

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**20-784**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

**RHÔNE-POULENC RORER PHARMACEUTICALS INC.**

500 ARCOLA ROAD  
P.O. BOX 1200  
COLLEGEVILLE, PA 19426-0107  
TEL. 610-454-8000

**New Drug Application #20-784  
Form FDA 356h  
Item 13**

**Nasacort® HFA-134a  
Nasa! —  
(triamcinolone acetonide)**

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**Item 13: *Patent Information***

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Patent Information for the Nasacort ® HFA-134a Nasa! — (triamcinolone acetonide) original New Drug Application is found on the following pages.

**APPEARS THIS WAY  
ON ORIGINAL**

### **Item 13 -Patent/Exclusivity Information**

- 1) Active Ingredient(s): triamcinolone acetonide
- 2) Strength(s): 55 mcg/actuation
- 3) Trademark: N/A
- 4) Dosage Form (Route of Administration): Metered dose inhaler (Nasal)
- 5) Application Firm Name: Rhône-Poulenc Rorer Pharmaceuticals Inc.
- 6) IND Number: 43,841
- 7) NDA Number: 20-784
- 8) Approval Date: N/A
- 9) Exclusivity -- date first ANDA could be submitted or approved and length of exclusivity period: Pursuant to Section 505(j)(4)(D)(iii) and 505(c)(3)(D)(iii) of the Federal Food, Drug and Cosmetic Act, no ANDA may be approved with an effective date which is prior to 3 years after the date of approval of this application.
- 10) Applicable patent numbers and expiration date of each: N/A
- 11) To the best of our knowledge, each of the clinical investigations included in this application meets the definition of "new clinical investigation" set forth in 21 CFR 314.108(a).

A list of all published studies or publicly available reports of clinical investigations known to the applicant through a literature search that are relevant to the conditions for which we are seeking approval is attached. We have thoroughly searched the scientific literature and, to the best of our knowledge, the list is complete and accurate and, in our opinion, such published studies or publicly available reports do not provide a sufficient basis for the approval of the conditions for which we are seeking approval without reference to the new clinical investigation(s) in the application. The reasons that these studies or reports are insufficient are presented in the attachment as well.

### **Item 13- Patent/ Exclusivity Information**

A search of the Medline database for any reports or clinical investigations of triamcinolone acetonide with the new non-CFC propellant revealed no publicly available reports on this subject. Therefore, the studies conducted by Rhône-Poulenc Rorer, contained within this submission, meet the definition of "new clinical investigation" set forth in 21 CFR 314.108(a).

### Item 13. Patent Information

- |                         |     |
|-------------------------|-----|
| 1) Patent number        | N/A |
| 2) Date of expiration   | N/A |
| 3) Type of patent       | N/A |
| 4) Name of patent owner | N/A |
| 5) U.S. representative  | N/A |

The applicant believes that there are no patents which claim the drug or the drug product or which claim a method of using the drug product and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product

Signed:

Name:

Title:



Ross J. Oehler

Assistant General Counsel, Patents and Trademarks  
Rhône-Poulenc Rorer Pharmaceuticals Inc.

Date: 11/15/96

**RHÔNE-POULENC RORER PHARMACEUTICALS INC.**

500 ARCOLA ROAD  
P.O. BOX 1200  
COLLEGEVILLE, PA 19426-0107  
TEL. 610-454-8000

**New Drug Application #20-784  
Form FDA 356h  
Item 14**

**Nasacort® HFA-134a  
Nasal —  
(triamcinolone acetonide)**

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**Item 14: *Patent Certification***

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Patent Certification is not applicable for the Nasacort® HFA-134a Nasal —  
(triamcinolone acetonide) original New Drug Application.

## PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA # 20-784 Supplement Type (e.g. SE5): \_\_\_\_\_ Supplement Number: \_\_\_\_\_

Stamp Date: October 7, 2003 Action Date: April 7, 2004

HFD 570 Trade and generic names/dosage form: Nasacort (triamcinolone acetonide) HFA

Applicant: Aventis Therapeutic Class: 3S

Indication(s) previously approved:

**Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.**

Number of indications for this application(s): 2

Indication #1: Seasonal allergic rhinitis

Is there a full waiver for this indication (check one)?

Yes: Please proceed to Section A.

No: Please check all that apply:  Partial Waiver  Deferred  Completed  
NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

### Section A: Fully Waived Studies

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: \_\_\_\_\_

*If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.*

### Section B: Partially Waived Studies

Age/weight range being partially waived:

Min \_\_\_\_\_ kg \_\_\_\_\_ mo. 0 yr. \_\_\_\_\_ Tanner Stage \_\_\_\_\_  
Max \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. 2 Tanner Stage \_\_\_\_\_

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: \_\_\_\_\_

*If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is*

complete and should be entered into DFS.

**Section C: Deferred Studies**

Age/weight range being deferred:

Min \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. >2 Tanner Stage \_\_\_\_\_  
Max \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. <6 Tanner Stage \_\_\_\_\_

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other: \_\_\_\_\_

Date studies are due (mm/dd/yy): April 1, 2007

*If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.*

**Section D: Completed Studies**

Age/weight range of completed studies:

Min \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. 6 Tanner Stage \_\_\_\_\_  
Max Adult kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. \_\_\_\_\_ Tanner Stage \_\_\_\_\_

Comments:

**Attachment A**

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: Perennial Allergic Rhinitis

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
- No: Please check all that apply:  Partial Waiver  Deferred  Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

**Section A: Fully Waived Studies**

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: \_\_\_\_\_

*If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.*

**Section B: Partially Waived Studies**

Age/weight range being partially waived:

Min _____	kg _____	mo. <u>0</u>	yr. _____	Tanner Stage _____
Max _____	kg _____	mo. _____	yr. <u>&lt;2</u>	Tanner Stage _____

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: \_\_\_\_\_

*If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.*

**Section C: Deferred Studies**

Age/weight range being deferred:

Min \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. >2 Tanner Stage \_\_\_\_\_  
Max \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. <6 Tanner Stage \_\_\_\_\_

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: \_\_\_\_\_

Date studies are due (mm/dd/yy): April 1, 2007

*If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.*

**Section D: Completed Studies**

Age/weight range of completed studies:

Min \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. 6 Tanner Stage \_\_\_\_\_  
Max Adult kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. \_\_\_\_\_ Tanner Stage \_\_\_\_\_

Comments:

NDA 20-784

Page 5

This page was completed by:

*{See appended electronic signature page}*

---

Regulatory Project Manager

cc: NDA 20-784  
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG  
DEVELOPMENT, HFD-960, 301-594-7337.

