results obtained from a single concentration of the test substance. For the absorption phase all four soils and solutions were equilibrated for 24 hours at 20°C in the dark. Soil samples were then desorbed twice with fresh calcium chloride solutions for 24 hours each time.
Solution and soil extracts were analysed by TLC to determine the actual concentrations of ^{14}C-Novaluron present in solution and soil extracts during the equilibration phases.

^{14}C-Novaluron was strongly adsorbed to the four soils tested. Simple adsorption constant (K_a) and desorption constants (K_d, second desorption) are shown in the table below. Based on these results ^{14}C-Novaluron can be classified as being immobile in soil. K_{oc} values calculated from the simple adsorption constants for the four soils do not correlate with the organic carbon content of the soil but suggest that other mechanisms were important in the adsorption of ^{14}C-Novaluron to soil.

Soil	Soil type	Organic carbon content %	Simple adsorption constant K_a	Organic carbon normalised adsorption constant K_{oc}	Simple desorption constant K_d
Spreyer 2.2	Loamy sand	2.4	247	10271	1477
Arrow	Sandy loam	2.0	133	6650	953
Evesham 3	Clay loam	1.9	184	9658	699
Wick	Sandy loam	0.8	95	11813	307

Ref. (R – 9667)

Soil column leaching ^{14}C"RIMON"

The study was performed according to European Community Council Directive 91/414/EEC, US EPA Guidelines 163 – 1.

Four different soils were used to assess leaching potential of "RIMON" labeled with carbon-14 uniformly in both aromatic rings.

The column leaching of "RIMON" was investigated after application to 30cm columns of clay loam, sandy loam (2 soil types) and silty clay loam soil at a rate of 20 µg/column which is equivalent to the use rate of 100 g a.i./ha. The columns were eluted with 0.0114 calcium chloride solution to a height of 50 cm over the cross-sectional area of the column. Total recoveries of radioactivity from the eluted columns were in the range 94.0 – 105.5% of the amounts applied.

Based on the results of the study, "RIMON" can be classified as having a very low potential for leaching in soil.

Ref. (R – 10005)

ISAGRO
Direzione e Uffici - Centro Direzionale Milano Oltre - Palazzo Raffaello
Via Cassanese, 224 - 20090 Segrate - Milano - Tel. (02) 26996.425 - Fax (02) 26996 287

Milan, 26/01/1996

TO WHOM IT MAY CONCERN

We hereby declare that ISAGRO S.p.A., Milano, Italy has given MAKTESHIM CHEMICAL WORKS LTD., Beer Sheva, Israel, the right to use all data generated by ISAGRO on GR-572, containing the active ingredient 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoro-methoxy) phenyl]-3-[2,6-difluorobenzoiyl] urea, for the purpose of registration of any crop protection product containing the active ingredient mentioned above.

ISAGRO S.p.A.
Managing Director
(Ottorino Polla)

RIMON® TECHNICAL

(Novaluron)

For The Manufacture of Insecticides Only

	% BY WT.
ACTIVE INGREDIENT: Novaluron: 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	98.5%
INERT INGREDIENTS:	1.5%
Total	100.0%

CAUTION

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

STATEMENT OF PRACTICAL TREATMENT (FIRST AID)

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.
IF SWALLOWED: Call a doctor or get medical attention. Do not induce vomiting. Do not give anything by mouth to an unconscious person. Avoid alcohol.
IF IN EYES: Flush eyes with plenty of water. Call a physician if irritation persists.

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

Harmful if absorbed through skin. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters except in accordance with the requirements of a 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 treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. This pesticide is for the further manufacture of formulated insecticides only. Formulators using this product are responsible for obtaining EPA registration for their formulated products.

Only for formulation into a insecticide for the following uses:
(1) Ornamentals (greenhouse and outdoor)
(2) Uses for which USEPA has accepted the required data and/or citations of data that the formulator has submitted in support of registration; and
(3) Uses for experimental purposes that are in compliance with USEPA requirements.

STORAGE AND DISPOSAL

STORAGE: Do not contaminate water, food, or feed by storage or disposal. Open dumping is prohibited.
PESTICIDE DISPOSAL: Wastes resulting from the use of this product may be disposed of at an approved waste disposal facility.
CONTAINER DISPOSAL: Completely empty liner by shaking and tapping sides and bottom to loosen clinging particles. Empty residue into equipment. Then dispose of liner in a sanitary landfill or by incineration if allowed by State and local authorities. If drum is contaminated and cannot be reused, dispose of in the same manner.

WARRANTY STATEMENT

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 but 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 instruction, or under abnormal conditions, or under conditions not reasonably foreseeable to seller, and buyer assumes the risk of any such use. Buyer assumes all risks of use, storage or handling of this material not in strict accordance with directions given herewith.

NET CONTENTS _____ POUNDS

Makhteshim Chemical Works, Ltd.
c/o Makhteshim-Agan of North America, Inc.
551 Fifth Avenue, Suite 1100
New York, NY 10176

EPA Reg. No. 11678-xx
EPA Est. No. 11678-IS-1

RIMON® TECHNICAL

(Novaluron)

For The Manufacture of Insecticides Only

	% BY WT.
ACTIVE INGREDIENT: Novaluron: 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea	98.5%
INERT INGREDIENTS:	1.5%
Total	100.0%

CAUTION

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle. (If you do not understand the label, find someone to explain it to you in detail.)

