CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-043

ADMINISTRATIVE DOCUMENTS

NDA Labeling Review

NDA 21-043

Submission Date: August 31, 1998
Review Date: June 24, 1999

Applicant:	Soltec Research PTY Ltd. 8 Macro Court Rowville, Victoria Australia 3178
Applicant's Representative	Thomas Blake, R.Ph. 973-347-5129
Drug:	RID® Mousse pyrethrum extract (equivalent to 0.33% pyrethrins) and piperonyl butoxide 4% aerosolized foam
Pharmacologic Category:	Pediculicide (lice treatment)
Submitted:	Carton and can labels, and Consumer Information Insert labeling
Background:	The combination of pyrethrum extract (0.17 to 0.33%), as a pediculicide, with piperonyl butoxide (2 to 4%), as a synergistic adjuvant, is included as active ingredients in a non-aerosol dosage form in the OTC pediculicide drug products monograph under 21 CFR § 358.610. Aerosol dosage forms were declared to be new drugs. The applicant has submitted this NDA deviation to include the aerosol dosage form of the same combination of ingredients for use as an OTC pediculicide.
Reviewer's comments:	The sponsor submitted proposed carton, can labels, and Consumer Information Insert labeling with the initial submission. Subsequently, the sponsor resubmitted revised labeling in conformance with the final rule for labeling format requirements published on March 17, 1999. On June 10, 1999, the sponsor resubmitted a third version of its proposed labeling after the tele-conference with the Agency regarding information related to the sponsor's Australian labeling. On June 16, 1999, the sponsor submitted a 4th version of their proposed labeling. This review has included the latest labeling submission. A single strikeout is used to indicate the Agency's recommendation for deletion, and shading indicates addition. Since many parts of the labeling repeat the same information, the reviewer's comment will occur only the first time a change is required.

13 pages of revised draft labeling have been redacted from this portion of the document.

Reviewer's recommendation: A copy of the prototype labeling should be telefaxed to the sponsor prior to the action letter and the sponsor should be informed to revise their labels and labeling in accordance with the attached draft labeling. Once, the sponsor accepts the recommended changes, an approval letter can be sent the sponsor requesting final printed labeling identical to the draft labeling.

/S/

Michael T. Benson, R. Ph., J.D.

/S/

Linda Hu, M.D.

/S/

Marina Chang, R. Ph.

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

NDA Labeling Review Addendum

NDA 21-043

Submission Date: August 31, 1998
Review Date: July 8, 1999

Applicant:	Soltec Research PTY Ltd. 8 Macro Court Rowville, Victoria Australia 3178
Applicant's Representative	Thomas Blake, R.Ph. 973-347-5129
Drug:	RID® Mousse pyrethrum extract (equivalent to 0.33% pyrethrins) and piperonyl butoxide 4% aerosolized foam
Pharmacologic Category:	Pediculicide (lice treatment)
Submitted:	Carton and can labels, and Consumer Information Insert labeling
Reviewer's Comment:	A copy of the agency's draft labeling was faxed on June 29, 1999 with a request that the sponsor respond with comments or a commitment to implement the labeling as supplied. Subsequently on July 1, 1999, the Agency informed the Sponsor to make new changes to the "Do not use" and "Ask a doctor before use if you have" sections of the "Warnings". (see attachment 1) These new changes were determined to be necessary or an improvement to the labeling. The following revised, prototype labeling should be sent to the Sponsor as the attachment to the action letter.

9 pages of revised draft labeling have been redacted from this portion of the document.

Stop use and ask a doctor if

- skin irritation or infection is present or develops
- infestation of eyebrows or eyelashes occurs

Keep out of reach of children. If swallowed, get medical help or contact a Poison Control Center right away.

OTHER INFORMATION

- store at 20°-25°C (68°-77°F)
- do not store at temperature above 43°C (110°F)
- keep in a cool place out of the sun

QUESTIONS? Call **1-800-RID LICE (1-800-743-5423)**

Recommendation: Enclose the attached proptotype labeling with the Action Letter to the Sponsor.

/S/

Marina Y. Chang, R. Ph.

/S/

Linda Hu, M.D.

Attachment 1 - Memorandum of telephone converstation dated July 1, 1999

APPEARS THIS WAY
ON ORIGINAL

- **Review of OTC Drug Labeling**

NDA #21-043	Sponsor:Soltec Research USA
Drug Product:Rid Mousse	
Submission Dates: August 31, 1998 and November 10, 1999 Amendment: January 31, 2000 and February 14, 2000	Review Date: February 17, 2000 (of amendment)
Type of Submission: Labeling Amendment to Pending Application	Reviewer: Michael T. Benson

Stock Keeping Unit: a 5.5 ounce can of aerosol foam in a carton

Information Included in the Submission

Content of Submission	Yes	No
1. A cover letter stating that the submission includes new labeling in the Drug Facts format for the drug product and shelf keeping unit(s);	X	
2. A table of contents or index		X
3. The most recent approved labeling *;	N/A	
4. A representation of the proposed labeling, including any outserts, panel extensions, or other graphical or package techniques intended to be used with the product.	X	
5. Information on formatting, text style, and text size as illustrated in 64 FR 13254 at 13293.	X	

*Additional labeling submitted under 21 CFR 314.70(c) or (d) since the last approved labeling should be included in the submission with the date of submission referenced and how they were submitted (e.g. annual report, pending supplement).