(revised 10-14-03)

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**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
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/s/

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Colette Jackson  
4/5/04 03:16:57 PM

# PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

<b>NDA/BLA Number:</b>	<u>20784</u>	<b>Trade Name:</b>	<u>NASACORT HFA NASAL</u> <u>(TRIAMCINALONE)</u>
<b>Supplement Number:</b>		<b>Generic Name:</b>	<u>TRIAMCINOLONE ACETONIDE</u>
<b>Supplement Type:</b>		<b>Dosage Form:</b>	<u>Spray, Metered; Nasal</u>
<b>Regulatory Action:</b>	<u>AE</u>	<b>Proposed Indication:</b>	<u>for the nasal treatment of seasonal and perennial allergic rhinitis symptoms in adults and children 6 years of age and older</u>

**ARE THERE PEDIATRIC STUDIES IN THIS SUBMISSION?**

YES, Pediatric data exists for at least one proposed indication which supports pediatric approval

**What are the INTENDED Pediatric Age Groups for this submission?**

<input type="checkbox"/> NeoNates (0-30 Days )	<input type="checkbox"/> Children (25 Months-12 years)
<input type="checkbox"/> Infants (1-24 Months)	<input type="checkbox"/> Adolescents (13-16 Years)
<input checked="" type="checkbox"/> Other Age Groups (listed): <u>6 years and older</u>	

<b>Label Adequacy</b>	<u>Adequate for SOME pediatric age groups</u>
<b>Formulation Status</b>	-
<b>Studies Needed</b>	-
<b>Study Status</b>	-

Are there any Pediatric Phase 4 Commitments in the Action Letter for the Original Submission? NO

COMMENTS:

This Page was completed based on information from a PROJECT MANAGER/CONSUMER SAFETY OFFICER, SANDRA BARNES



Signature

2/3/00

Date



April 7, 2004

Badrul Chowdhury, M.D., Ph.D.  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Pulmonary Drug Products (HFD-570)  
Document Control Room 10B-03  
5600 Fishers Lane  
Rockville, MD 20857-1706

**NDA 20-784**  
**Nasacort<sup>®</sup> (triamcinolone acetonide) HFA**  
**Nasal Inhaler**

**TYPE OF SUBMISSION – OTHER**  
**Proposed Labeling for Nasacort HFA**

Dear Dr. Chowdhury,

Reference is made to the above referenced NDA, submitted to the Agency on December 17, 1996. Reference is made to proposed labeling for Nasacort HFA submitted to the Agency on March 30, 2004. Reference is made to a telefax received from the Agency on April 5, 2003 providing comments for labeling revisions. Reference is made to a teleconference held on April 6, 2004 between the Ms. Colette Jackson, Dr. Badrul Chowdhury, and Dr. Peter Starke (FDA) and Dr. Eric Floyd (Aventis) during which labeling comments on proposed labeling for Nasacort HFA were discussed. Reference is further made to a telephone conversation between Colette Jackson (FDA) and Dr. Eric Floyd (Aventis) on April 7, 2004 during which typographical corrections were identified for labeling. Aventis is hereby providing revised labeling based upon those discussions.

This labeling submission is provided in paper format. As an attachment to this letter, we are providing the following:

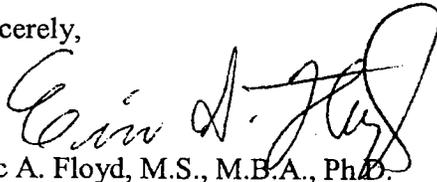
- Proposed Labeling
- Annotations to Proposed Labeling

07 April 2004  
NDA 20-784  
Page -2-

We consider the information included in this submission to be a confidential matter, and request that the Food and Drug Administration not make its content, nor any future communications in regard to it, public without first obtaining the written permission of Aventis Pharmaceuticals.

If you have any questions or need additional information please contact Dr. Eric A. Floyd (908) 231-2474 or, in my absence, Dr. Steve Caffé (908) 231-5863.

Sincerely,

A handwritten signature in black ink, appearing to read "Eric A. Floyd". The signature is fluid and cursive, with a large loop at the end.

Eric A. Floyd, M.S., M.B.A., Ph.D.  
Sr. Director, US Regulatory Affairs  
Aventis Pharmaceuticals

Attch: Proposed Labeling

A

38 Page(s) Withheld

           Trade Secret / Confidential

  /   Draft Labeling

           Deliberative Process

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338  
Expiration Date: August 31, 2005  
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, Parts 314 & 601)

FOR FDA USE ONLY.

APPLICATION NUMBER  
20-784

APPLICANT INFORMATION

NAME OF APPLICANT Aventis Pharmaceuticals Inc	DATE OF SUBMISSION 4/7/04
TELEPHONE NO. (Include Area Code) 908-231-4000	FACSIMILE (FAX) Number (Include Area Code) 908-541-5274
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Aventis Pharmaceuticals Inc Bridgewater, NJ 08807-0890 Phone: 908-304-7000 Fax: 908-541-5274	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Aventis Pharmaceuticals Inc Bridgewater, NJ 08807-0890 Phone: 908-304-7000 Fax: 908-541-5274

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) Triamcinolone acetonide	PROPRIETARY NAME (trade name) IF ANY Nasacort® HFA Nasal	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) RG 5029, RGW 5029, triamcinolone acetonide, Nasacort HFA-134a, Nasacort HFC-134a, Nasacort-134a, 9-Fluoro-11β, 16a, 17, 21-tetrahydroxypregena-1 4-diene-3, 20-dione cyclic 13, 17-acetal with acetone, C 24H31 P06	CODE NAME (If any)	
DOSAGE FORM: Aerosol Inhaler	STRENGTHS: 55 mcg actuation	ROUTE OF ADMINISTRATION: Inhaler

PROPOSED INDICATION(S) FOR USE:

Nasal treatment of seasonal and perennial allergic rhinitis symptoms

PRODUCT DESCRIPTION

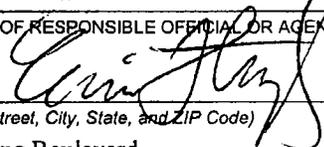
APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)
IF AN ANDA, OR 505(b)(2), 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) <input type="checkbox"/> ORIGINAL APPLICATION <input type="checkbox"/> AMENDMENT TO PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input checked="" type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)
REASON FOR SUBMISSION Draft Labeling
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)  
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.

