

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-004

ADMINISTRATIVE DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 22-004

SUPPL #

HFD # 570

Trade Name Omnaris

Generic Name ciclesonide

Applicant Name ALTANA Pharma

Approval Date, If Known 10/20/2006

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3, SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

5 years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !
IND # !
 YES ! NO
 ! Explain:

Investigation #2 !
IND # !
 YES ! NO
 ! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1 !
YES ! NO
Explain: ! Explain:

Investigation #2

YES

Explain:

!

!

! NO

! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES

NO

If yes, explain:

Name of person completing form: Colette Jackson

Title: Regulatory Health Project Manager

Date: October 2, 2006

Name of Office/Division Director signing form: Curtis Rosebraugh, M.D., M.P.H.

Title: Deputy Division Director, ODE II, OND, CDER

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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/s/

Curtis Rosebraugh
10/23/2006 07:45:50 AM

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA # 22-004 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: December 22, 2005 Action Date: October 20, 2006

HFD 570 Trade and generic names/dosage form: OMNARIS (ciclesonide) Nasal Spray

Applicant: ALTANA Pharma Therapeutic Class: 1S

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 or is difficult to diagnose 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. 16 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: We are approving the indication for patients 12 years of age and older but we are requesting a growth study under PREA.

Date studies are due (mm/dd/yy): December 31, 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. >16 Tanner Stage _____
Max _____ 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. 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. 16 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: We are approving the indication for patients 12 years of age and older but we are requesting a growth study under PREA.

Date studies are due (mm/dd/yy): December 31, 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. >16 Tanner Stage _____
Max _____ kg _____ mo. _____ yr. _____ Tanner Stage _____

Comments:

I

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

cc: NDA 22-004
HFD-960/ Grace Carmouze

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-796-1654.

(revised 10-14-03)

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/s/

Colette Jackson
10/24/2006 01:47:30 PM

MEMORANDUM OF TELECON

DATE: October 18, 2006

APPLICATION NUMBER: NDA 22-004

BETWEEN:

Name: Tushar Shah, MD Senior VP, Scientific and Clinical Development
Mark Wingertzahn, Ph.D. Director of Clinical Research, Allergic Rhinitis
Kathleen Waldron Manager, Regulatory Affairs
Ruediger Nave, Ph.D. Senior Research Scientist
Anton Drollman, MD, Ph.D. Head Therapeutic Area Respiration
Peter Fernandes, M Pharm, Senior Director, Regulatory Affairs
Phone: 1-866-953-2116
Representing: ALTANA Pharma

AND

Name: Badrul A. Chowdhury, M.D., Ph.D., Division Director
Lydia Gilbert-McClain, M.D., Clinical Team Leader
Carol Bosken, M.D., Clinical Reviewer
Arthur Shaw, Ph.D., Chemistry Reviewer
Emmanuel Fadiran, Ph.D., Clinical Pharmacology Team Leader
Colette Jackson, Project Manager
Division of Pulmonary and Allergy Products

SUBJECT: October 17, 2006, Meeting Request Submission

ALTANA Pharma sent in a meeting request and meeting package dated October 17, 2006, to discuss the Division's October 16, 2006, Phase 4 commitment facsimile. ALTANA agreed to those Phase 4 commitments as outlined in their October 19, 2006, commitment letter submitted to the Agency.

Colette Jackson
Project Manager

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/s/

Colette Jackson
10/20/2006 03:25:24 PM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-004

ALTANA Pharma
210 Park Avenue
Florham Park, NJ 07932

Attention: Cheryl Czachorowski
Senior Manager, Regulatory Affairs

Please refer to your October 17, 2006, correspondence, received October 17, 2006, requesting an advice meeting for OMNARIS (ciclesonide) Nasal Spray.

Based on the statement of purpose, objectives, and proposed agenda, we consider the meeting a type C meeting as described in our guidance for industry titled *Formal Meetings with Sponsors and Applicants for PDUFA Products* (February 2000). The meeting is scheduled for:

Date: October 18, 2006
Time: 4:30 PM to 5:30 PM
Location: via teleconference

FDA participants:

Badrul A. Chowdhury, MD, PhD, Division Director
Lydia Gilbert McClain, MD, Clinical Team Leader
Carol Bosken, MD, Clinical Reviewer
Emmanuel Fadiran, PhD, Clinical Pharmacology/Biopharmaceutics Team Leader
Arthur Shaw, Ph.D., Chemistry Reviewer
Colette Jackson, Project Manager

If there are additional attendees, please fax that information to me at (301) 796-9718.

If you have any questions, call Colette Jackson, Regulatory Project Manager, at (301) 796-1230.

Sincerely,

(See appended electronic signature page)

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

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

/s/

Colette Jackson
10/19/2006 11:19:56 AM
Signed for S. Barnes.

CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; WO 22, MAIL STOP 4447)**

DATE RECEIVED:

August 29, 2006

DESIRED COMPLETION DATE:

October 1, 2006

OSE REVIEW #: 2006-129

DATE OF DOCUMENT:

August 28, 2006

PDUFA DATE:

October 22, 2006

TO: Badrul Chowdhury, M.D.
Director, Division of Pulmonary and Allergy Products, HFD-570

THROUGH: Linda Y. Kim-Jung, Pharm.D., Team Leader
Denise Toyer, Pharm.D., Deputy Director
Carol Holquist, R.Ph., Director
Division of Medication Errors and Technical Support, HFD-420

FROM: Todd D. Bridges, R.Ph., Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

PRODUCT NAME:

Omnaris
(Ciclesonide Nasal Spray) 50 mcg/spray

NDA SPONSOR: Altana Pharma US, Inc.

NDA#: 22-004

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Omnaris. DMETS considers this a final review. However, if approval of the application is delayed beyond 90 days from the signature date of this review then the name and its labels and labeling must be re-evaluated. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.
2. DMETS recommends the implementation of the label and labeling revisions outlined in Section III of this review in order to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name, Omnaris, acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact the medication errors Project Manager, Diane Smith, at 301-796-0538.

**Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
WO 22, Mail Stop 4447
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: September 6, 2006
NDA#: 22-004
NAME OF DRUG: **Omnaris**
(Ciclesonide Nasal Spray)
50 mcg/spray
NDA HOLDER: Altana Pharma US, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Pulmonary and Allergy Products (HFD-570), for assessment of the proprietary name, Omnaris, regarding potential name confusion with other proprietary or established drug names. DMETS initially reviewed the proprietary names, [REDACTED] for this drug product (OSE Review #06-0030/06-0030-1, dated September 13, 2006). DMETS did not recommend use of the names, [REDACTED]

[REDACTED] Therefore, the sponsor has submitted the alternate name, Omnaris, for review. Revised container labels and carton labeling were provided for review and comment at this time. Additionally, the sponsor submitted a proprietary name assessment conducted by the [REDACTED] for review and comment.

PRODUCT INFORMATION

Omnaris (Ciclesonide) is an intranasal corticosteroid indicated for seasonal and perennial allergic rhinitis. Omnaris will be available as an aqueous nasal spray in a 12.5 gram amber glass bottle that yields 120 metered sprays. Each spray delivers 50 mcg of Ciclesonide to the patient. The recommended dose for adults and children [REDACTED] years of age and older is 200 mcg per day administered as 2 sprays (50 mcg/spray) in each nostril once daily. [REDACTED]

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2} as well as several FDA databases^{3,4} for existing drug names which sound-alike or look-alike to Omnaris to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁵. The SAEGIS⁶ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Omnaris. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC has no objections to the proposed proprietary name, Omnaris, from a promotional perspective.
2. The Expert Panel identified two proprietary names which were thought to have the potential for confusion with Omnaris. These products are listed in Table 1 (see page 4), along with the dosage form available and usual dosage.

**Appears This Way
On Original**

¹ MICROMEDEX Integrated Index, 2006, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, Facts and Comparisons, St. Louis, Missouri.

³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-06, and the electronic online version of the FDA Orange Book.

⁴ Phonetic and Orthographic Computer Analysis (POCA)

⁵ www location <http://www.uspto.gov/tmdb/index.html>.