The information provided is adequate for review: ___X___Yes _____No

Reviewer's Comments

This amendment serves as the Sponsor's response to the labeling issues identified in the approvable letter dated July 8, 1999. The Sponsor has made the labeling changes suggested by the Agency and they are acceptable. The attached review serves to identify those areas that have been changed by the Sponsor. Type sizes were reviewed in the September 2, 1999 submission and were found to meet the specifications set forth in Drug Facts regulations. The Sponsor has not altered any of the type sizes in the resubmissions.

A. Carton Label

Principal Display Panel

Paragraph 21 CFR	Description of Paragraph	Adequate (yes/no)	Comments	Resubmission
201.60	Principal Display Panel	**No**	**The sponsor objects to removing "Lice Killing" from trade name RID Lice Killing Mousse in which the name RID appears in a red stop sign logo. The sponsor claims the name RID Lice Killing Mousse distinguishes the product from other company products using the name RID in**	**"Lice Killing" was removed from the trade name.**

A. Carton Label

Principal Display Panel

Paragraph 21 CFR	Description of Paragraph	Adequate (yes/no)	Comments	Resubmission
201.60	Principal Display Panel	**No**	**The sponsor objects to removing "Lice Killing" from trade name RID Lice Killing Mousse in which the name RID appears in a red stop sign logo. The sponsor claims the name RID Lice Killing Mousse distinguishes the product from other company products using the name RID in a red stop sign logo, and differentiates this drug product from other cosmetic mousses. The Agency reaffirms its requirement for the removal of "Lice Killing" from the trade name, and has no objection to it appearing elsewhere on the PDP. Sponsor deleted the "Head...Crab...& Body Lice" statement from the PDP. The Agency has no objection to the deletion. The words are included adjacent to "uses" in the Drug Facts panel.**	**"Lice Killing" was removed from the trade name.**
201.61	Statement of Identity • Established name of drug	**No**	**An established name was included as proposed in Agency's July 8, 1999 approvable letter. There is no official or compendial name for pyrethrum extract and piperonyl butoxide aerosolized foam. The Agency had wanted the Sponsor to voluntarily use its proposed name on the PDP. The Agency will accept the Sponsor's**	**"Pyrethrum extract/piperonyl butoxide aerosolized foam" was included.**

Paragraph 21 CFR	Description of Paragraph	Adequate (yes/no)	Comments	Resubmission
	• Statement of general pharmacological category(ies) or the principal intended actions • Bold type • Size related to the most prominent printed matter	Yes Yes Yes	**proposal to include "pyrethrum extract/piperonyl butoxide" as the established name. The official dosage form is an aerosolized foam recognized by the Agency and will be required to appear on the PDP to inform the consumer that this is an aerosolized foam product.**	
201.62	Declaration of net quantity of contents	Yes		
201.63	Pregnancy/breast feeding warnings	N/A		
201.1	Name and place of business of manufacturer, packer, or distributor	Yes		
201.17	Location of expiration dates	Yes		
201.18	Control numbers	Yes		

Labeling Content [21 CFR 201.66 (c)]

Paragraph	Description of Paragraph	Adequate (yes/no)	Comments	Resubmission
(c)(1)	Drug Facts, Drug Facts (continued)	Yes		
(c)(2)	Active ingredient, established name, quantity	No	**Sponsor deleted the zero after the decimal (i.e., 4% rather than 4.0%), an acceptable change. The phrase "calculated without propellent" needs to be bolded and in same font size as heading. If space is insufficient to accommodate the change, the sponsor can submit a request for exemption to reduce the font**	**The phrase "calculated without propellent" had been bolded, but in a smaller font size than "Active ingredients." The font sizes were made equal (8-point) in the February 14, 2000 submission. The Agency recommendation spelled the third word in parentheses as "propellent." The Sponsor spelled the word as "propellant." Webster's**

Labeling Content [21 CFR 201.66 (c)]

Paragraph	Description of Paragraph	Adequate (yes/no)	Comments **size for that phrase.**	Resubmission **Dictionary allows either spelling.**
(c)(3)	Purpose(s)	**Yes**		
(c)(4)	Use(s)	**Yes**		
(c)(5)	Warning(s)	**Yes**		
(c)(5)	(i) For external use only	**Yes**		
(c)(5)	(ii) All applicable warnings	**Yes**		
	(A) Allergic reaction warnings	**N/A**		
	(C) Flammability warning, with appropriate signal word	**Yes**	**Chemist review dated 10/19/99 noted that a report was provided showing that Rid Mousse meets the CPSC definition of "flammable." The period after the word "flammable" needs to be deleted.**	**The period after "flammable" was removed. A colon was inserted after "flammable."**
(c)(5)	(iii) "Do not use" followed by all contraindications	**No**	**The period after "eyes" needs to be deleted.**	**The period after "eyes" was removed.**
(c)(5)	(iv) "Ask a doctor before use if you have"	**No**	**The period after "ragweed" needs to be deleted.**	**The period after "ragweed" was removed.**
(c)(5)	(vi) When using this product	**Yes**		
(c)(5)	(vii) Stop use and ask a doctor if	**Yes**		
(c)(5)	(viii) Any required warnings	**N/A**		
(c)(5)	(x) Keep out of reach of children	**Yes**		
(c)(6)	Directions	**No**	**The statement "Important: Read warnings before using" needs to be preceded by a bullet to appear vertically aligned with other bullets. The period in the next to last bulleted statement needs to be deleted.**	**A bullet precedes the Direction "Important: Read warnings before using." The period after "hair" in the next to last bulleted statement is removed.**
(c)(7)	Other information and additional information not included in (c)(2) – (c)(6), (c)(8), (c)(9) of this section. Storage Statement	**Yes**		