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

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This application contains the following items: <i>(Check all that apply)</i>	
<input type="checkbox"/>	1. Index
<input checked="" type="checkbox"/>	2. Labeling <i>(check one)</i> <input checked="" type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input checked="" type="checkbox"/>	20. OTHER <i>(Specify)</i> Draft Labeling

<b>CERTIFICATION</b>		
<p>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:</p> <ol style="list-style-type: none"> <li>1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.</li> <li>2. Biological establishment standards in 21 CFR Part 600.</li> <li>3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.</li> <li>4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.</li> <li>5. Regulations on making changes in application in FD&amp;C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.</li> <li>6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.</li> <li>7. Local, state and Federal environmental impact laws.</li> </ol> <p>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 reviewed and, to the best of my knowledge are certified to be true and accurate.  <b>Warning:</b> A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.</p>		
SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE:
	Eric A. Floyd, Ph.D, Sr. Director US Regulatory Affairs	4/7/04
ADDRESS <i>(Street, City, State, and ZIP Code)</i>		Telephone Number
200 Crossing Boulevard P. O. Box 6890 Bridgewater, NJ 08807-0890		( 908 ) 231-2474



May 6, 2004

Food and Drug Administration  
Central Document Room  
5901-B Ammendale Road  
Beltsville, MD 20705

**NDA 20-784**  
**Nasacort® (triamcinolone acetonide) HFA**  
**Nasal Inhaler**

**FPL for Approved NDA 20-784**

Dear Dr. Chowdhury,

Reference is made to NDA 20-784 for Nasacort® (triamcinolone acetonide) HFA Nasal Inhaler and to the April 7, 2004 approval letter for the indication of the treatment of the nasal symptoms of allergic rhinitis (seasonal and perennial) in adults and children 6 years of age and older.

An electronic version of the FPL is hereby being provided according to the guidance for industry titled "*Providing Regulatory Submissions in Electronic Format – NDA.*"

Aventis considers the information included in this submission to be a confidential matter, and request that the Food and Drug Administration not make its content, nor any future communications in regard to it, public without first obtaining the written permission of Aventis Pharmaceuticals.

If you have any questions or need additional information please contact Dr. Eric A. Floyd (908) 231-2474 or, in my absence, Dr. Steve Caffè (908) 231-5863.

Sincerely,

A handwritten signature in black ink that reads "Eric A. Floyd".

Eric A. Floyd, M.S., M.B.A., Ph.D.  
Sr. Director, US Regulatory Affairs  
Aventis Pharmaceuticals

Enclosure: CD-ROM



April 6, 2004

Badrul Chowdhury, M.D., Ph.D.  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Pulmonary Drug Products (HFD-570)  
Document Control Room 10B-03  
5600 Fishers Lane  
Rockville, MD 20857-1706

**NDA 20-784**  
**Nasacort<sup>®</sup> (triamcinolone acetonide) HFA**  
**Nasal Inhaler**

**TYPE OF SUBMISSION – OTHER**  
**Proposed Labeling for Nasacort HFA**

Dear Dr. Chowdhury,

Reference is made to the above referenced NDA, submitted to the Agency on December 17, 1996. Reference is made to proposed labeling for Nasacort HFA submitted to the Agency on March 30, 2004. Reference is made to a telefax received from the Agency on April 5, 2003 providing comments for labeling revisions. Reference is further made to a teleconference held on April 6, 2004 between the Ms. Colette Jackson, Dr. Badrul Chowdhury, and Dr. Peter Starke (FDA) and Dr. Eric Floyd (Aventis) during which labeling comments on proposed labeling for Nasacort HFA were discussed. Aventis is hereby providing revised labeling based upon those discussions.

This labeling submission is provided in paper format. As an attachment to this letter, we are providing the following:

- Proposed Labeling
- Annotations to Proposed Labeling

06 April 2004

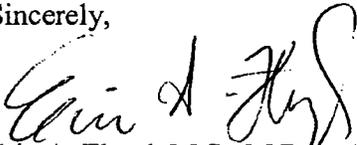
NDA 20-784

Page -2-

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Sincerely,

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Eric A. Floyd, M.S., M.B.A., Ph.D.  
Sr. Director, US Regulatory Affairs  
Aventis Pharmaceuticals

Attch: Proposed Labeling

B

34 Page(s) Withheld

       Trade Secret / Confidential

✓ Draft Labeling

       Deliberative Process

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**This is a representation of an electronic record that was signed electronically and  
this page is the manifestation of the electronic signature.**  
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/s/

-----  
Colette Jackson  
4/5/04 02:54:01 PM  
CSO



April 6, 2004

Badrul Chowdhury, M.D., Ph.D.  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Pulmonary Drug Products (HFD-570)  
Document Control Room 10B-03  
5600 Fishers Lane  
Rockville, MD 20857-1706

**NDA 20-784**  
**Nasacort<sup>®</sup> HFA Inhaler**  
**(triamcinolone acetonide)**  
**GENERAL CORRESPONDENCE**

**Subject: Phase-IV Commitment for One-Year Growth Study**

Dear Dr. Chowdhury,

Reference is made to Nasacort<sup>®</sup> HFA Inhaler (NDA 20-784) and to a teleconference between Ms. Colette Jackson, Dr. Badrul Chowdhury, and Dr. Peter Starke (FDA) and Dr. Eric Floyd (Aventis) on April 6, 2004. During the discussion, the Agency requested a Phase-IV commitment from the sponsor to conduct a one-year pediatric growth study with Nasacort<sup>®</sup> HFA Inhaler. Aventis Pharmaceuticals is hereby responding to the Agency's request.

**FDA Request:** Please provide a written commitment to the Agency to conduct a one-year pediatric growth study with Nasacort<sup>®</sup> HFA Inhaler. With the agreement, please provide timelines for the following:

- timeline for submission of a study protocol;
- timeline for study initiation;
- and a timeline for submission of a final study report to the Agency.

**Aventis Response:** With this letter, Aventis Pharmaceuticals hereby agrees to conduct a one-year pediatric growth study with Nasacort<sup>®</sup> HFA Inhaler. Aventis proposes the following timelines for protocol submission, study initiation, and completion of the one-year growth study:

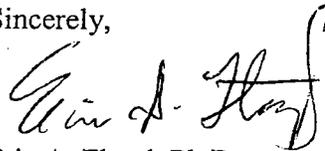
NDA 20-784  
Nasacort<sup>®</sup> HFA Inhaler  
Phase-IV Commitment for One-Year Growth Study  
April 6, 2004  
Page 2 of 2

- Aventis will submit to the Agency a study protocol to conduct a one-year pediatric growth study with Nasacort<sup>®</sup> HFA Inhaler
- Aventis Pharmaceuticals will initiate a one-year pediatric growth study with Nasacort<sup>®</sup> HFA Inhaler
- Based upon enrollment rates, Aventis Pharmaceuticals will submit a final study report to the Agency

We consider the information included in this submission to be a confidential matter, and request that the Food and Drug Administration not make its content, nor any future communications in regard to it, public without first obtaining the written permission of Aventis Pharmaceuticals.

If you have any questions or need additional information please contact Eric A. Floyd, Ph.D. (908) 231-2474 or, in my absence, Dr. Steve Caffè (908) 231-5863.