⁶ Data provided by Thomson & Thomson's SAEGIS™ Online service, available at www.thomson-thomson.com

Table 1: Potential Look-Alike Names Identified for Omnaris.

Product Name	Dosage form(s), Established name	Usual adult dose*	Other**
Omnaris	Ciclesonide Nasal Spray 50 mcg per spray	2 sprays in each nostril once daily.	N/A
Amicar	Aminocaproic Acid Injection 250 mg/mL Aminocaproic Acid Syrup 1.25 gram/5 mL Aminocaproic Acid Tablets 500 mg, 1000 mg	16 mL to 20 mL (4 gram to 5 gram) in 250 mL of diluent administered by intravenous infusion during the first hour of treatment, followed by a continuing intravenous infusion at a rate of 4 mL (1 gram) per hour in 50 mL of diluent. 10 tablets (5 grams) or 4 teaspoonfuls of syrup (5 grams) administered during the first hour of treatment, followed by a continuing rate of 2 tablets (1 gram) or 1 teaspoonful of syrup (1.25 grams) per hour. Treatment would ordinarily be continued for about 8 hours or until the bleeding situation has been controlled.	LA
Omacor	Omega-3-Acid Ethyl Ester Capsules 1 gram	4 grams daily either as 4 capsules once daily or 2 capsules twice daily.	LA
*Frequently used, not all-inclusive. **LA (look-alike)			

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Omnaris with other U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 119 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Omnaris (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
<p data-bbox="310 199 467 226"><u>Outpatient RX:</u></p> <p data-bbox="332 254 987 493">Omnaris #1 2 sprays into each nostril daily</p>	<p data-bbox="1047 405 1369 506">Omnaris Quantity of 1 2 sprays each nostril daily</p>
<p data-bbox="310 527 451 554"><u>Inpatient RX:</u></p> <p data-bbox="310 583 987 674">Omnaris 2 sprays into each nostril qd</p>	

2. Results:

One respondent in the voice prescription study interpreted the proposed proprietary name as Climaris. Climaris can potentially sound similar to the currently marketed U.S. product Climara. See Appendix A (page 9) for the complete listing of interpretations from the verbal and written studies.

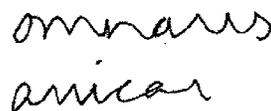
C. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Omnaris, the primary concerns relating to look-alike and sound-alike confusion with Omnaris are Amicar and Omacor.

Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, one respondent in the voice prescription study interpreted the proposed proprietary name as Climaris. Climaris can potentially look similar to the currently marketed U.S. product Climara. Despite this finding, Climara was not further reviewed due to a lack of convincing look-alike and sound-alike similarities with Omnaris, in addition to differentiating product characteristics such as the product strength, indication for use, frequency of administration, route of administration, and dosage form. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Omnaris.

1. Amicar was found to have look-alike potential with Omnaris. Amicar is indicated for use in enhancing hemostasis when fibrinolysis contributes to bleeding.

Both names begin with letters which may look similar when scripted (“A” vs. “O”) and share the letter “m” as the second letter which contributes to the look-alike similarities between Amicar and Omnaris. However, the endings of each name (“icar” vs. “naris”) are orthographically different. Although, neither name contains an upstroke or downstroke letter, the length of Omnaris when scripted is noticeably longer which helps distinguish the two products (see below).

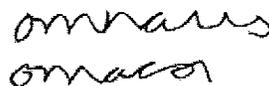


The image shows two lines of handwritten text. The top line is 'omnaris' and the bottom line is 'amicar'. The 'omnaris' is significantly longer than the 'amicar'.

We note that the potential for confusion is more likely in an outpatient setting since the route of administration (oral or intravenous vs. intranasal) would be required on inpatient prescriptions. However, since Amicar is available in two strengths (500 mg and 1000 mg), a strength would either be indicated on an order for Amicar or need to be obtained from the prescriber prior to filling and dispensing the prescription. The necessity for a strength on a prescription for Amicar may help to differentiate this name pair on an order. Additionally, since Amicar is available in two different *oral* dosage forms (syrup and tablet), there is the potential that this information may be included on a prescription for Amicar which may aid in furthering distinguishing Amicar from Omnaris. DMETS believes the multiple product strengths and dosage forms of Amicar coupled with differences in orthographic characteristics minimize the likelihood for confusion between these two drug products.

2. Omacor was identified to have similar appearance to Omnaris when scripted. Omacor (Omega-3-acid ethyl ester capsules), a lipid-regulating agent, is indicated as an adjunct to diet to reduce the triglyceride levels in adult patients with Fredrickson and Lees’ type IIb, IV, and V hyperlipidemia. The usual dose of Omacor is 4 grams per day taken as a single 4 gram dose or as two 2 gram doses.

Although both names begin with the letters “Om” and neither name contains an upstroke or downstroke letter, the length of Omnaris when scripted is noticeable longer (see below). The letter “n” in Omnaris lengthens the orthographic appearance of the name which helps distinguish the two products. Additionally, unless written with the instructions “use as directed”, the directions for use on an order for Omnaris may contain the dosing unit “spray” and route of administration “each nostril” (e.g., 2 **sprays each nostril** once daily) which may further help to differentiate this name pair. Although these products have some overlapping product characteristics such as frequency of administration (qd), the orthographic differences between the two proprietary names will help to differentiate Omacor and Omnaris.



The image shows two lines of handwritten text. The top line is 'omnaris' and the bottom line is 'omacor'. The 'omnaris' is significantly longer than the 'omacor'.

D. _____ NAME ANALYSIS

The _____ a subsidiary of _____ submitted a Proprietary Name Promotional Assessment in support of the proposed proprietary name, Omnaris. The assessment findings indicate that Omnaris is not confusingly similar in sound or appearance to proprietary or nonproprietary names of drugs in the United States. DMETS acknowledges _____ conclusion.

The analysis conducted by _____ discusses the following names: Banaril, Bromarest, Cefdinir, Cialis, Norisc, Omacor, Omeprazole, Omnicef, Omnicol, Omnihib, Omnihist, Omnipaque, Omnipen, Omniscan, Ponaris, and Rhinaris.

DMETS did not identify the following names as potential sound or look-alike products with Omnaris: Banaril, Bromarest, Cefdinir, Cialis, Norisc, Omeprazole, Omnicol, Omnipaque, Omnipen, Ponaris, and Rhinaris. Following review of these proprietary names, DMETS concurs that none of the aforementioned names pose a significant safety risk due to lack of lack of convincing sound-alike and look-alike properties and differentiating product characteristics such as strength, indication for use, frequency of administration, route of administration, and dosage formulation.

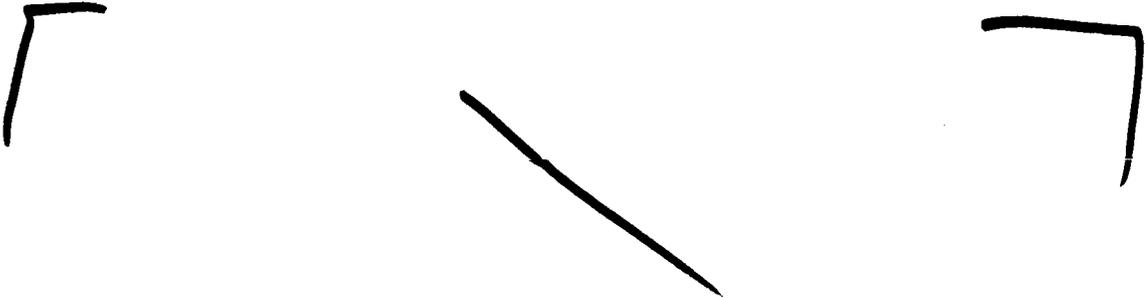
Both DMETS and _____ identified the names, Omacor, Omnicef, Omnihist, and Omniscan, as having potential confusion with Omnaris. We concur that the names Omacor, Omnicef, Omnihist, and Omniscan may safely co-exist in the marketplace with Omnaris.