Labeling Content [21 CFR 201.66 (c)]

Paragraph	Description of Paragraph	Adequate (yes/no)	Comments	Resubmission
(c)(7)	(iii) additional information	N/A		
(c)(8)	Inactive ingredients	Yes		
(c)(9)	Questions	No	**The word "Questions" should be italicized, bolded, and colored red to be consistent with other subheadings. The word "call" should be unbolded and use a lower case c.**	**The subsection heading "Questions" is italicized, bolded, and red. The word "call" used a lower case c, but it was still bolded. The February 14, 2000 submission debolded the word "call."**

Labeling Format [21 CFR 201.66 (d)]

Paragraph	Description of Paragraph	Adequate (yes/no)	Comments	Resubmission
(d)(1)	Drug Facts: first letter of words uppercase	Yes		
(d)(1)	Headings, subheadings: first letter of first word uppercase	Yes		
(d)(1)	Left justification	Yes		
(d)(2)	Drug Facts type size greater than largest type size used in Drug Facts labeling	Yes		
(d)(2)	Heading 8 pt or 2 point sizes greater than text point size	Yes		
(d)(2)	Type size 6 pt size for information in Drug Facts	Yes		
(d)(2)	Subheadings ≥ 6 point type size	Yes		
(d)(3)	No reverse type	Yes		
(d)(3)	Letters do not touch	Yes		
(d)(3)	≥.5 pt leading (space between lines)	Yes		
(d)(3)	No more than 39 characters per inch	Yes		
(d)(3)	Bold Italic headings and title	Yes	**Except "Questions" which is not**	**Now is corrected. See paragraph (c)(9) above.**
(d)(3)	Bold subheading except (continued)	Yes		
(d)(3)	Black or dark type	Yes		
(d)(3)	White or neutral background	Yes		
(d)(3)	Contrasting dark color for title and heading	Yes		
(d)(4)	Bullet: solid circle or square 5 pt type, same shape and color, left justified or separated from heading or subheading by at least two square "EMS"	Yes		
(d)(4)	Vertical alignment of bulleted statements	Yes		
(d)(5)	Appear on more than one panel	No		

Labeling Format [21 CFR 201.66 (d)]

Paragraph	Description of Paragraph	Adequate (yes/no)	Comments	Resubmission
(d)(6)	Left justification of information required by (c)(2)	Yes		
(d)(6)	Right justification of information required by (c)(3)	Yes		
(d)(6)	Alphabetical order of active ingredients	Yes		
(d)(6)	Information required by (c)(4), (c)(6) - (c)(9) may start on same line as required headings	Yes		
(d)(6)	None of information required in (c)(5) shall appear on same line as Warnings	Yes		
(d)(7)	Graphical images should not interrupt the heading, subheading and information. Hyphens should not be used except to punctuate compound words.	Yes		
(d)(8)	Enclosed box using barline	Yes		
(d)(8)	Horizontal barline separates headings listed in (c)(2) - (c)(9)	Yes		
(d)(8)	Horizontal hairline precedes heading immediately after Drug Facts	Yes		
(d)(8)	Horizontal hairline follows the title	Yes		
d)(8)	Horizontal hairline extending within 2 spaces on either side of the Drug Facts box shall immediately follow the title and precede the subheadings set forth in (c)(5) [except (c)(5)(ii) A-G]	Yes		

In accordance with section 501(b) of the Federal Food, Drug, and Cosmetic Act. since pyrethrum extract 50% is not official in the USP, an asterisk should appear next to it with a reference asterisk anywhere else in the labeling followed by "50% extract (not USP)." The January 31, 2000 submission showed that an asterisk appears next to pyrethrum extract, and under the Questions section. It states "50% extract (not USP)."

B. Can label – The sponsor included a modified "drug facts" labeling for the can which is round and has no edging. The title "drug facts" is not enclosed in a box with barline nor any edging to separate the panels. As an inner container, the "Drug Facts" format is not required and the Agency will accept this type of labeling. The sponsor should be advised to make the following changes:

1. to include a visual graphic (e.g., an arrow) to signal the continuation of the "Drug Facts" labeling to the next adjacent panel [21 CFR 201.66(d)(5)]

2. to add "Drug Facts (continued)" to the beginning of the second column to indicate that this column is the continuation of the previous column.

3. Carton label changes also apply to the can label.

In the January 31, 2000 submission, the Sponsor made changes comparable to those in the carton label. A triangle appears under the first column of Drug Facts which appears to be the visual graphic that signals the continuation of Drug Facts labeling on the next adjacent panel. The second panel to Drug Facts is headed "Drug Facts (continued)." The subsection heading Questions is italicized, bolded and red. The next word "call" used a lower case c, but it was still bolded. The February 14, 2000 submission debolded the word "call."

C. Consumer Information Insert – It includes capitalized subheadings on the sponsor's submitted insert. The comments listed below are shown together with changes to be made to be in compliance with the Agency's July 8, 1999 approvable letter (except for the Prevent Reinfestation statement). In the Sponsor's January 31, 2000 submission, the statement of identity includes "aerosolized foam" as the official dosage form.