Sincerely,



Eric A. Floyd, Ph.D.  
Senior Director, Regulatory Affairs

Hard Copy – UPS Express  
Desk Copy (1): Ms. Colette Jackson, Regulatory Project Manager, HFD-570, Rm. 10B45

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338  
Expiration Date: August 31, 2005  
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, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

20-784

**APPLICANT INFORMATION**

NAME OF APPLICANT Aventis Pharmaceuticals Inc	DATE OF SUBMISSION 4/6/04
TELEPHONE NO. (Include Area Code) 908-231-4000	FACSIMILE (FAX) Number (Include Area Code) 908-541-5274
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): Aventis Pharmaceuticals Inc Bridgewater, NJ 08807-0890 Phone: 908-304-7000 Fax: 908-541-5274	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Aventis Pharmaceuticals Inc Bridgewater, NJ 08807-0890 Phone: 908-304-7000 Fax: 908-541-5274

**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) Triamcinolone acetonide	PROPRIETARY NAME (trade name) IF ANY Nasacort® HFA	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) RG 5029, RGW 5029, triamcinolone acetonide, Nasacort HFA-134a, Nasacort HFC-134a, Nasacort-134a, 9-Fluoro-11B, 16a, 17, 21-tetrahydroxypregena-1 4-diene-3, 20-dione cyclic 13, 17-acetal with acetone, C 24H31 P06	CODE NAME (If any)	
DOSAGE FORM: Aerosol Inhaler	STRENGTHS: 55 mcg actuation	ROUTE OF ADMINISTRATION: Inhaler
PROPOSED INDICATION(S) FOR USE: Nasal treatment of seasonal and perennial allergic rhinitis symptoms		

**PRODUCT DESCRIPTION**

APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)
IF AN ANDA, OR 505(b)(2), 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) <input type="checkbox"/> ORIGINAL APPLICATION <input type="checkbox"/> AMENDMENT TO PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input checked="" type="checkbox"/> OTHER
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)
REASON FOR SUBMISSION General Correspondence / Phase-IV Commitment
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)
NUMBER OF VOLUMES SUBMITTED      1      THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC
ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.) 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.

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

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This application contains the following items: <i>(Check all that apply)</i>	
<input type="checkbox"/>	1. Index
<input type="checkbox"/>	2. Labeling <i>(check one)</i> <input checked="" type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input checked="" type="checkbox"/>	20. OTHER <i>(Specify)</i> General Correspondence / Phase-IV Commitment

**CERTIFICATION**

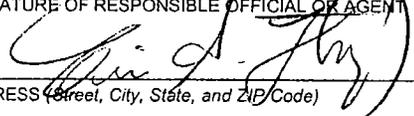
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. 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 Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 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 Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 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 reviewed 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 Eric A. Floyd, Ph.D, Sr. Director US Regulatory Affairs	DATE: 4/6/04
ADDRESS <i>(Street, City, State, and ZIP Code)</i> 200 Crossing Boulevard P. O. Box 6890 Bridgewater, NJ 08807-0890		Telephone Number ( 908 ) 231-2474



Food and Drug Administration  
Center for Drug Evaluation and Research  
OFFICE OF DRUG EVALUATION II

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE: April 5, 2004**

<b>To: Eric Floyd</b>	<b>From: Colette Jackson</b>
<b>Company: Aventis Pharmaceuticals</b>	Division of Pulmonary and Allergy Drug Products
<b>Fax number: 908-541-5274</b>	<b>Fax number: 301-827-1271</b>
<b>Phone number: 908-231-2474</b>	<b>Phone number: 301-827-9388</b>

**Subject: NDA 20-784 Nasacort HFA FDA proposed labeling**

**Total no. of pages including cover:** 19

**Comments: Dr. Floyd, see attached FDA proposed labeling in response to your March 30, 2004, proposed labeling. Please respond by 12 PM (noon) on April 6, 2004.**

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**Document to be mailed:** YES                      xNO

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C

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  /   Draft Labeling

           Deliberative Process



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation II

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** March 18, 2004

<b>To:</b> Dr. Eric Floyd	<b>From:</b> Colette Jackson
<b>Company:</b> Aventis Pharmaceuticals	Division of Pulmonary and Allergy Drug Products
<b>Fax number:</b> 908-541-5274	<b>Fax number:</b> 301-827-1271
<b>Phone number:</b> 908-231-2474	<b>Phone number:</b> 301-827-9388

**Subject:** NDA 20-784

**Total no. of pages including cover:** 23

**Comments:**

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**Document to be mailed:**                      YES                      xNO

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NDA 20-784  
Nasacort HFA

We are reviewing your submission dated February 11, 2004, and we have the following comments regarding your proposed product label:

1. We have revised your proposed labeling. In the copy of the label that follows, ~~strikethrough~~ characters represent deletions and underlined characters represent additions. Editorial comments and directions are included throughout the document, and appear in *blue italic font* enclosed in brackets starting with an 'Ed.'. A red X appears where a number needs to be inserted.
2. Submit both proposed and annotated versions of the PI. The annotated version should include the clinical trial number as well as the submission reference (NDA, Submission date, Submission number, Volume and Page numbers).

If there are any questions, please contact Ms. Colette Jackson, Project Manager, at 301-827-9388.

Enclosure: FDA proposed labeling.

D

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  ✓   Draft Labeling

       Deliberative Process

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/s/

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Colette Jackson  
3/18/04 01:58:44 PM  
CSO



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation II

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** January 13, 2004

<b>To:</b> Dr. Eric Floyd	<b>From:</b> Colette Jackson
<b>Company:</b> Aventis Pharmaceuticals	Division of Pulmonary and Allergy Drug Products
<b>Fax number:</b> 908-541-5274	<b>Fax number:</b> 301-827-1271
<b>Phone number:</b> 908-231-2474	<b>Phone number:</b> 301-827-9388
<b>Subject:</b> NDA 20-784	

**Total no. of pages including cover:** 3

**Comments:**

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**Document to be mailed:** YES xNO

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NDA 20-784  
Nasacort HFA

We are reviewing your new drug application for Nasacort HFA. Please acknowledge the following agreements by COB Wednesday, January 28, 2004.

1. Develop and institute an improved method for the control of the APSD of the drug product (DP) to replace the current \_\_\_\_\_ method. The new methodology will utilize the \_\_\_\_\_ and will be provided to the Agency in a Prior Approval Supplement, containing all pertinent validation data, supportive batch analysis data, and proposed associated APSD acceptance criteria by no later than March 30, 2004.

The Agency acknowledges your concern regarding the associated controls for the mass balance of emitted drug substance as collected by the \_\_\_\_\_ equipment. However, we would like to emphasize that since CI testing determinations will be based on a collection of *multiple* actuations from single inhaler units, CI mass balance controls are more closely related to mean dose delivery not individual dose delivery control limits. Address this issue and the apparent higher than target mass balance observed (average of \_\_\_\_\_ in the preliminary data presented (p. 024 of the Dec. 09, 2003, submission) in the upcoming PAS providing for implementation of the new specifications and test method.