STATEMENT OF PRACTICAL TREATMENT (FIRST AID)

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.
IF SWALLOWED: Call a doctor or get medical attention. Do not induce vomiting. Do not give anything by mouth to an unconscious person. Avoid alcohol.
IF IN EYES: Flush eyes with plenty of water. Call a physician if irritation persists.

PRECAUTIONARY STATEMENTS
HAZARDS TO HUMANS AND DOMESTIC ANIMALS

Harmful if absorbed through skin. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling.

ENVIRONMENTAL HAZARDS

This pesticide is extremely toxic to aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters except in accordance with the requirements of a 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 treatment plant authority. For guidance contact your State Water Board or Regional Office of the EPA.

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling. This pesticide is for the further manufacture of formulated insecticides only. Formulators using this product are responsible for obtaining EPA registration for their formulated products.

Only for formulation into a insecticide for the following uses:
(1) Ornamentals (greenhouse and outdoor)
(2) Uses for which USEPA has accepted the required data and/or citations of data that the formulator has submitted in support of registration; and
(3) Uses for experimental purposes that are in compliance with USEPA requirements.

STORAGE AND DISPOSAL

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PRATS
11/3/99
JAV

****
NEW CHEMICAL/FIRST FOOD USE SCREEN
****

1. FILE SYMBOL/REG NO (ISB) 11678-LT
2. TOLERANCE PETITION NO. (RSB) _____
3. CHEMICAL NAME (RSB) NOVALURON
4. PESTICIDE CHEMICAL CODE (RSB) 124002 (CAS: 116714-46-6)
5. PRODUCT NAME (ISB) Rimon(R) Technical
6. PM (ISB) 04 7. PM TEAM REVIEWER (PM) _____
8. DATE OF RECEIPT (ISB) 11/2/99
9. [illegible]E PATTERN (PM) _____
0. DATE OF TRANSMISSION TO PM (ISB) To SIG: 11/4/99
(EPA Receipt Date plus 3 days)
1. DATE OF TRANSMISSION TO HED/EFED/RSB (PM) _____
(PM Receipt Date plus 5 days)
2. HED/EFED/RSB DUE DATE FOR COMPLETION OF SCREEN _____
(HED/EFED Receipt Date plus 10 days)
3. HED/EFED/RSB REVIEWERS:

HED:
TB _____
DEB _____
OREB _____
RD/RSB _____

EFED:
EEB _____
EFGWB _____

14. HED/EFED/RSB COMPLETION DATE (HED) _____ (EFED) _____ (RSB) _____
15. SUBMISSION BARCODE (PM) _____

REGISTRANT PHONE CONTACT INFORMATION (PM)

DATE OF CONTACT _____

PERSON CONTACTED _____

TITLE _____

DECISION & COMMENTS _____

STATUS OF PACKAGE

☐ PASSED SCREEN

☐ FAILED SCREEN (Documentation attached)

CHEMICAL NAME/PESTICIDE CHEMICAL CODE (PCC) REQUEST FORM*

CR#: 99-0518

REQUESTOR NAME: Jim Hollis REQUEST DATE: 11/12/99
TEL.: (703) 305-5761 ORG.: ERSD/ISB ROOM: 224 MAIL CODE: 7502C
(DIV./BR./SEC.)

CSF ATTACHED:
- [x] YES If CSF is attached complete Item A and the chemical name in Item B.
- [ ] NO If CSF is not attached complete Items A through C.

A. INFORMATION REQUIRED:
✓Check Applicable Category
- [ ] Provide PCC and Tolerance Exemption Status For Food-Use Inert Ingredient(s)
- [ ] Provide PCC for Non-Food Use Inert Ingredient (s)
- [x] Provide PCC for Active Ingredient(s)
- [ ] Provide PCC for Dye
- [ ] Determine if Fragrance is Acceptable for Use in Formulation
- [ ] Other (Describe): _____

B. INGREDIENT INFORMATION:

Ingredient No. 1:
Chem. Name: NOVALURON
Trade Name:
CAS Reg. No.: 116714-46-6

Ingredient No. 2:
Chem. Name:
Trade Name:
CAS Reg. No.:

Ingredient No. 3:
Chem. Name:
Trade Name:
CAS Reg. No.:

Ingredient No. 4:
Chem. Name:
Trade Name:
CAS Reg. No.:

C. PESTICIDE PRODUCT INFORMATION:

EPA Reg. No./File Symbol: 11678-LT Product Name: Rimon(R) Technical
Registrant: MAKHTeshim Chemical Works Food-Use Pesticide: [ ] YES [ ] NO
Percent in Formulation (For Fragrance/Dyes only): _____

INFORMATION REPORTED:

Ingredient No. 1:
PCC: 124002
TOL. STATUS:
OTHER INF.:

Ingredient No. 2:
PCC:
TOL. STATUS:
OTHER INF.:

Ingredient No. 3:
PCC:
TOL. STATUS:
OTHER INF.:

Ingredient No. 4:
PCC:
TOL. STATUS:
OTHER INF.:

Completed By: LINDA FAN Date Completed: 11/03/99

*Once completed, this form may be entitled to treatment as CBI under section 10 of FIFRA. Also, a red FIFI CBI cover should be affixed to the request form and the document handled accordingly.

Confidential Statement of Formula may be entitled to confidential treatment

11/05/99