PREVENT REINFESTATION (in the 5th bulleted statement)

"For anything that cannot be washed, dry cleaned or stored in a plastic bag, you may want to use a lice control spray." should say " Personal articles of clothing or bedding that cannot be washed may be dry-cleaned, sealed in a plastic bag for a period of about 2 weeks, or sprayed with a product specifically designed for this purpose." The latter labeling statement is consistent with the final monograph. The draft labeling accompanying the Agency's July 8, 1999 approvable letter suggested [redacted] The monograph statement is preferred at this time. In the January 31, 2000 submission, the Sponsor included the statement recommended above.

WARNINGS

In the January 15, 2000, a period appears after "occur" in the 5th bulleted statement under the subheading "When using this product," as requested.

Reviewer's Recommendation:

The following information should be relayed to the Sponsor:

The consumer information insert submitted on January 31, 2000 and the carton and immediate container labels submitted on February 14, 2000 are acceptable. Therefore, an approval letter should be sent to the Sponsor requesting 20 copies of final printed labeling identical to the submitted draft labeling.

Carton and Can labels – Remind Sponsor that the flag "New" is to be deleted 6 months after marketing.

Consumer Information Insert – Remind Sponsor that the Agency will not comment on foreign language labeling. It is the Sponsor's responsibility to ensure that the foreign language be identical in meaning to the English language labeling.

/S/

Michael T. Benson, R.Ph., J.D.

APPEARS THIS WAY
ON ORIGINAL

RID MOUSSE

PATENT INFORMATION

The formulation (formula #262-1) described in the attached dNDA application is covered by the enclosed patent (patent number 5,783,202) entitled Pediculicidal Mousse Composition for Killing Head Lice, assigned to Soltec Research Pty. Ltd., Australia. The labeling will be revised to include this patent number.

Solte
RESEARC
A C N 006 353
8 MACRO CO
ROWVILLE, VICT
AUSTRALIA.
TEL: + 61 3 9763
FAX: + 61 3 9763

SOLTEC RESEARCH PTY LTD certifies it did not and will not use in any capacity the services of any person debarred under Section 306 of the Food Drug and Cosmetic Act in connection with this application.

Thomas Blake 8/30/98

Thomas Blake, R.Ph. Date
REGULATORY CONSULTANT
TO SOLTEC
48 Mt. Olive Road
Budd Lake, NJ 07828
Phone: 973-347-5129 Fax: 973-448-0837

ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: **NDA 21043/000**
Priority: **S** Org Code: **560**
Stamp: **02-SEP-1998** Regulatory Due: **09-SEP-1999**
Action Goal: District Goal: **11-JUL-1999**
Applicant: **SOLTEC**
S MARCO CT, ROWVILLE, 3178
VICTORIA, , AS
Brand Name: **RID MOUSSE(PIPERONYL BUTOXIDE 4.0%/PYRET**
Established Name:
Generic Name: **PIPERONYL BUTOXIDE 4.0%/PYRETHRINS 0.33%**
Dosage Form: **AER (AEROSOL)**
Strength: **4.0/0.33%**

FDA Contacts:			
	K. ROTHSCHILD	**(HFD-560)**	**301-827-2284 , Project Manager**
	C. YACIW	**(HFD-830)**	**301-827-2296 , Review Chemist**
	H. PATEL	**(HFD-550)**	**301-827-2507 , Team Leader**

Overall Recommendation:

ACCEPTABLE on 19-JAN-1999 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: [redacted]
DMF No:
AADA No:

Profile: **ADM** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **01-DEC-1998**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**
Responsibilities: **FINISHED DOSAGE MANUFACTURER**

Establishment: **2211583**
PFIZER INC
100 JEFFERSON RD
PARSIPPANY, NJ 07054
DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **19-JAN-1999**
Decision: **ACCEPTABLE**
Reason: **DISTRICT RECOMMENDATION**
Responsibilities: **FINISHED DOSAGE RELEASE TESTER**

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER
NDA 21-043

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
SOLTEC RESEARCH PTY LTD	9/8/99
TELEPHONE NO. *(Include Area Code)* 011 61 3 9763 0022	**FACSIMILE (FAX) Number** *(Include Area Code)* 011 61 3 9763 0354
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):* 8 Macro Court Rowville, Victoria 3178 AUSTRALIA	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE Ms. Terri Deer 2034 Eisenhower Avenue, Suite 107 Alexandria, VA 22314 Phone: (703) 299-6629 Fax: (703) 299-9623

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Pyrethrins, piperonyl butoxide	RID MOUSSE

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*

CODE NAME *(If any)*

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
MOUSSE	Pyrethrins 0.33%, Piperonyl butoxide 4%	Topical

(OPOSED) INDICATION(S) FOR USE:
For the treatment of head, pubic (crab), and body lice

APPLICATION INFORMATION

APPLICATION TYPE (check one)
☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b)(1) ☐ 505 (b)(2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION (check one)
☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

REASON FOR SUBMISSION
Response to Item 18 of the FDA Approvable Letter dated 8 July 1999: SAMPLE INFORMATION

PROPOSED MARKETING STATUS (check one) ☐ PRESCRIPTION PRODUCT (Rx) ☒ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 — THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

N/A. Provided in original NDA

)ss References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current -pplication)

N/A. Provided in original NDA

This application contains the following items: *(Check all that apply)*

	1. Index
	2. Labeling (check one) ☐ Draft Labeling ☐ Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
X	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2) SAMPLE INFORMATION
	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
	12. Case report forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C 355 (b) (2) or (j) (2) (A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.50 (k) (3))
	18. User Fee Cover Sheet (Form FDA 3397)
X	19. OTHER (Specify) Separate response to Item 18 of the 8 July 1999 FDA Approvable Letter

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been review and, to the best of my knowledge are certified to be true and accurate.