2. Collect extractables data from \_\_\_\_\_, manufacturing campaigns \_\_\_\_\_ and to revise the acceptance criterion to reflect these data for the \_\_\_\_\_. This re-evaluation and revision will take place 18-24 months post approval.
3. Work with the supplier of the actuator, \_\_\_\_\_ to decrease the dimensional tolerance of the orifice diameter from the current allowed limits of \_\_\_\_\_. The improvements will be reported in the first annual report for the application. Be aware that \_\_\_\_\_ would also be required to update their supporting Drug Master File accordingly.

If there are any questions, please contact Ms. Colette Jackson, Project Manager, at 301-827-9388.

Initialed by: Jafari for Barnes/January 13, 2004  
Bertha/January 13, 2004

Finalized: CCJ/January 13, 2004

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/s/

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Colette Jackson  
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CSO

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NDA 20-784

Aventis Pharmaceuticals  
200 Crossing Boulevard  
P.O. Box 6890  
Bridgewater, NJ 08807-0890

Attention: Dr. Eric Floyd  
Senior Director, US Regulatory Affairs

Dear Dr. Floyd:

We acknowledge receipt on October 7, 2003, of your October 6, 2003, resubmission to your new drug application for Nasacort (triamcinolone acetonide) HFA Nasal

We consider this a complete, class 2 response to our September 23, 2003, action letter. Therefore, the user fee goal date is April 7, 2004.

If you have any questions, call Colette Jackson, Project Manager, at (301) 827-5584.

Sincerely,

*{See appended electronic signature page}*

Sandy Barnes  
Supervisory CSO  
Division of Pulmonary and Allergy Drug Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

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/s/

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Colette Jackson  
10/9/03 02:57:59 PM  
Signed for S. Barnes.



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation II

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** August 13, 2003

<b>To:</b> Dr. Eric Floyd	<b>From:</b> Colette Jackson
<b>Company:</b> Aventis Pharmaceuticals	Division of Pulmonary and Allergy Drug Products
<b>Fax number:</b> 908-541-5274	<b>Fax number:</b> 301-827-5586
<b>Phone number:</b> 908-231-2474	<b>Phone number:</b> 301-827-5584
<b>Subject:</b> NDA 20-784	

**Total no. of pages including cover:** 3

**Comments:**

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NDA 20-784  
Nasacort HFA

We have completed the pharmacology/toxicology consultation of your submission dated March 21, 2003, and we have the following comment:

Provide data demonstrating that the following three potential \_\_\_\_\_  
leachables are not present in the formulation of the product during shelf-life:

\_\_\_\_\_ Alternatively, you may  
tighten your acceptance criteria for \_\_\_\_\_ and provide  
qualification data supporting the lower limits. For \_\_\_\_\_ additional  
qualification data are not needed if it is shown that the concentration of this potential  
leachable would not exceed \_\_\_\_\_ canister during product shelf life.

If there are any questions, please contact Ms. Colette Jackson, Project Manager, at  
301-827-5584.

Initialed by: Barnes/August 6, 2003  
Bertha/August 11, 2003  
Schroeder for Poochikian/August 11, 2003  
Pei/August 11, 2003  
Sun/August 11, 2003

Finalized: CCJ/August 13, 2003

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/s/

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Colette Jackson  
8/13/03 11:39:50 AM  
CSO

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Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation II

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** September 10, 2003

<b>To:</b> Eric Floyd	<b>From:</b> Colette Jackson
<b>Company:</b> Aventis Pharmaceuticals	Division of Pulmonary and Allergy Drug Products
<b>Fax number:</b> 908-541-5274	<b>Fax number:</b> 301-827-5586
<b>Phone number:</b> 908-231-2474	<b>Phone number:</b> 301-827-5584
<b>Subject:</b> NDA 20-784 July 18 <sup>th</sup> Meeting Minutes	

**Total no. of pages including cover:** 31

**Comments:**

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## MEMORANDUM OF MEETING MINUTES

**MEETING DATE:** July 18, 2003  
**TIME:** 2:00 PM  
**LOCATION:** Food and Drug Administration/Conference Room C  
**APPLICATION:** NDA 20-784/Nasacort HFA/Aventis Pharmaceuticals  
**TYPE OF MEETING:** CMC Meeting

### FDA ATTENDEES, DIVISION OF PULMONARY AND ALLERGY DRUG PRODUCTS

Badrul A. Chowdhury, MD, Ph.D., Division Director  
Craig Bertha, Ph.D., Chemistry Reviewer  
Guiragos Poochikian, Ph.D., Chemistry Team Leader  
Eric Duffy, Ph.D., DNDC II, Director  
Colette Jackson, Project Manager

### EXTERNAL CONSTITUENT ATTENDEES AND TITLES:

Mike Dey, Ph.D.,- Head of Respiratory Technology  
Steve Simmons, Ph.D., Vice-President Quality Operations, North America  
Mark Broughton, B.Sc.- Quality Manager for QC Analytics  
Dhiren N. Shah, Ph.D., Director, U.S. Drug Regulatory Affairs  
Eric Floyd, Ph.D., Senior Director, U.S. Regulatory Affairs

**BACKGROUND:** The purpose of this meeting is to discuss Aventis' proposal for specifications of drug product.

### DISCUSSION:



G

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**cc:**

**HFD-570/Chowdhury**

**HFD-570/Duffy**

**HFD-570/Poochikian**

**HFD-570/Bertha**

**Drafted: CCJ/July 21, 2003**

**Initialed: Bertha/August 14, 2003**

**Poochikian/August 25, 2003**

**Chowdhury/September 9, 2003**

**Finalized: CCJ/September 10, 2003**

**File: C:\My Documents\N20784\20784 july18 2003 MM.doc**

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/s/

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Colette Jackson  
9/10/03 10:27:16 AM

Minutes of Pre NDA Meeting

March 1, 1995

IND 43,841 Nasacort HFA-134a (triamcinolone acetonide)

Rhone-Poulenc Rorer

Meeting Attendees

FDA - Robert Temple, Martin Himmel, Cheung Kwong, Guirag Poochikian, Dale Koble, Virgil Whitehurst, Mehul Mehta, Gretchen Strange, Sandy Barnes

Rhone-Poulenc Rorer (RPR) - Judith Plon, Gary Feiss, Michael Doherty, Joseph Smith, Frank Deluccia, Greg Alcorn, Cynthia Obetz, Donald Heald, Vivian Alderfer, Steven Lerman, Lee Geiger

-----  
Background Packages dated June 21, 1994 and January 30, 1995.

Following opening remarks by RPR the meeting proceeded with technical discussions focusing on the issues outlined on pages 8 - 10 (paraphrased in *italics* below) of the January 30, 1995 submission.

CMC

Three pairs of large, hand-drawn, curved lines, resembling parentheses or brackets, arranged in two rows of three.

A.2. In previous discussion with the Pilot Drug Evaluation Staff an agreement was reached that \_\_\_\_\_ of RT, real time stability data for three batches of at least \_\_\_\_\_ scale, manufactured at the commercial site with \_\_\_\_\_ data available during the review period would be acceptable to file the NDA for Nasacort HFA-134a.