Additionally, DMETS identified Amicar, Claravis, Omnipred, Orinase, and the medical term, nares, as having orthographic and/or phonetic similarities with Omnaris. These names and medical term were not identified in the _____ evaluation. We have concluded that the names, Amicar, Claravis, Omnipred, Orinase, and the medical term, nares, do not pose a significant safety risk due to differing product characteristics in conjunction with phonetic and/or orthographic differences.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels and carton labeling of Omnaris, DMETS has focused on safety issues relating to possible medication errors. We have identified the following areas of improvement, in the interest of minimizing potential user error and patient safety.

1. GENERAL COMMENTS



1 Page(s) Withheld

 § 552(b)(4) Trade Secret / Confidential

 § 552(b)(5) Deliberative Process

 ✓ § 552(b)(5) Draft Labeling

Appendix A. DMETS prescription study results for Omnaris.

Voice Inpatient Outpatient

Climaris	Ameraris	Omanus
Omnares	Omerasis	Omnares or Omnaus
Omnaris	Omnaris	Omnaris
Omnaris	Omnaris	Omnaris
Omnaris	Omnaris	Omnaris
Omneris	Omnaris	Omnaus
Omneris	Omnaris	Omnaus
Palmeris	Omnaris	Omnaus
Promeras	Omnaris	Omnaus
	Omnaris	

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/s/

Todd Bridges
10/17/2006 03:41:15 PM
DRUG SAFETY OFFICE REVIEWER

Linda Kim-Jung
10/17/2006 03:41:42 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
10/17/2006 03:51:54 PM
DRUG SAFETY OFFICE REVIEWER
Also signing for Carol Holquist, Director DMETS



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

FACSIMILE TRANSMITTAL SHEET

DATE: October 16, 2006

To: Cheryl Czachorowski Senior Manager, Regulatory Affairs	From: Colette Jackson Regulatory Health Project Manager
Company: ALTANA Pharma	Division of Pulmonary and Allergy Products
Fax number: 973-236-1695	Fax number: 301-796-9718
Phone number: 973-514-4271	Phone number: 301-796-1230

Subject: NDA 22-004

Total no. of pages including cover: 3

Comments:

Document to be mailed: YES xNO

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NDA 22-004

Ciclesonide Nasal Spray

We are reviewing your new drug application (NDA) and we ask that you submit a correspondence committing to performing the postmarketing studies as listed below.

1. An adequate HPA axis safety study in patients with allergic rhinitis who are 12 years of age or older. The objective of this study is to evaluate the effects of ciclesonide nasal spray on the HPA axis. The study should be conducted using the labeled dose and at least one higher dose of ciclesonide nasal spray. The study should include one or more 24-hour measurements of cortisol and be of adequate size and duration to meet the objective. The study should include efficacy assessments, PK measurements, or both to ensure compliance with study medication and also include a positive control arm. Submit the final study report as a labeling supplement.

Protocol Submission Date: _____

Study Start Date: _____

Final Report Submission Date: _____

2. A one-year linear growth study with a dose of ciclesonide nasal spray that is relevant to the proposed ciclesonide nasal spray dose in children with allergic rhinitis. The objective of this study is to assess the effects of ciclesonide nasal spray on growth velocity. The study should be conducted in prepubescent children with allergic rhinitis and should be of adequate size to meet the objective. Alternatively, a linear growth study conducted with a formulation of ciclesonide other than the nasal formulation may be adequate, provided the systemic exposure from that formulation is higher than the systemic exposure from the nasal formulation. Submit the final study report as a labeling supplement.

Protocol Submission Date: _____

Study Start Date: _____

Final Report Submission Date: _____

If there are any questions, please contact Ms. Colette Jackson, Project Manager, at 301-796-1230.

Drafted: CCJ/October 12, 2006

Initialed:

Barnes/ October 12, 2006
Bosken/ October 12, 2006
Gilbert-McClain/October 12, 2006
Chowdhury/October 13, 2006
Ripper/October 13, 2006
Rosebraugh/October 13, 2006

Finalized: CCJ/October 16, 2006

File: 22004 October 2006 PMC fax.doc

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/s/

Colette Jackson
10/16/2006 09:54:39 AM
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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: October 12, 2006

To: Cheryl Czachorowski Senior Manager, Regulatory Affairs	From: Colette Jackson
Company: ALTANA PHARMA	Division of Pulmonary and Allergy Products
Fax number: 973-236-1695	Fax number: 301-796-9718
Phone number: 973-514-4271	Phone number: 301-796-1230

Subject: NDA 22-004 FDA Proposed Patient's Instructions for Use and Carton/Container
comments

**Total no. of pages including
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 ✓ § 552(b)(5) Draft Labeling

Drafted: CCJ/October 11, 2006

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Bosken/ October 10, 2006

Gilbert-McClain/ October 10, 2006

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Fadiran/ October 10, 2006

Zhou/ October 10, 2006

Davi/ October 10, 2006

Hao/ October 10, 2006

McGovern/ October 10, 2006

Shaw/ October 10, 2006

Peri/ October 10, 2006

Shaw/ October 10, 2006

Chowdhury/ October 11, 2006

Ripper/October 12, 2006

Rosebraugh/October 12, 2006

Finalized: CCJ/ October 12, 2006

Filename: 22004 October 2006 PPI and CC comments.doc

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/s/

Colette Jackson
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Food and Drug Administration
 Center for Drug Evaluation and Research
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FACSIMILE TRANSMITTAL SHEET

DATE: October 11, 2006

To: Cheryl Czachorowski Senior Manager, Regulatory Affairs	From: Colette Jackson
Company: ALTANA PHARMA	Division of Pulmonary and Allergy Products
Fax number: 973-236-1695	Fax number: 301-796-9718
Phone number: 973-514-4271	Phone number: 301-796-1230

Subject: NDA 22-004 FDA Proposed Package Insert Label

Total no. of pages including cover:

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NDA 22-004

Ciclesonide Nasal Spray

Please refer to your December 22, 2005, new drug application (NDA) for ciclesonide nasal spray. We also acknowledge receipt of your submission dated October 6, 2006. Please refer to the enclosed labeling with our preliminary labeling comments and/or recommendations. These comments are not all inclusive and we may have additional comments from the Office of Drug Evaluation II. Submit revised draft labeling incorporating the changes outlined in our enclosed labeling.

If there are any questions, please contact Ms. Colette Jackson, Project Manager, at 301-796-1230.

Enclosure: Recommendations to the Proposed Label

14 Page(s) Withheld

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✓ § 552(b)(5) Draft Labeling

Adus - 27

Drafted: CCJ/October 11, 2006

Initialed:

Bosken/ October 10, 2006
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Fadiran/ October 10, 2006
Zhou/ October 10, 2006
Davi/ October 10, 2006
Hao/ October 10, 2006
McGovern/ October 10, 2006
Shaw/ October 10, 2006
Peri/ October 10, 2006
Shaw/ October 10, 2006
Chowdhury/ October 11, 2006
Ripper/October 11, 2006
Rosebraugh/October 11, 2006

Finalized: CCJ/ October 11, 2006

Filename: 22004 October 11 2006 labeling fax.doc

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/s/

Colette Jackson
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**FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications**

Memorandum

Date: October 2, 2006

To: Colette Jackson, Regulatory Project Manager
Division of Pulmonary and Allergy Products

From: Michelle Safarik, PA-C, Regulatory Review Officer
Division of Drug Marketing, Advertising, and Communications

Subject: NDA 22-004
DDMAC labeling comments for TRADENAME (ciclesonide) Nasal
Spray, 50 mcg

Per your e-mail consult request dated October 2, 2006, DDMAC has reviewed the revised proposed product labeling (PI) for TRADENAME (ciclesonide) Nasal Spray, 50 mcg, and we have no comments at this time. We have also reviewed Dr. Badrul Chowdhury's comments on this revised proposed PI and concur with his recommendations.

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/s/

Michelle Safarik
10/2/2006 12:57:02 PM
DDMAC REVIEWER



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

FACSIMILE TRANSMITTAL SHEET

DATE: October 4, 2006

To: Cheryl Czachorowski Senior Manager, Regulatory Affairs	From: Colette Jackson
Company: ALTANA PHARMA	Division of Pulmonary and Allergy Products
Fax number: 973-236-1695	Fax number: 301-796-9718
Phone number: 973-514-4271	Phone number: 301-796-1230

Subject: NDA 22-004 FDA Proposed Package Insert Label

Total no. of pages including cover:

Comments:

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NDA 22-004
Ciclesonide Nasal Spray

Please refer to your December 22, 2005, new drug application (NDA) for ciclesonide nasal spray. We also acknowledge receipt of your submission dated September 29, 2006. Please refer to the enclosed labeling with our preliminary labeling comments and/or recommendations. These comments are not all inclusive and we may have additional comments from the Office of Drug Evaluation II. Submit revised draft labeling incorporating the changes outlined in our enclosed labeling.