Warning: a willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
Thomas B Blake	Thomas Blake, R.Ph. Regulatory Consultant to Soltec	9/8/99

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
48 Mt. Olive Road, Budd Lake, New Jersey 07828	(973) 347-5129

Public reporting burden for this collection of information is estimated to average 40 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

HHS, Reports Clearance Officer
aperwork Reduction Project (0910-0338)
Hubert H. Humphrey Building, Room 531-H
200 Independence Avenue, S.W.
Washington, DC 20201

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Please DO NOT RETURN this form to this address.

FORM FDA 356h (7/97)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on page 2.

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER
NDA 21-043

APPLICANT INFORMATION

NAME OF APPLICANT
SOLTEC RESEARCH PTY LTD

DATE OF SUBMISSION
2/14/00

TELEPHONE NO. (Include Area Code)
011 61 3 9763 0022

FACSIMILE (FAX) Number (Include Area Code)
011 61 3 9763 0354

APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):
8 Macro Court
Rowville, Victoria 3178
AUSTRALIA

AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE
Ms. Terri Deer
2034 Eisenhower Avenue, Suite 107
Alexandria, VA 22314
Phone: (703) 299-6649
Fax: (703) 299-9623

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued)

ESTABLISHED NAME (e.g., Proper name, USP/USAN name)
Pyrethrins, piperonyl butoxide

PROPRIETARY NAME (trade name) IF ANY
RID Mousse

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any)

CODE NAME (If any)

DOSAGE FORM
Mousse

STRENGTHS: Pyrethrins 0.33%, Piperonyl butoxide 4%

ROUTE OF ADMINISTRATION:
Topical

(PROPOSED) INDICATION(S) FOR USE:
For the treatment of head, pubic (crab), and body lice

APPLICATION INFORMATION

APPLICATION TYPE (check one)
☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b) (1) ☐ 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION (check one)
☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

REASON FOR SUBMISSION
LABELING

PROPOSED MARKETING STATUS (check one) ☐ PRESCRIPTION PRODUCT (Rx) ☒ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1

THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

N/A. Provided in original NDA

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

N/A. Provided in original NDA

This application contains the following items: *(Check all that apply)*	
	1. Index
	2. Labeling (check one) ☒ Draft Labeling ☐ Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
	12. Case report forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C 355 (b) (2) or (j) (2) (A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.50 (k) (3))
	18. User Fee Cover Sheet (Form FDA 3397)
	19. OTHER (Specify)

TIFICATION

ge to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been review and, to the best of my knowledge are certified to be true and accurate.

Warning: a willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
Thomas Blake	Thomas Blake, R.Ph. Regulatory Consultant to Soltec	2/14/00

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
48 Mt. Olive Road, Budd Lake, New Jersey 07828	(973) 347-5129

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FORM FDA 356h (7/97)

NDA FILEABILITY CHECKLIST

NDA Number: 21-043 **Applicant:** Soltec **Stamp Date:** 9/2/98 **Clock Date:** 9/9/98
Drug Name: Rid Mousse (piperonyl butoxide and pyrethrum extract)

IS THE CMC SECTION OF THE APPLICATION FILEABLE? (Yes or No) yes

The following parameters are necessary in order to initiate a full review, i.e., complete enough to review but may have deficiencies.

	Parameter	Yes	No	Comment
1	On its face, is the section organized adequately?	X		Poor but reviewable
2	Is the section indexed and paginated adequately?	X		
3	On its face, is the section legible?	X		
4	Are ALL of the facilities (including contract facilities and test laboratories) identified with full street addresses and CFNs?	X		Not all have CFNs
5	Is a statement provided that all facilities are ready for GMP inspection?		X	The DP site is ready. Most of the others have a status statement but not all
6	Has an environmental assessment report or categorical exclusion been provided?	X		Wrong citation in summary; EA section 12 in index is missing
7	Does the section contain controls for the drug substance?	X		Only info submitted for DS. Referenced to monograph product.
8	Does the section contain controls for the drug product?	X		
9	Has stability data and analysis been provided to support the requested expiration date?	X		
10	Has all information requested during the IND phase, and at the pre-NDA meetings been included?	X see →		Full DS information was requested but was neither submitted nor referenced to DMFs – not needed per CW Chen E-mail
11	Have draft container labels been provided?	X		
12	Has the draft package insert been provided?	X		
13	Has an investigational formulations section been provided?	NA		
14	Is there a Methods Validation package?	X		
15	Is a separate microbiological section included?	NA		

If the NDA is not fileable from a manufacturing and controls perspective state why it is not.

Review Chemist: /S/ Date: 10/8/98

Team Leader: /S/ Date: 10-20-98

cc:
Original NDA 21-043
HFD-560/Division File
HFD-550/Chem/Yaciw
HFD-560/PM/Merritt
HFD-830/DivDir/CW Chen

pplicant: Soltec
duct: R.L Mousse

45 DAY MEETING CHECKLIST

FILEABILITY:

On initial overview of the NDA application	YES	NO

PROJECT MANAGEMENT:

		YES	NO
(1)	Do any of the following apply to this application (i.e., if yes, the application MUST BE REFUSED TO FILE under 314.100(e) and there is no filing over protest):		
	(a) Is the drug product already covered by an approved application?		X
	(b) Does the submission purport to be an abbreviated application under 314.55; however the drug product is not one for which FDA has made a finding that an abbreviated application is acceptable under 314.55(b)?		X
	(c) Is the drug product subject to licensing by FDA under the Public Service Act and Subchapter F of Chapter I of Title 21 of the CFR (Biologics)?		X
(2)	Do any of the following apply to this application (i.e., if NO, the application MAY BE REFUSED TO FILE under 314.100(d) and there is the potential for filing over protest):		
	(a) Does the application contain a completed application form as required under 314.50 or 314.55?	X	
	(b) On its face, does the application contain the sections of an application required by regulation and Center guidelines?	X	
	(c) Has the applicant submitted a complete environmental assessment which addresses each of the items specified in the applicable format under 25.31 or has the applicant submitted evidence to establish that the product is subject to categorical exclusion under 25.24 of the CFR?	X	
	(d) On its face, is the NDA formatted in compliance with Center guidelines including integrated efficacy and safety summaries?		X (Not Applicable)
	(e) Is the NDA indexed and paginated?	X	

		YES	NO
(f)	On its face, is the NDA legible?	X	
(g)	Has the applicant submitted all required copies of the submission and various sections fo the submission?	X	
(h)	Has the sponsor submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?	X	
(I)	Does the application contain a statement that all nonclinical laboratory studies was conducted in compliance with the requirements set forth in Part 58 or a statement why a study was not conducted in compliance with those requirements? (GLP statement)		X
(j)	If required, has the applicant submitted carcinogenicity studies?	(None submitted)	X
(k)	On its face, does the application contain at least two adequate and well-controlled clinical trials? (Clinical section references OTC monograph)		X
(l)	Does the application contain a statement that all clinical trials were conducted in accord with the IRB/ Declaration of Helsinki provisions of the CFR? (Not applicable)		X
(m)	Have all articles/study reports been submitted in English or translated into English?	X	
(n)	Has the applicant submitted draft labeling in compliance with 210.56 and 210.57 of the CFR?	X	
(o)	Has the applicant submitted the required FRAUD POLICY (Debarment Certification) notice?		X
(p)	Has the applicant submitted copies of all package inserts (or their equivalent) from all countries in which this product has been previously approved for marketing? Have all non-English package inserts been translated?		X
(q)	Has the applicant stated that the integrated summary of safety includes all safety data for this product of which they are aware from all sources, domestic and foreign? What is the cut-off date for the preparation of the ISS?	(Not Applicable)	

		YES	NO
(r)	If this is a CANDA submission, has the applicant submitted to the archival NDA that the text, tables, and data in the CANDA and the archival hardcopy NDA are identical? If they are not identical, is there a letter to the archival NDA that specifies distinctly ALL of the differences in the two submissions?	(Not Applicable)	
(3)	From a project management perspective, is this NDA fileable? If "No", please state on the reverse side why it is not.	X	

Comments: The following were not submitted and are judged to be not applicable:

1. Biopharm 2. Statistical 3. Microbiology 4. Case Report Forms
5. Integrated safety and efficacy summaries.

Provided that additional carcinogenicity studies are not required, the NDA is judged to be fileable from the Project Manager's perspective. However, the applicant will be requested to submit the following: 1) GLP statement; 2) Debarment Certification; and 3) Package inserts if applicable.
(foreign marketing)

/S/
Project Manager

10/19/98
Date

/S/
Supervisory Project Manager

10/20/98
Date

APPEARS THIS WAY
ON ORIGINAL

d NDA 21-043

45 DAY MEETING CHECKLIST

:ABILITY:

On initial overview of the NDA application:	YES	NO

MICROBIOLOGY:

(1) On its face, is the microbiologic section of the NDA organized in a manner to allow substantive review to begin?	✓	
(2) Is the microbiologic section of the NDA indexed and paginated in a manner to allow substantive review to begin	✓	
(3) On its face, is the microbiologic section of the NDA legible so that substantive review can begin?		
(4) On its face, has the applicant <u>submitted</u> *in vitro* data in necessary quantity, using necessary clinical and non-clinical strains, and using necessary numbers of approved laboratories to meet current divisional standard for approvability of the submitted draft labeling?	✓	
(5) Has the applicant <u>submitted</u> any required animal model studies necessary for approvability of the product based on the submitted draft labeling?	N/A	
(6) Has the applicant <u>submitted</u> draft breakpoint and interpretive criteria in a manner consistent with contemporary standards, in a manner which attempts to correlate criteria with clinical results of NDA studies, and in a manner to allow substantive review to begin?	N/A	
(7) Has the applicant <u>submitted</u> all special studies/data requested by the Division during pre-submission discussions?	N/A	
(8) Has the applicant submitted draft labeling consistent with 201.56 and 201.57, current divisional policy, and the design of the development package?	✓	

(9) If necessary for this product, has the applicant submitted the sterilization procedures and documentation required for approval of the manufacturing and controls elements of this NDA?

N/A

(9) From a microbiology perspective, is this NDA fileable? If "no", please state on reverse why it is not.