Dr. Koble stated that the FDA had concerns with the stability data, based upon trends in the accelerated data and had doubts whether \_\_\_\_\_ of data would be adequate at the time of filing. Dr. Poochikian added that he had seen a number of trends in \_\_\_\_\_ data which cause serious concern. No conclusion could be reach at this time; RPR will submit the \_\_\_\_\_ stability data to the IND for our review and a determination regarding the NDA filing.

Dr. Koble noted that the stability protocol changed between the June and the January package. RPR stated that this was due to ICH guidance. Dr. Koble stated that the testing should be done at 30°C/60%RH.

Dr. Koble had several other issues and concerns regarding the drug substance and drug product:

1. Particle size distribution data is needed for both the Drug Product and Drug Substance.
2. The USC (unit spray content) specifications are too broad and need to be tightened.
3. Spray pattern should be added as a release test and a one-time determination of plume geometry should be performed.

Additional CMC comments are attached.

#### PHARMACOLOGY

B.1. RPR requested FDA comment on the overall adequacy of the Pharm/Tox program.

Dr. Whitehurst stated that the \_\_\_\_\_ Nasacort \_\_\_\_\_ program was acceptable with the addition of either a two week or three month rat study as discussed at the \_\_\_\_\_

CLINICAL

C.1. Study RG-5029T-311 is intended to provide an assessment of the comparability of Nasacort HFA-134a with the original Nasacort Nasal Inhaler. RPR would like to discuss FDA's intended method of assessment.

Dr. Kwong presented assessment of comparability as:

1. Pharmacokinetics Comparison
2. Dose-ranging Efficacy Comparison
  - 14 mcg/day, 110 mcg/day and 440 mcg/day of each formulation
  - double blind, placebo control, double dummies, parallel group trial
  - primary variables will be the mean change from baseline for nasal stuffiness, nasal discharge, sneezing and nasal index for the 24-hour symptom scores

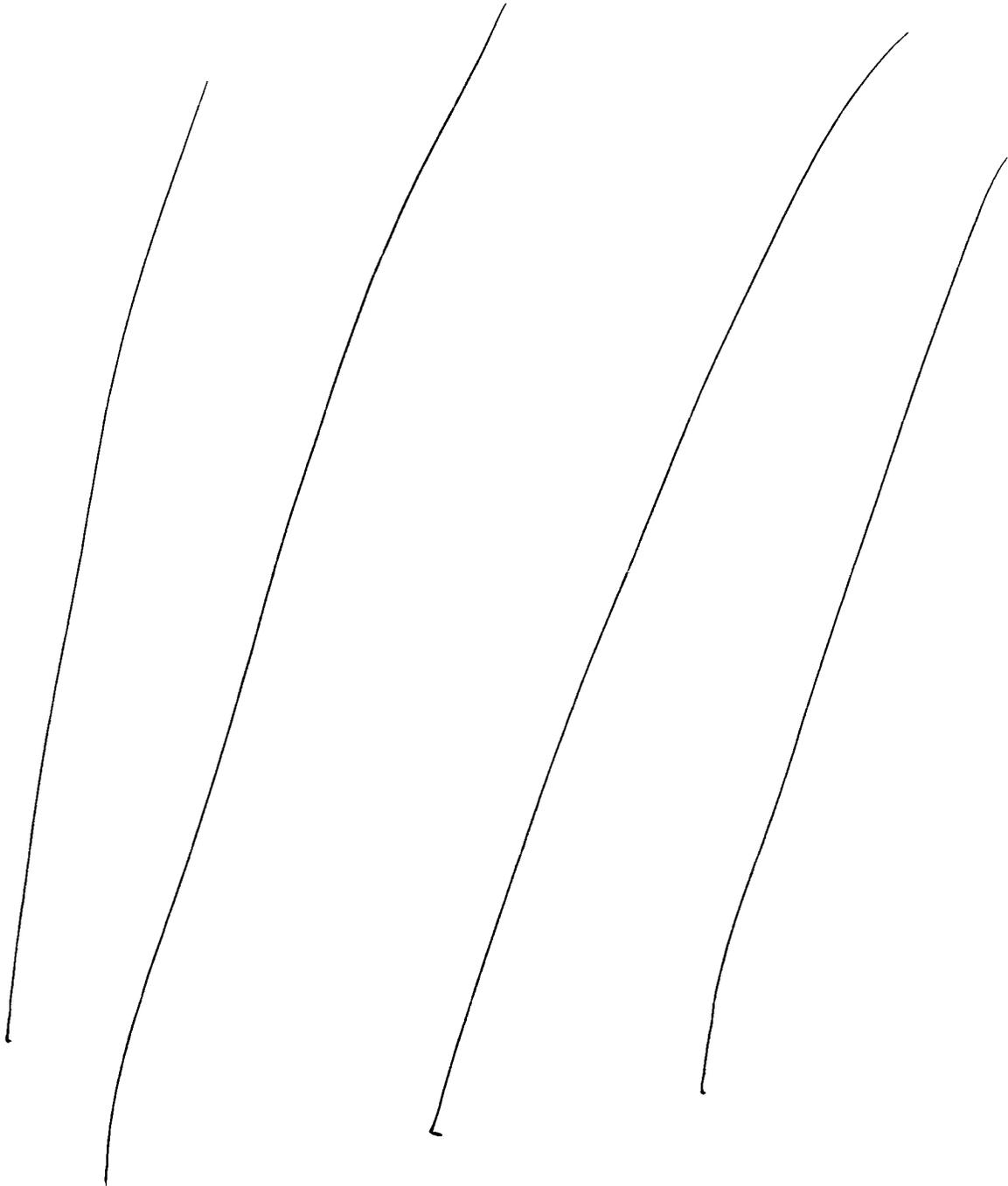
DOPDP - preferred Efficacy analysis:

1. Comparison across the two products using evaluable patients
    - a. comparability will be determined by inspection of both dose response curves in the same graph after taking into account the magnitude of the difference in response between the active treatment and the placebo. (no preset criteria)
    - b. Comparing the day of onset of action of each product
  2. Comparison within each formulation using intent-to-treat conventional analysis
    - for determining statistical significance in mean change from baseline of symptom scores for each dose as compared to placebo or other dose of the same product.
- C.2. RPR is proposing to submit the NDA with the first six months of safety data and submit the additional data in the four month Safety Update and additional data in a final safety update.

Drs. Kwong and Himmel indicated that this is acceptable as the Four Month Safety Update would include 300 patients with 6 month exposure @ 440 mcg and at least 150 of those patients with 12

IND 43,841  
Page 4

months exposure.



This concluded the meeting.