If there are any questions, please contact Ms. Colette Jackson, Project Manager, at 301-796-1230.

Enclosure: Recommendations to the Proposed Label

19 Page(s) Withheld

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Drafted: CCJ/October 4, 2006

Initialed:

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Shaw/ October 4, 2006
Peri/ October 4, 2006
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Finalized: CCJ/ October 4, 2006

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/s/

Colette Jackson
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Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: September , 2006

To: Cheryl Czachorowski	From: Colette Jackson
Company: ALTANA Pharma	Division of Pulmonary and Allergy Products
Fax number: 973-236-1695	Fax number: 301-796-9718
Phone number: 973-514-4271	Phone number: 301-796-1230
Subject: NDA 22-004 CMC Request for Information	

Total no. of pages including cover: 3

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NDA 22-004

Ciclesonide Nasal Spray

Please refer to your December 22, 2005, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ciclesonide Nasal Spray.

We also refer to your submission dated September 15, 2006, which was a response to our September 6, 2006, Discipline Review Letter. We have the following comments. We request a prompt response in order to continue our evaluation of your NDA.

1. The stability protocol provided in section 3.2.P.8.2 does not contain instructions for taking samples for out-of-pouch testing. Submit an amended stability protocol as requested in comment 2 of our Discipline Review Letter.
2. Provide a method that is specific for measuring weight loss of bottles stored out-of-pouch over the proposed shelf life of the product.
3. You have provided the new test procedure for _____ in the specifications in 3.2.P.5.1. However, the actual test procedure is not included under 3.2.P.5.2. Analytical Procedures. Amend 3.2.P.5.2 to include this analytical procedure.

If there are any questions, please contact Ms. Colette Jackson, Project Manager, at 301-796-1230.

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/s/

Colette Jackson
9/22/2006 02:10:40 PM
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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation II

FACSIMILE TRANSMITTAL SHEET

DATE: September 15, 2006

To: Cheryl Czachorowski Senior Manager, Regulatory Affairs	From: Colette Jackson
Company: ALTANA PHARMA	Division of Pulmonary and Allergy Products
Fax number: 973-236-1695	Fax number: 301-796-9718
Phone number: 973-514-4271	Phone number: 301-796-1230

Subject: NDA 22-004

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NDA 22-004
Ciclesonide Nasal Spray

Please refer to your December 22, 2005, new drug application (NDA) for ciclesonide nasal spray. We also acknowledge receipt of your submission dated May 4, 2006. Please refer to the enclosed labeling with our preliminary labeling comments and/or recommendations. These comments are not all inclusive and we may have additional comments from the Office of Drug Evaluation II. Submit revised draft labeling incorporating the changes outlined in our enclosed labeling.

If there are any questions, please contact Ms. Colette Jackson, Project Manager, at 301-796-1230.

Enclosure: Recommendations to the Proposed Label

18 Page(s) Withheld

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/s/

Anthony Zeccola
9/15/2006 05:03:01 PM
CSO
For Colette Jackson



NDA 22-004

DISCIPLINE REVIEW LETTER

ALTANA Pharma
210 Park Avenue
Florham Park, NJ 07932

Attention: Cheryl Czachorowski
Senior Manager, Regulatory Affairs

Dear Ms. Czachorowski:

Please refer to your December 21, 2005, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ciclesonide Nasal Spray.

We also refer to your submissions dated March 2, and 24, April 14, and 21, June 2, July 21, and August 2, 10, 11, 14, 17, 18, and 21, 2006.

Our review of the Chemistry, Manufacturing and Controls section of your submission is complete, and we have identified the following deficiencies. Please respond to the following comments promptly.

1. Revise the acceptance criterion for  for in-pouch stability to  with a 24 month expiration date.
2. Regarding the long-term stability testing protocol (in-pouch).

Amend the stability protocol for long-term testing to include taking samples for "out-of-pouch" (OOP) testing at the following time intervals:

0, 3, 6, 9, 12, 18 and 24 months

This protocol may be reduced based upon data from the first three batches placed on the full long-term in-pouch and complete OOP testing.

3. Regarding the stability protocol for OOP testing.

When the data from the comparison of the "in-use" model and your proposed OOP testing protocol are available, your proposed OOP protocol will be evaluated for its ability to be used for routine OOP stability testing.

4. The out-of-pouch use should be limited to four months until sufficient stability data is available to evaluate a longer-term use. (with an acceptance criterion for [REDACTED])
5. Amend the post-approval stability protocol in Section 3.2.P.8.2.1 to include the additional acceptance criteria for [REDACTED] stored in-pouch and out-of-pouch.
6. Amend the "Patient's Instructions for Use" to specify that the storage time for the bottle out of the pouch is four months.
7. Comment 10.b in our July 27, 2006, letter stated:

[REDACTED]

[REDACTED]

The following comments may be addressed by providing data or by providing a time-frame in which you will be able to provide the data.

8.

[REDACTED]

9. In regard to the stability data for [REDACTED] reported in your submissions dated April 21, and June 2, 2006, explain the following:
 - a. The data in the SAS Transport file (Amendment 10, June 2, 2006) for Lot number GD507017 are blank.
 - b. The average data were reported in the table shown on Page 403 in Section 3.2.P.8.3 of your submission dated April 21, 2006, rather than individual data, especially because the individual data reported in your submission dated July 21, 2006, showed out-of specification results for batch GD505017.
 - c. The out-of specification results, which were collected in October 2005, were not reported until July 21, 2006.
10. Provide the data to support the statement in 3.2.P.5.6 (Page 14) in the original submission:

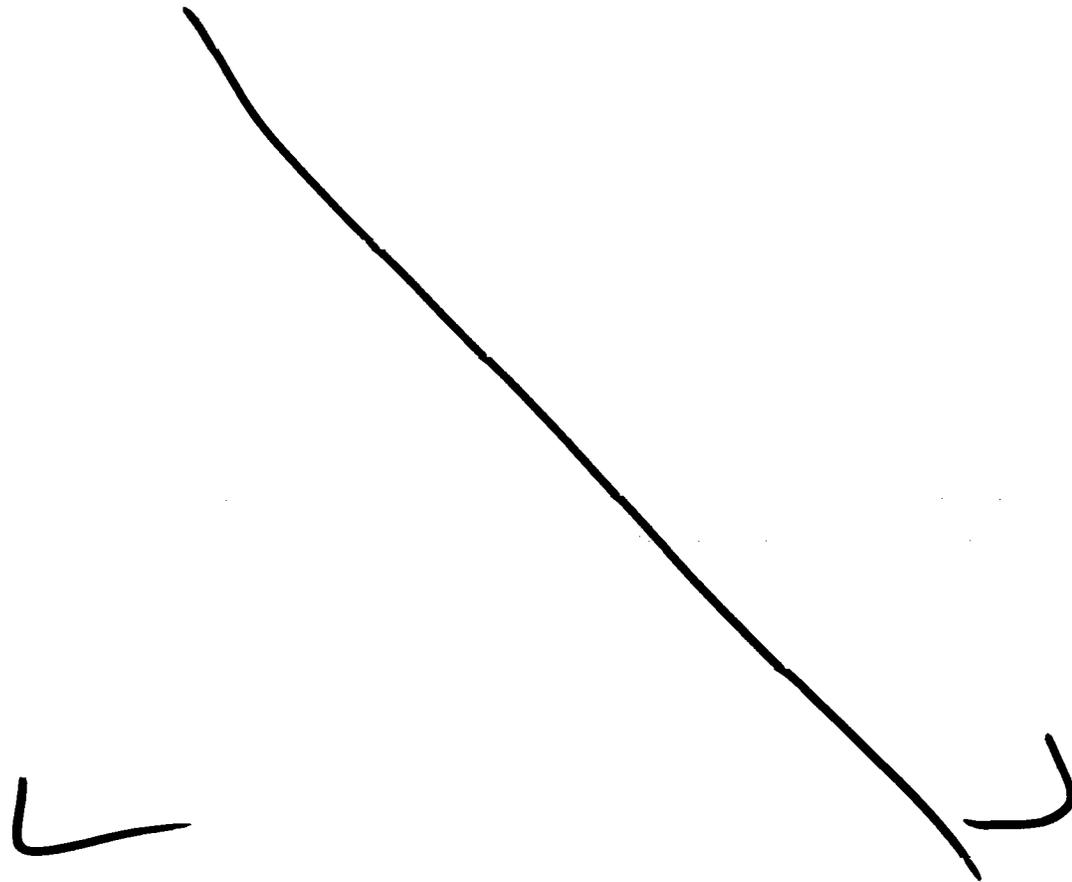
[REDACTED]

11.