✓

APPEARS THIS WAY
ON ORIGINAL

APPEARS THIS WAY
ON ORIGINAL

/S/ 10/20/98
Reviewing Microbiology Officer

/S/ 10/21/98
Supervisory Microbiology Officer

Memorandum of Meeting Minutes

Meeting Date:	October 21, 1998
Time:	11:00 a.m.
Location:	Corporate Building, Room S200B
Type of Meeting:	Fileability/Forward Planning Meeting
Product:	Rid Mousse
Sponsor:	Soltec Research
Project Manager:	Babette Merritt

FDA Participants:

Debra Bowen, M.D., Deputy Director, ODE-V, HFD-105
Linda M. Katz, M.D., M.P.H., Deputy Director, DOTCDP, HFD-560
Linda Hu, M.D., Medical Officer, DOTCDP, HFD-560
James R. King, Microbiologist, HFD-520
Lynnda L. Reid, Pharmacologist, DDDDP, HFD-540
Charolette Yaciw, Chemist, DONDC, HFD-550
Tony DeCamp, Chemist, DONDC, HFD-830
Michael Benson, Regulatory Review Pharmacist, HFD-560
Maria R. R. Cook, M.B.A., Chief, Project Management Staff, HFD-560

Objective:

To determine if the application for Rid Mousse is fileable.

Discussion:

- The FDA microbiologist stated that the studies (in terms of in-vitro or kill) are adequate, and therefore the microbiology is considered fileable.
- The FDA pharmacologist indicated that assays alone are deemed not acceptable. The strain of lice being assesssed is a body louse created in the laboratory which does not mimic the actual use (example when put on corduroy). There are no data on the breaking down of ingredients. Adequate data have been submitted for review, however, approvability is a critical issue.

- It was then concluded that if the in-vitro meets the specifications, then it is acceptable. The monograph doesn't allow for aerosolized products.

- The FDA chemist indicated that from the chemistry point of view, the application is fileable. There are review issues for the IR letter. The sponsor has formulated to the maximum of the OTC monograph concentration range for the active ingredients to be delivered. There is not enough room for manufacturing deviations, or analytical variations, and concern about what's on the skin and how it breaks down. For the they need to include a flammability statement. The sponsor is referencing the monograph to support safety and efficacy. The applicant needs to submit case report forms for adverse events reported for the aerosol formulation from previous manufacturing.

- The Medical Officer indicated that no clinical data were submitted. The Agency needs additional information on 11 reports.

- The Pharmacist pointed out that the direction, USE ON DRY HAIR was capitalized and cited a Pharmacy Times article stating that water tends to close the operculum of the louse to inhibit inflow of the active ingredients. At that time, the article was sent for consult to HFD-540.

- In follow-up, the HFD-560 chemist said that the formulation contains a great deal of water.

Conclusion: The decision was made that the application is fileable. All checklists will be submitted to the Project Manager.

Action Items: The Project Manager will complete the IR letter, Gantt chart and set up monthly team meetings.

/S/

Babette Merritt, Project Manager
Minutes Preparer

/S/

Maria Rossana R. Cook, M.B.A.
Concurrence

OTC CONSULT

Review and Evaluation of Fileability of
Pharmacology and Toxicology Data
Division of Dermatologic and Dental Drug Products (HFD-540,)

NDA 21-043

Drug: Rid Mousse (Pyrethrins 0.33%; Piperonyl Butoxide 4.0%)
Sponsor: SOLTEC RESEARCH PTY LTD

Fileability Date: October 21, 1998
Date Assigned: October 9, 1998
Review Draft Completed: October 15, 1998

FILEABILITY:

On initial overview of the NDA application:		Yes/No
1	On its face, it the pharmacology section of the NDA organized in a manner to allow substantive review to begin?	Yes
2	Is the pharmacology section of the NDA indexed and paginated in a manner to allow substantive review to begin?	Yes
3	On its face, is the pharmacology section of the NDA legible so that substantive review can begin?	Yes
4	Are all required(*) and requested IND studies completed and submitted in this NDA (carcinogenicity, mutagenicity, teratogenicity*, effects on fertility, juvenile studies, acute and adult studies*, chronic adult studies*, maximum tolerated dosage determination, dermal irritancy, ocular irritancy, photocarcinogenicity, animal pharmacokinetic studies, etc)?	N/A
5	If the formulation to be marketed is different from the formulation used in the toxicology studies, has the sponsor made an appropriate effort to either repeat the studies using the to be marketed product or to explain why such repetition should not be required?	N/A
6	Are the proposed labeling sections relative to pharmacology appropriate (including human dose multiples expressed in either mg/m^2 or comparative serum/plasma levels) and in accordance with 201.57?	N/A
7	Has the sponsor submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?	N/A
8	On its face, does the route of administration used in the animal studies appear to be the same as the intended human exposure route? If not, has the sponsor submitted a rationale to justify the alternative route?	See Comments

9	Has the sponsor submitted a statement(s) that all of the pivotal pharm/tox studies been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations?	N/A
10	Has the sponsor submitted a statement(s) that the pharm/tox studies have been performed using acceptable, state-of-the-art protocols which also reflect agency animal welfare concerns?	N/A
11	From a pharmacology perspective, is this NDA fileable? If "no", please state below why it is not.	See Comments

Pharmacology/Toxicology Comments on Fileability: Only *in vitro* pediculicidal and ovicidal assays were submitted to support claims of bioequivalence and efficacy. Generally, these assays are used as screening studies performed prior to demonstrating efficacy in human clinical trials. Alone, these assays are deemed inadequate to support either bioequivalence or efficacy for the following reasons:

1) The Sponsors have not submitted any justification or rationale for use of the *in vitro* assays as a surrogate for clinical trials; or the use of the body lice strain *Pediculus humanus humanus* as a surrogate for wild type head, pubic or body lice.

2) The strain of lice used in the *in vitro* study, *Pediculus humanus humanus*, is a body louse perpetuated in the laboratory. As such, it lacks the robust nature of wild type strains and cannot be used to evaluate either resistance or sensitivity.