IND 43,841  
Page 5

Sandy Barnes  
Consumer Safety Officer

cc:

Orig IND 43,841  
Division File  
Meeting Attendees  
HFD-570CSchumaker  
HFD-570/SBarnes/4-6-95  
RD/initialed byVWhitehurst  
DKoble/11-16-95  
GPoochikian/11-17-95  
CKwong/1-22-96  
MHimmel/1-24-96

17

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Deliberative Process



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this page is the manifestation of the electronic signature.**  
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/s/

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Raymond Anthracite  
1/28/04 02:37:21 PM  
MEDICAL OFFICER

Record of Telephone Conversation

**Date:** Dec. 10, 2003  
**NDA No:** NDA 20-784  
**Product Name:** Nasacort HFA (triamcinolone acetonide) Nasal Aerosol

**Firm Name:** Aventis

**Telecon  
Initiated by:** Applicant

**Name and Title of Persons with whom conversation was held:**  
Eric Floyd, Ph.D., Regulatory Affairs

**Telephone No:** (908)-231-2474

**Background:** The Agency had issued a DR letter for CMC on 14-Nov-2003. This succeeded the last AE action that was made on 24-Sep-2003.

**Content of Telecon:** Dr. Floyd called to inform me that Aventis was submitting the response to the DR letter shortly and that Aventis has provided everything that the Agency had asked for. He noted that in terms of the status of DMF



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Craig M. Bertha, Ph.D.  
Chemistry Team Leader (Acting), HFD-570/820

cc:  
Orig. NDA 20-784  
HFD-570/Division File  
HFD-570/CBertha/12/16/03  
HFD-570/CJackson  
F/T by: CBertha 12/16/03

N20-983, Telecon of 3/14/01

doc. name 03-12-10.tel.doc

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ON ORIGINAL**

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this page is the manifestation of the electronic signature.**  
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/s/  
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Craig Bertha  
12/17/03 06:45:46 AM  
CHEMIST

Barnes

**Memorandum of Telephone Facsimile Correspondence**

Date: June 11, 1997  
To: Mary Allis Rauinbush  
Rhone-Poulenc Rorer

From: Cheung H. Kwong M.D., Ph.D.  
Medical Reviewer  
Division of Pulmonary Drug Product  
HFD-570  
FDA  
FAX (301) 827-1271  
TEL (301) 827-1062

Through: Peter Honig M.D. *PH* 6/11/97

Subject: Nasal septum adverse events associated with Nasacort HFA, NDA 20-784

Total number of pages faxed (including cover page): 3

We are providing the attached information via telephone facsimile for your convenience, to expedite the progress of your drug development program. This material should be viewed as unofficial correspondence. Please feel free to contact me if you have any questions regarding the contents of this transmission.

**THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.** If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone at (301) 827-1062 and return it to us at FDA, 5600 Fishers Lane, Room 10B-45, Rockville, Md. 20857, ATTN: HFD-570.

The table below contains information from Study 405 who experienced adverse event(s) at the nasal septum while on treatment with Nasacort HFA.

<i>Patient Allocation Number</i>	<i>Adverse Experience (synonym term)</i>	<i>Study Day that the Event was recorded*</i>
33	<i>nasal septal bleeding</i>	
40	<i>nasal septal bleeding</i>	
44	<i>nasal septal bleeding</i>	
49	<i>nasal septal bleeding</i>	
52	<i>nasal septal bleeding</i>	
53	<i>erosion of septum anterior</i>	
67	<i>nasal sepum ulceration</i>	
87	<i>ulceration septum nasal</i>	
127	<i>nasal septal bleeding</i>	
130	<i>nasal septal bleeding</i>	
134	<i>nasal septal bleeding</i>	
140	<i>nasal septal bleeding</i>	
141	<i>nasal septal bleeding</i>	
143	<i>nasal septal bleeding</i>	
341	<i>nasal septal bleeding</i>	
345	<i>nasal septal bleeding</i>	
348	<i>nasal septal bleeding</i>	
364	<i>ulceration septum nasal</i>	
369	<i>ulcer anterior nasal septum</i>	
405	<i>excoriation nasal septum</i>	
411	<i>excoriation nasal septum</i>	
427	<i>ulceration nasal</i>	

*Shaded cells: nasal septum injury (excluding bleeding)*

\* refer to the day that the event was recorded either by the patient or by the physician who did the physical examination.

Please provide the Study Day in the table above, and identify any other patients in this study who had adverse event(s) at the nasal septum that may have been omitted.

Cheung Kwong

Cheung H. Kwong, M.D., Ph.D.

Medical Reviewer

CC:  
HFD-570 Orig NDA 20-784  
HFD-570/ Division File for N20784  
HFD-570/ Barnes  
HFD-570/ Peter Honig

## RECORD OF TELEPHONE CONVERSATION

APPLICATION NUMBER: N20784

DATE: June 9, 1997

INITIATED BY:  APPLICANT  FDA

FIRM NAME: Rhone Poulenc Rorer

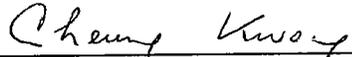
NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD:  
Mary Allis Raudinbush, Regulatory Affairs

TELEPHONE NUMBER: 610-454-8268

---

I requested the sponsor to provide me the following:

1. The p-value of the mean change from baseline of nasal index, as calculated from snap shot symptom scores, for Day 5-14 for all patients who took Nasacort HFA in Study 311.
2. The listing of all adverse events classified as 'unevaluable reaction' in the Summary of Adverse Clinical Experience table (Table 6 of Study 405 clinical report).
3. The listing of all patients who complained of nasal septal discomfort in table 6 who had nasal septal ulceration in their physical examination. On June 10, I asked her to provide us the list of all patients in Study 405 who had nasal septal ulceration regardless of whether they had complaint of nasal septal discomfort.

  
Cheung H. Kwong, M.D., Ph.D.  
Medical Review Officer

cc:

HFD-570/Division File for N20784

HFD-570/ Honig

HFD-570/CSO/ Sandy Barnes

I

23 Page(s) Withheld

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Deliberative Process

**RECORD OF TELEPHONE CONVERSATION**

APPLICATION NUMBER: N20-468

DATE: January 3, 1997

INITIATED BY:  APPLICANT  FDA

FIRM NAME: Rorer Poulenc Rorer

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD:

Mary Allis Raudinbush

TELEPHONE NUMBER: 610-454-8268

I asked her why efficacy analysis for Study 312 was performed with and without Dr. Ziering data. She told me that this was done to expedite NDA review as his

As the sponsor is \_\_\_\_\_, I requested the sponsor to submit tabulation of the number of patients for each age by treatment. In addition, for the perennial allergic rhinitis study, I requested the tabulation of mean change from baseline of nasal index over the primary time point for each age and for each treatment group.