12.

13.

14.



We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified and subject to change as we finalize our review of your application. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Colette Jackson, Regulatory Health Project Manager, at 301-796-1230.

Sincerely,

Blair A. Fraser, Ph.D
Chief, Branch II
Division of Pre-Marketing Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Prasad Peri
9/6/2006 03:58:14 PM
Signing for Blair Fraser, Ph. D.

MEMORANDUM

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH**

CLINICAL INSPECTION SUMMARY

DATE: August 9, 2006

TO: Colette Jackson
Regulatory Health Project Manager
Carol Bosken, Medical Officer
Lydia Gilbert-Mclain, Team Leader
Division of Pulmonary and Allergy Drug Products, HFD- 570

THROUGH: Leslie K. Ball, M.D.
Branch Chief
Good Clinical Practice Branch II
Division of Scientific Investigations

FROM: Sharon K. Gershon, Pharm.D., CSO

SUBJECT: Evaluation of Clinical Inspections

NDA: #22-004

APPLICANT: Altana Pharma

DRUG: Ciclesonide Nasal Spray

CHEMICAL CLASSIFICATION: 1S (NME)

THERAPEUTIC CLASSIFICATION: Priority Review

INDICATION: _____

CONSULTATION REQUEST DATE: 2 March 2006

ACTION GOAL DATE: 13 August 2006

PDUFA DATE: 13 August 2006

I. BACKGROUND:

This NDA was submitted to support the approval of ciclesonide nasal spray for the treatment of symptoms of allergic rhinitis in subjects 2 years of age and older. The adult and adolescent pivotal trials (Y9010/M1-401 (287/2004) and BY9010-405 (144/2005) included one 4-week trial in subjects with seasonal allergic rhinitis (SAR), one 6-week trial in subjects with PAR (perennial allergic rhinitis), and one 52-week safety study in subjects with PAR. All three used ciclesonide nasal spray 200 mcg as the active treatment, and all three were randomized, placebo controlled, and double blind. The primary efficacy endpoint was the average of AM and PM patient-reported reflective Total Nasal Symptom Score (TNSS) over the first 2 weeks of treatment. The planned sample size was 302 subjects; 327 were enrolled. There were a total of 6 sites that participated in this study. Two (5202 and 5203, Freeland and Hampel) of the six sites were selected for auditing because of their relatively high enrollment numbers. Site 5202 had efficacy results that were significantly higher than other sites, and a large number of moderate to severe adverse events. Site 5203 also had efficacy results that were higher than average and the number of moderate to severe adverse events was high.

The pediatric trials consisted of one 12-week study in subjects 5 to 11 years of age with PAR and one dose-ranging, PK, and safety trial in subjects 2 to 5 years of age.

Protocol BY9010/M1-405 was a randomized, double-blind, placebo-controlled, and parallel-group study to assess the safety of ciclesonide given at dosages of 200µg, 100µg, or 25µg once daily for six weeks, in patients 2-5 years of age, inclusive, with perennial allergic rhinitis (PAR). The primary objective was to assess safety of ciclesonide administered intranasally at 3 dose levels in the treatment of PAR in pediatric subjects. The planned sample size was 120 subjects; 133 were enrolled. Site 5724 (Herron) was selected for auditing because all of the subjects 2-5 years old in this study were enrolled from this site.

Dr. Jerry Herron has been inspected many times, he currently has ~~_____~~ studies in the COMIS database, and his last inspection in 2002 was classified as NAI. Dr. Daniel Freeland has never been inspected, and Dr. Hampel was inspected in 2000 with a NAI classification.

II. RESULTS (by site):

Clinical Investigator	Site No.	No. Subjects	Inspection Dates	Protocol No.	Field Classification
Jerry Herron, MD Arkansas Research Medical Testing 1207 Rebamen Park Road Little Rock, AR 72202	5724	133	5/2 to 5/16/2006	144/2005	OAI
Daniel V. Freeland, MD 8501 North Mopac Expressway Austin, Texas 78759	5202	44	5/24 to 5/29/2006	287/2004	VAI

Clinical Investigator	Site No.	No. Subjects	Inspection Dates	Protocol No.	Field Classification
Frank C. Hampel Jr., MD Central Texas Health Research 705 A Landa Street New Braunfels, Texas 78130	5203	60	5/9 to 5/11/2006	287/2004	NAI

Key to Classifications

NAI = No deviation from regulations. Data acceptable

VAI = Minor deviations(s) from regulations. Data acceptable

VAI= Deviation(s) form regulations, response requested. Data acceptable

OAI = Significant deviations for regulations. Data unreliable

Pending = Inspection not completed

Protocols Inspected:

Protocol 144/2005 (405): "A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Clinical Trial Designed to Assess the Safety of Ciclesonide, Applied as a Nasal Spray at Three Dose Levels, 200 µg, 100 µg, or 25 µg, Once Daily for Six Weeks, in the Treatment of Perennial Allergic Rhinitis (PAR) in Pediatric Patients 2-5 Years of Age"

Protocol 287/2004 (401): "A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Phase 3 Clinical Trial to Assess the Safety and Efficacy of Ciclesonide (200 µg Once Daily) Applied as a Nasal Spray in the Treatment of Seasonal Allergic Rhinitis (SAR) in Patients 12 Years and Older"

I. Sites:

Jerry Herron, MD Site 5724 Protocol 144/2005 or 405
Arkansas Research Medical Testing
1207 Rebamen Park Road
Little Rock, AR 72202

a. What was inspected? A total of 69 of 133 patient records was audited for inclusion/exclusion criteria, adverse events, concomitant medications, and adherence to study medication. Signed, witnessed and dated informed consent forms were verified for all 133 subjects enrolled. In all cases, consent was found to have been obtained prior to performance of study procedures. At the close of this inspection a 3-item FDA-483 was issued.

b. Limitations: There were no limitations to this inspection. Dr. Herron was unavailable at the close-out meeting due to back surgery the previous week.

c. General Observations: Properly signed and dated informed consent forms were obtained for each subject enrolled in the study. Serious adverse events and adverse events noted in the line listings were corroborated with the source records, and found accurate. A 3-item FDA-483 was issued to Dr. Herron for: failing to conduct the investigation in accordance with the investigational plan; drug disposition records not adequate with respect to quantity; and unused supplies of investigational drug not returned to the sponsor.

2 Page(s) Withheld

§ 552(b)(4) Trade Secret / Confidential

§ 552(b)(5) Deliberative Process

§ 552(b)(5) Draft Labeling

Daniel V. Freeland, MD Site 5202 Protocol 287/2004
8501 North Mopac Expressway, Suite 200
Austin, Texas 78759

- a. **What was inspected:** At this site, 44 subjects were randomized. The inspection reviewed 15 of 44 subject files. Subject files consisted of the source records, case report forms and patient diaries.
- b. **Limitations of inspection:** There were no limitations to this inspection.
- c. **General Observations:** The inspection confirmed that a signed and dated informed consent form was on file for each subject. Four observations were noted in the FDA-483 for failure to follow the investigational plan. The following deficiencies were noted: 1) two enrolled subjects took prohibited medications (Tylenol PM and Contact) during the baseline period, and one subject did not accurately complete the patient diary in that he/she had missing entries for more than 3 days; 2) diary dates were pre-dated by [redacted] staff; 3) a [redacted] technician, not the study physician, read the test allergy results; 4) patient randomization numbers were not allocated in sequential order.
- d. **Assessment of Data Integrity:** In general, the study at this site appears to have been conducted adequately, and the data appears acceptable in support of this NDA.