3) The surrogate *in vitro* assay does not mimic actual use, e.g., 2 minute stirring prior to application to body lice attached to corduroy, vs direct application to dry hair for the treatment of hair lice.

4) The Sponsors did not provide any data on the time necessary for the mousse matrix to "break down", releasing the active ingredients, or any 'actual use data' to insure 100 % mortality within the specified 10 minute treatment period allowable in the pediculicide monograph label.

/S/ 10/19/98

Lynnda Reid, Ph.D.
Pharmacologist/Toxicologist

Date

/S/ 10/20/98

Abby Jacobs, Ph.D.
Pharmacology/Toxicology Team Leader

Date

NDA Number: 21-043 **Applicant:** Soltec **Drug Name:** Rid Mousse

Have all DMF References been Identified?

DMF Number	Holder	Description	LOA Included	Status

Summary of Sites Used

Drug substance:

Manufacturing and In-process Controls:

Finished product release:

Pfizer Consumer Health Care
Research & Development
100 Jefferson Road
Parsippany, NJ 07054
[redacted]
Contact: Richard Norgard, Director Quality Control & Assurance; phone (973) 952-7600
Status statement: ready
Source: Form 356h attachment
Comments: Last inspection 5/98, control lab profile not listed
Page 074 (summary section) states that [redacted] may also do release testing This is not confirmed in the drug product section.

Stability testing:

Pfizer Consumer Health Care
400 Webro Road
Parsippany, NJ 07054
CFN: not in database
Status statement: none
Source: NDA page 074 (summary)
Comments: Not listed in 356h attachment
Stability testing site not specified in stability section.

Stability samples storage:

[redacted]

Additional Comments:

1. It has been decided that under 21 CFR 330.11, the drug substances (DS) can be referenced to the monograph product. Therefore, the information submitted (controls only) is adequate.

2. It is stated in several places that [redacted] has submitted DMFs for the drug substances. A search of the DMF database found no hits for [redacted] none for pyrethrins and one

for piperonyl butoxide [redacted] Since the DS is referenced to the monograph product, these DMFs are not needed.

3. The incorrect CFR citation was provided in the Summary for the claim of categorical exclusion for environmental assessment. Soltec referenced 25.24 which was eliminated in the rewrite. They should submit a statement as provided for in 25.15(d) in the current 21 CFR if they qualify under 25.31. The part 12 which was listed in the index as containing the EA information is missing from the CMC copy.

4. Letters of Authorization for DMFs should be sent to the DMF, not to the reviewing division. The correct address is

   Food and Drug Administration
   Center for Drug Evaluation and Research
   Central Document Room
   12229 Wilkins Avenue
   Rockville, Maryland 20852

5. There are discrepancies between the Summary and the main body of the NDA especially regarding the facilities which will be used for release and stability testing. Soltec should provide a list with the name, full street address and responsibilities for each facility used, including all testing laboratories. The name and address should be for the site which actually performs each task.

/

45 DAY MEETING CHECKLIST

EABILITY: Rid Mouse - NDA division

On initial overview of the NDA application:	YES	NO
CLINICAL:		
(1) On its face, is the clinical section of the NDA organized in a manner to allow substantive review to begin?	N.A.	
(2) Is the clinical section of the NDA indexed and paginated in a manner to allow substantive review to begin?	N.A.	
(3) On its face, is the clinical section of the NDA legible so that substantive review can begin?	N.A.	
(4) If needed, has the sponsor made an appropriate attempt to determine the most appropriate dosage and schedule for this product (*i.e.*, appropriately designed dose-ranging studies)?	N.A.	
(5) On its face, do there appear to be the requisite number of adequate and well-controlled studies in the application?	N.A.	
(6) Are the pivotal efficacy studies of appropriate design to meet basic requirements for approvability of this product based on proposed draft labeling?	N.A.	
(6) Are all data sets for pivotal efficacy studies complete for all indications (infections) requested?	N.A	
(7) Do all pivotal efficacy studies appear to be adequate and well-controlled within current divisional policies (or to the extent agreed to previously with the applicant by the Division) for approvability of this product based on proposed draft labeling?	N.A.	
(8) Has the applicant submitted line listings in a format to allow reasonable review of the patient data? Has the applicant submitted line listings in the format agreed to previously by the Division?	N.A.	

(9) Has the application submitted a rationale for assuming the applicability of foreign data (disease specific microbiologic specific) in the submission to the US population?

N.A.

(10) Has the applicant submitted all additional required case record forms (beyond deaths and drop-outs) previously requested by the Division?

applicant needs to submit case report forms for adverse events reported for the aerosol formulation from previous marketing

(11) Has the applicant presented the safety data in a manner consistent with Center guidelines and/or in a manner previously agreed to by the Division?

(12) Has the applicant presented a safety assessment based on <u>all</u> current world-wide knowledge regarding this product?

(13) Has the applicant submitted draft labeling consistent with 201.56 and 201.57, current divisional policies, and the design of the development package?

has submitted draft labeling

(14) Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions with the sponsor?

yes, for clinical section

(15) From a clinical perspective, is this NDA fileable? If "no", please state below why it is not.

yes, but needs to submit more. Sponsor is referencing the monograph to support safety and efficacy.

If certain claims are not filable, please state which claims they are and why they are not filable.

APPEARS THIS WAY
ON ORIGINAL

/S/

viewing Medical Officer

/S/

isory Medical Officer

APPEARS THIS WAY
ON ORIGINAL