Cheung Kwong  
Cheung H. Kwong, M.D., Ph.D.  
Medical Review Officer

cc:

HFD-570/Division File for N20-468

HFD-570/ Honig

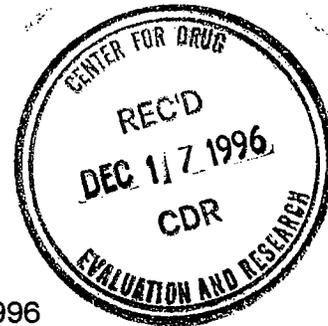
HFD-570/Medical Reviewer/ Kwong

HFD-570/CSO/ Sandra Barnes

**RHÔNE-POULENC RORER PHARMACEUTICALS INC.**

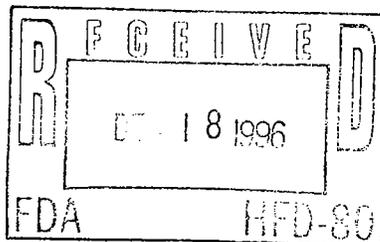
500 ARCOLA ROAD  
P.O. BOX 1200  
COLLEGEVILLE, PA 19426-0107

JUDITH R. PLON  
DIRECTOR  
REGULATORY AFFAIRS  
TEL: 610-454-3024  
FAX: 610-454-5299  
VM# 610-454-8666, BOX 3024



December 16, 1996

Food and Drug Administration  
Center for Drug Evaluation and Research  
Central Document Room  
Park Building, Room 214  
12420 Parklawn Drive  
Rockville, MD 20852



**NDA #20-784**  
**Nasacort® HFA**  
**(triamcinolone acetonide)**  
**Nasal**

**ORIGINAL NEW DRUG**  
**APPLICATION**

Dear Sir/Madam:

In accordance with 21 CFR 314, and Section 505(b) of the Federal Food, Drug and Cosmetic Act, Rhône-Poulenc Rorer Pharmaceuticals Inc. is submitting an Original New Drug Application for Nasacort® HFA (triamcinolone acetonide) Nasal

This product was developed by reformulating the currently marketed Nasacort® Nasal Inhaler with a non-CFC propellant; i.e., HFA-134a. This reformulation was necessary because in recent years, it has been determined that CFC propellants, such as the P-12 in the currently marketed Nasacort® Nasal Inhaler, may be contributing to the depletion of the stratospheric ozone. Based on this environmental factor, many nations, including the U.S. and the European Union members, are signatories to an international agreement calling for the phase-out of CFCs.

The active ingredient in Nasacort® HFA Nasal is triamcinolone acetonide which is a synthetic glucocorticoid with anti-inflammatory and anti-allergin properties. The clinical development for this new formulation was an extension of RPR's vast clinical experience with this corticosteroid. Information concerning triamcinolone acetonide



Food and Drug Administration  
Page Two  
December 16, 1996  
RE: NDA #20-784  
Original New Drug Application

utilized in the clinical program was derived primarily from experience with the previously approved CFC aerosol formulation in the treatment of seasonal and perennial allergic rhinitis (Nasacort® Nasal Inhaler, NDA #19-798), asthma (Azmacort® Oral Inhaler, NDA #18-117), and the aqueous formulation also for the treatment of seasonal and perennial allergic rhinitis (Nasacort® AQ Nasal Spray, NDA #20-468).

The development program to specifically evaluate this new formulation was created with input from the Division of Pulmonary Drug Products and in accordance with the FDA Guidance entitled, "Points to Consider: Clinical Development Programs for New Nasal Spray Formulation" (dated January 23, 1996). A meeting with the Division was held on March 1, 1995 to review the development of Nasacort® HFA (RPR meeting minutes were submitted to the Division on April 19, 1995, Serial No. 019). Based on this guidance, RPR conducted a clinical program comprised of therapeutic comparability, long-term safety, and a pharmacokinetic study. The data from these new studies, in combination with all of the data generated to date by RPR with triamcinolone acetonide, support the safety and effectiveness of Nasacort® HFA Nasal — in adults and children ages six and above for the treatment of seasonal and perennial allergic rhinitis.

In advance of this submission, on October 18, 1996 (IND #43,841, Serial No. 024), a pre-NDA Briefing Document was submitted to the Division which presented both an overview of the above-referenced studies, as well as an outline and overview of the enclosed NDA. Subsequently, in several discussions with Ms. Sandra Barnes, Project Manager, FDA's Division of Pulmonary Drug Products, it was relayed that RPR could proceed with the submission of this NDA since none of the Reviewers had identified any major issues to preclude the filing of this application.

In addition to the hard copy filing of this NDA, it is our intent to provide an electronic review system which will contain both the key textual documents and individual patient profiles. RPR is prepared to provide this electronic review system shortly following the filing of this NDA and would like to discuss the delivery method for this system with the appropriate representatives from the Division of Pulmonary Drug Products. Rhône-Poulenc Rorer is also providing the SAS data sets and corresponding SAS programs necessary for the generation of the primary efficacy analysis. The SAS sets and supporting documentation can be found in Volume 1.21, Item 10. It is our hope that these tools will greatly assist the Reviewers with their review of this NDA.

In accordance with 21 CFR 314.50, this application contains the following Technical Sections: 1) Chemistry, Manufacturing and Controls; 2) Nonclinical Pharmacology and Toxicology; 3) Human Pharmacokinetics and Bioavailability; 5) Clinical Data; and, 6) Statistical Data. The NDA consists of a total of 129 volumes distributed as follows: a Blue Copy, or "Archival Copy" - 52 volumes (Items 1 through 14); and a Review Copy.



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Page Three  
December 16, 1996  
RE: NDA #20-784  
Original New Drug Application

The "Review Copy" contains a copy of each "Technical Section" (Items 3 through 10). With each "Technical Section" a copy of Volume 1 which contains an Overall Index (Item 1), and an Overall Summary (Item 2) of the entire New Drug Application is submitted in the appropriate color-coded binder. A Statement of Organization describing the NDA format and content immediately follows this Cover Letter.

In accordance with the Prescription Drug User Fee Act of 1992, a check (Check No. 001645), in the amount of \$116,500, was sent to the Food and Drug Administration, Pittsburgh, Pennsylvania, on November 14, 1996. The application was assigned the User Fee Identification Number 3114.

As required by Section 306(k)(1) of the Generic Drug Enforcement Act [21 U.S.C. 335a(k)(1)], we hereby certify that, in connection with this application, Rhône-Poulenc Rorer did not and will not use in any capacity, the services of any person debarred under subsections 306(a) or (b) of the act.

Rhône-Poulenc Rorer Pharmaceuticals Inc. considers the information in this application to be confidential and proprietary, and we request that no portions thereof be disclosed to third parties, under FOI or otherwise, without prior discussion with us.

If you have any questions or require any additional information concerning this NDA, please contact me at (610) 454-3024, or, in my absence, Ms. Mary Alice Raudenbush, Manager, Regulatory Affairs, at (610) 454-8268.

Sincerely,

Judith R. Plon  
Director,  
Regulatory Affairs

JRP/mar/sb  
Enclosure