Frank C. Hampel Jr., MD Site 5203
Central Texas Health Research
705 A Landa Street
New Braunfels, Texas 78130

- a. **What was inspected:** The inspection reviewed 15 of 55 subject files. Subject files consisted of case report forms, source records, and patient diaries.
- b. **Limitations of Inspection:** There were no limitations to this inspection.
- c. **General Observations:** No deficiencies were noted; no discrepancies were noted with the sponsor's data listings. A signed informed consent form was on file for each subject. A form FDA-483 was not issued at the end of the inspection. At the conclusion of the inspection, the investigator held a discussion with Dr. Hampel regarding patient diaries. The copies at the site were certified copies, as the original diaries were retrieved by [redacted] personnel.
- d. **Assessment of Data Integrity:** The study appears to have been conducted adequately, and the data generated at this site appear acceptable in support of the NDA.

III. OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS

The data submitted in support of this NDA appear to be acceptable for the studies conducted at the Freeland and Hampel sites.

Follow-up action: none needed.

Sharon K. Gershon, Pharm.D.
Good Clinical Practice Branch II, HFD-47
Division of Scientific Investigations

CONCURRENCE:

Supervisory comments

Leslie K. Ball, M.D.
Branch Chief
Good Clinical Practice Branch II
Division of Scientific Investigations

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/s/

Sharon Gershon
8/10/2006 10:43:06 AM
CSO

Leslie Ball
8/15/2006 12:53:56 PM
MEDICAL OFFICER



NDA 22-004

DISCIPLINE REVIEW LETTER

ALTANA Pharma
210 Park Avenue
Florham Park, NJ 07932

Attention: Cheryl Czachorowski
Senior Manager, Regulatory Affairs

Dear Ms. Czachorowski:

Please refer to your December 21, 2005, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ciclesonide Nasal Spray.

We also refer to your submissions dated March 2, and 24, April 14, and 21, and June 2, 2006.

Our review of the Chemistry, Manufacturing and Controls section of your submission is complete, and we have identified the following deficiencies:

1. The following request pertains to the Particle Size distribution for the ciclesonide:

a.

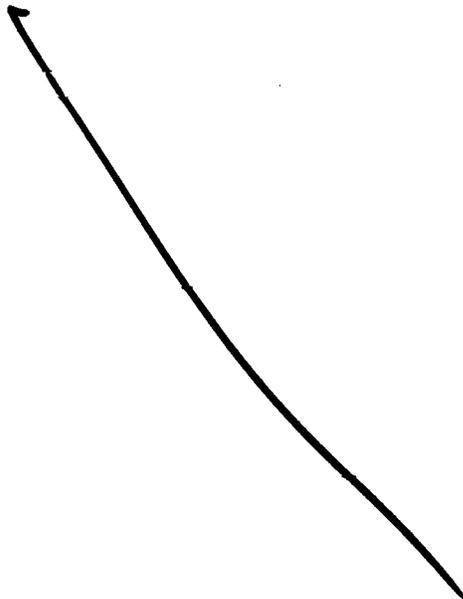
b.

c.

2.

b

c.



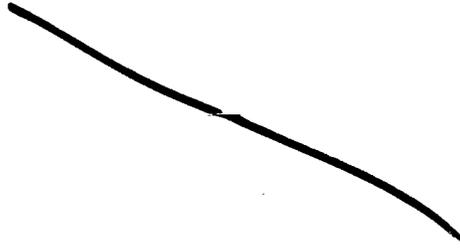
6 Page(s) Withheld

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 § 552(b)(5) Deliberative Process

 § 552(b)(5) Draft Labeling

i.



j.

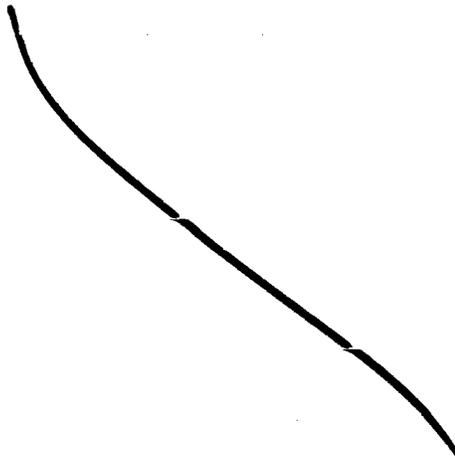


9. The following request pertains to the Stability:

a.



b.



c.



10. The following request pertains to the labeling:

a.



b.



We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified and subject to change as we finalize our review of your application. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not

be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Colette Jackson, Regulatory Health Project Manager, at 301-796-1230.

Sincerely,

Blair A. Fraser, Ph.D
Chief, Branch II
Division of Pre-Marketing Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Blair Fraser

7/27/2006 01:00:58 PM



Frank C. Hampel, Jr., M.D.
Central Texas Health Research
705 Landa St., Ste A
New Braunfels, TX 78130

Dear Dr. Hampel:

Between May 9 and May 11, 2006, Mr. Joel Martinez, representing the Food and Drug Administration (FDA), conducted an investigation and met with you to review your conduct of a clinical investigation (protocol number 287/2004 (401) entitled "A Randomized, Double-Blind, Placebo-Controlled Parallel-Group, Phase 3 Clinical Trial to Assess the Safety and Efficacy of Ciclesonide (200 µg Once Daily) applied as a Nasal Spray in the Treatment of Seasonal Allergic Rhinitis (SAR) in Patients 12 Years and Older, ") of the investigational drug ciclesonide nasal spray, performed for Altana, Inc.

This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to evaluate the conduct of research and to ensure that the rights, safety, and welfare of the human subjects of the study have been protected.

From our review of the establishment inspection report and the documents submitted with that report, we conclude that except for minor deficiencies, you adhered to the applicable statutory requirements and FDA regulations governing the conduct of clinical investigations and the protection of human subjects.

We appreciate the cooperation shown Investigator Martinez during the inspection. Should you have any questions or concerns regarding this letter or the inspection, please contact me by letter at the address given below.

Sincerely,

{See appended electronic signature page}

Leslie K. Ball, M.D.
Branch Chief
Good Clinical Practice Branch 2, HFD-47
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
7520 Standish Place, Room 125
Rockville, MD 20855

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/s/

Leslie Ball
7/16/2006 11:20:07 PM



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

FACSIMILE TRANSMITTAL SHEET

DATE: April 24, 2005

To: Cheryl Czachorowski Senior Manager, Regulatory Affairs	From: Colette Jackson Regulatory Health Project Manager
Company: ALTANA Pharma	Division of Pulmonary and Allergy Products
Fax number: 973-236-1695	Fax number: 301-796-9718
Phone number: 973-514-4271	Phone number: 301-796-1230
Subject: NDA 22-004	

Total no. of pages including cover: 4

Comments:

Document to be mailed: YES xNO

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NDA 22-004

Ciclesonide Nasal Spray

We are reviewing your new drug application (NDA) dated December 22, 2005. We also refer to your March 21, 2006, submission which requested review of your proposed proprietary names for ciclesonide nasal spray. We have received the following preliminary comment regarding your proposed trade names.

We have no objection to the proposed trade name _____ from a promotional perspective. However, trade names such as _____ make representations about the therapeutic use of the drug. While these names may be true and non-misleading statements about the indication or use, the names may preclude the sponsor from disseminating reminder advertisements or labeling. Specifically, embedding such claims within the trade name will require appropriate communication of the indication and risks associated with product therapy. Please refer to 21 CFR §§ 200.200. Considering the limitations on the use of these names, please advise if you wish to continue our review of the proposed names.

If there are any questions, please contact Ms. Colette Jackson, Project Manager, at 301-796-1230.

Drafted: CCJ/April 13, 2006

Initialed:

Barnes/ April 14, 2006

Chowdhury/April 14, 2006

Finalized: CCJ/April 24, 2006

File: 22004 april 2006 dmets fax.doc

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/s/

Colette Jackson
4/24/2006 02:56:08 PM
CSO

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): Director, Division of Medication Errors and Technical Support (DMETS), HFD-420 WO Rm 4414		FROM: Colette Jackson Project Manager Division of Pulmonary and Allergy Drug Products, HFD-570		
DATE April 4, 2006	IND NO.	NDA NO. 22-004	TYPE OF DOCUMENT N	DATE OF DOCUMENT March 21, 2006
NAME OF DRUG Ciclesonide	PRIORITY CONSIDERATION Standard	CLASSIFICATION OF DRUG Pro-corticosteroid	DESIRED COMPLETION DATE August 31, 2006	
NAME OF FIRM: ALTANA Pharma				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:				
<p>This is a request for a consult on ALTANA Pharma's NDA 22-004 for Ciclesonide. This submission is electronic only and is located on the EDR under the submission dated March 21, 2006. ALTANA is proposing 2 new names for DMETS approval. The original submission is dated December 21, 2005. DMETS has completed 2 prior tradename reviews for ciclesonide under IND 65,488.</p> <p>PDUFA DATE: October 22, 2006 ATTACHMENTS: CC: Archival NDA 22-004 HFD-570/Division File HFD-570/Jackson</p>				
SIGNATURE OF REQUESTER		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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/s/

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

FACSIMILE TRANSMITTAL SHEET

DATE: March 20, 2005

To: Cheryl Czachorowski Senior Manager, Regulatory Affairs	From: Colette Jackson Regulatory Health Project Manager
Company: ALTANA Pharma	Division of Pulmonary and Allergy Products
Fax number: 973-236-1695	Fax number: 301-796-9718
Phone number: 973-514-4271	Phone number: 301-796-1230

Subject: NDA 22-004

Total no. of pages including cover: 4

Comments:

Document to be mailed: YES xNO

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§ 552(b)(5) Deliberative Process

§ 552(b)(5) Draft Labeling

Drafted: CCJ/March 17, 2006

Initialed:

Barnes/ March 17, 2006

Zhou/ March 20, 2006

Davi/March 20, 2006

Finalized: CCJ/March 20, 2006

File: 22004 march 2006 stats fax.doc

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Colette Jackson
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NDA 22-004

INFORMATION REQUEST LETTER

ALTANA Pharma
210 Park Avenue
Florham Park, NJ 07932

Attention: Cheryl Czachorowski
Senior Manager, Regulatory Affairs

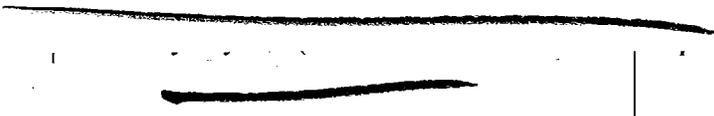
Dear Ms. Czachorowski:

Please refer to your December 22, 2005, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ciclesonide Nasal Spray.

We also refer to your submission dated March 2, 2006.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Provide drawings showing the identification and dimensions of all the pump components.
2. Regarding the Drug Master Files (DMFs) for the Pump Assembly:
 - a. The following DMFs have Letters of Authorization (LOAs) in the NDA but the letters have not been entered into the DMF. Request that the DMF holders send two copies of the LOAs to the following DMFs.

DMF Number	Holder	Description	Part of Pump Assembly
			

The DMF holder should use the following address for all submissions:

Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville MD 20705-1266

- b. Update Request letters were sent to the following DMFs on February 17, 2006:

DMF Number	Holder	Description	Part of Pump Assembly
------------	--------	-------------	-----------------------

c. _____

d. _____

e. _____

When the DMFs cited above are amended, you must notify the Agency of the dates of the amendments.

3. _____

4. The requested expiration period of 24 months will be evaluated based upon the available data, taking into account the following points.

a. Regarding the drug product used in the primary stability studies:

- i. _____
- ii. _____

b. Regarding the drug product to be marketed:

- i. No stability data has been provided.
- ii. Regarding the differences between the drug product to be marketed and the drug product used in the primary stability studies.

(1) _____

(2) The products use different _____

If you have any questions, call Colette Jackson, Regulatory Health Project Manager, at 301-796-1230.

Sincerely,

Blair A. Fraser, Ph.D
Chief, Branch II
Division of Pre-Marketing Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

Prasad Peri
3/17/2006 11:45:35 AM
Signing for Blair Fraser, Ph.D.



DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

DATE: March 2, 2006
FROM: Carol H. Bosken, MD
Division of Pulmonary and Allergy Drug Products, HFD(570)
THROUGH: Lydia I Gilbert-McClain, MD
Team Leader, Division of Pulmonary and Allergy Drug Products,
HFD(570)
TO: Ele Ibarra-Pratt
Division of Scientific Investigations
SUBJECT: NDA 22,004 Audit

NDA 22-004: Ciclesonide Nasal Spray, submitted by Altana on December 22, 2006.

We would like to audit sites that participated in 2 of the pivotal efficacy studies.

144/2005 (405) – Single-center US dose-ranging study in children 2 – 5 years of age with perennial rhinitis

287/2004 (401) – Multicenter US (Adult and adolescent with seasonal rhinitis)

We are requesting an audit of the following sites:

Site 5724 (Study 144/2005 or 405)
Investigator: Jerry Herron, MD
Arkansas Research Medical Testing
1207 Rebamen Park Road
Little Rock, AR 72202

Site 5202 (Study 287/2004)
Investigator: Daniel V. Freeland, MD
8501 North Mopac Expressway, Suite 200
Austin, Texas 78759

Site 5203 (Study 287/2004)
Investigator: Frank C. Hampel Jr, MD

Central Texas Health Research
705 A Landa Street
New Braunfels, Texas 78130

We would like a general survey of the trial conduct, IRB approval processes, and conduct of internal auditing by the sponsor at these three sites. We are submitting tables with selected laboratory values and adverse events taken from the SAS transport files submitted in this NDA. We would like you to check these data against the original data sources.

We are particularly interested in site 5724 because the investigators at this site enrolled all of the subjects age 2 to 5 years. Approval of the drug for this age range is, therefore, dependent wholly on the data obtained at this site. Because of the difficulty in obtaining reliable symptom scores in children this age, the efficacy determination will be made primarily on the basis of extrapolation from the results obtained from the studies in older subjects. The results of study 144/2005 are therefore of primary importance for interpreting safety: this includes adverse events, results of the ophthalmologic examinations, and laboratory analysis as well as pharmacodynamic measurements. Blood and 14-hour urine samples were obtained for cortisol determinations. The location of the data in the study report is under a Listing and a list of observations of particular interest will be found in the appendices at the end of this memo (Table 1).

Table 1. Location of the relevant listings

	Listing in Study Report	Observations of particular interest
Adverse Events	16.2.7.1	Appendix I
Ophthalmologic Exam	16.2.7.5	Appendix II
Serum Chemistry	16.2.7.5	Appendix III
Platelet Count	16.2.8.1	Appendix III
Cortisol (Urine and Blood)	16.2.8.2	Appendix III
PK	16.1.13*	Random Sample Requested

*These results are found in table 10 of the Bioanalytic Report (16.1.13) it begins on page 27/57 of the Bioanalytic Report (page 711/3226 of the study report).

Study 287/2004 was conducted in adults with seasonal allergic rhinitis. There were only six sites involved in this study and therefore, each site was responsible for a relatively large proportion of the total enrollment. The two sites that we have included in the audit request enrolled a large number of subjects. In addition, Site 5202 had efficacy results that were significantly better than the other sites, and also had a large number of moderate to severe adverse events. At Site 5203 the efficacy results were better than average, but not so much so that they affected the overall means. However, at this site, also, the number of moderate to severe adverse events was high for a 2-week study in a population with no other disease than rhinitis. We are submitting a list of adverse events to audit. For the efficacy endpoint we are submitting a list of subject IDs for those subjects who had better than expected results. We would appreciate it if the auditors would check a random selection of the diary entries for these subjects. Lastly, we would like the

pollen counts audited for each of these sites. The pollen count consists of one value per day per site.

Pollen counts (Listing 16.2.4.10) Site 5202 Dec 15, 2003 through February 26, 2004 and site 5203 December 17, 2003 through February 29, 2004.

Symptom scores: (Listing 16.2.6.3) The scoring is divided into “Nasal” and “Non-nasal” areas and the nasal scores include itching, stuffiness/congestion, runny nose, and sneezing. Each subject has a score (0 to 3) recorded in the morning and evening and there is an instantaneous and reflective score at each time-point. The primary endpoint for the study was an average of the two reflective nasal score, so we would like to audit these. Appendix V includes the IDs for subjects of particular interest. Please audit these and a random sample of as many additional subjects as you think appropriate to make up an adequate sample.

Adverse Events: (Listing 16.2.7.1) Appendix IV of audit request.

APPENDIX I

Adverse Events in Study 405(144/2005)

	Adverse Event	Start Date	End Date	Severity	id	DSI Comment
7.	Ear infection NOS	2004-10-27	2004-11-06	Moderate	5024	
9.	Varicella	2004-10-13	2004-11-05	Moderate	5031	
10.	Pneumonia NOS	2005-01-15	2005-01-24	Moderate	5045	
15.	Cough	2004-12-27	2004-12-27	Mild	5052	
16.	Body temperature increased	2005-01-01	2005-01-02	Mild	5052	
17.	Otitis media NOS	2005-01-01	2005-01-10	Moderate	5052	
18.	Headache	2004-12-29	2004-12-30	Mild	5054	
19.	Headache	2005-01-11	2005-01-12	Mild	5054	
20.	Nasopharyngitis	2005-01-09	2005-01-17	Moderate	5054	
26.	Epistaxis	2005-03-24	2005-03-24	Mild	5093	
27.	Abdominal pain NOS	2005-04-27		Severe	5093	
28.	Lymphadenopathy	2005-04-27		Severe	5093	
29.	Cough	2005-02-16	2005-02-18	Moderate	5098	
30.	Cough	2005-03-01	2005-03-07	Moderate	5098	
31.	Pyrexia	2005-03-06	2005-03-06	Moderate	5098	
35.	Viral infection NOS	2005-03-29	2005-04-15	Moderate	5104	
39.	Cough	2005-04-05	2005-04-10	Moderate	5118	
40.	Pharyngitis	2005-04-05	2005-04-10	Mild	5118	
41.	Upper respiratory tract infection NOS	2005-03-18	2005-04-11	Mild	5118	
45.	Pharyngitis streptococcal	2005-04-02	2005-04-07	Moderate	5126	
47.	Blood alkaline phosphatase NOS increased	2005-04-11		Moderate	5131	

APPENDIX II

Ophthalmologic Results: Study 405 (144/2005)

id	result	Eye	Date/Visit/Time	DSI Comment
29.	12	OD	2004-09-10T07:50	
30.	15	OS	2004-09-10T07:50	
31.	15	OD	2004-10-08T08:59	
32.	14	OS	2004-10-08T08:59	
33.	9	OD	2004-10-29T08:14	
34.	10	OS	2004-10-29T08:14	
205.	16	OD	2004-09-24T07:20	
206.	14	OS	2004-09-24T07:20	
207.	14	OD	2004-10-22T07:40	
208.	14	OS	2004-10-22T07:40	
209.	18	OD	2004-11-12T07:47	
210.	18	OS	2004-11-12T07:47	
319.	18	OD	2004-12-06T08:30	
320.	18	OS	2004-12-06T08:30	
321.	20	OD	2005-01-03T07:30	
322.	18	OS	2005-01-03T07:30	
323.	18	OD	2005-01-24T07:32	
324.	18	OS	2005-01-24T07:32	
355.	20	OD	2005-01-03T07:43	
356.	20	OS	2005-01-03T07:43	
357.	14	OD	2005-01-31T07:10	
358.	10	OS	2005-01-31T07:10	
359.	21	OD	2005-02-21T07:30	
360.	18	OS	2005-02-21T07:30	
519.	16	OD	2005-01-31T07:47	
520.	14	OS	2005-01-31T07:47	
521.	13	OD	2005-02-28T07:45	
522.	15	OS	2005-02-28T07:45	
523.	28	OD	2005-03-21T07:35	
524.	26	OS	2005-03-21T07:35	
551.	4	OD	2005-01-31T07:32	
552.	6	OS	2005-01-31T07:32	
553.	13	OD	2005-03-07T07:10	

554.	5092	8	OS	2005-03-07T07:10
555.	5092	6	OD	2005-03-28T07:15
556.	5092	8	OS	2005-03-28T07:15
701.	5117	14	OD	2005-02-21T07:57
702.	5117	14	OS	2005-02-21T07:57
703.	5117	17	OD	2005-03-24T07:30
704.	5117	15	OS	2005-03-24T07:30
705.	5117	15	OD	2005-04-13T07:25
706.	5117	15	OS	2005-04-13T07:25
725.	5121	12	OD	2005-02-21T08:19
726.	5121	6	OS	2005-02-21T08:19
727.	5121	12	OD	2005-03-21T07:20
728.	5121	12	OS	2005-03-21T07:20
729.	5121	26	OD	2005-04-11T07:18
730.	5121	24	OS	2005-04-11T07:18
813.	5134	17	OD	2005-03-03T07:30
814.	5134	15	OS	2005-03-03T07:30
815.	5134	8	OD	2005-03-28T07:45
816.	5134	10	OS	2005-03-28T07:45
817.	5134	12	OD	2005-04-18T07:30
818.	5134	18	OS	2005-04-18T07:30

APPENDIX III

Chemistry, cortisol and hematology values of interest from study 405(144(2005))

id	result	Date/Visit/time	tmtgp*	Test	DSI Comment
264.	5087	368	2005-03-21T08:30	1	Platelet Count
471.	5058	474	2005-02-21T08:30	1	Platelet Count
814.	5005	329	2004-09-10T09:20	1	Platelet Count
909.	5052	363	2005-01-24T08:59	1	Platelet Count
1133.	5087	355	2005-01-31T09:20	1	Platelet Count
1414.	5058	417	2005-01-03T08:08	1	Platelet Count
1471.	5052	344	2004-12-06T09:28	1	Platelet Count
1560.	5005	339	2004-10-29T00:00	1	Platelet Count
1998.	5092	405	2005-02-07T08:27	2	Platelet Count
3391.	5092	502	2005-03-28T09:00	2	Platelet Count
3643.	5121	433	2005-04-11T09:07	3	Platelet Count
3925.	5134	454	2005-04-18T09:18	3	Platelet Count
4244.	5121	479	2005-02-21T09:00	3	Platelet Count
4252.	5134	322	2005-03-03T08:30	3	Platelet Count
5692.	5117	418	2005-04-13T08:15	4	Platelet Count
6411.	5117	480	2005-02-21T08:50	4	Platelet Count
6713.	5033	378	2004-11-12T09:04	4	Platelet Count
6742.	5033	649	2004-09-24T08:15	4	Platelet Count
259.	5005	716	2004-10-29T00:00	1	Cortisol-AM
263.	5005	695	2004-09-10T09:20	1	Cortisol-AM
1636.	5033	260	2004-09-24T08:15	4	Cortisol-AM
1669.	5033	474	2004-11-12T09:04	4	Cortisol-AM
2626.	5052	516	2004-12-06T09:28	1	Cortisol-AM
2647.	5052	378	2005-01-24T08:59	1	Cortisol-AM
2946.	5058	217	2005-01-03T08:08	1	Cortisol-AM
2965.	5058	179	2005-02-21T08:30	1	Cortisol-AM
4406.	5087	288	2005-01-31T09:20	1	Cortisol-AM
4432.	5087	420	2005-03-21T08:30	1	Cortisol-AM
4725.	5092	424	2005-02-07T08:27	2	Cortisol-AM
4728.	5092	253	2005-03-28T09:00	2	Cortisol-AM

6043.	5117	393	2005-02-21T08:50	4	Cortisol-AM
6056.	5117	318	2005-04-13T08:15	4	Cortisol-AM
6253.	5121	243	2005-02-21T09:00	3	Cortisol-AM
6260.	5121	207	2005-04-11T09:07	3	Cortisol-AM
7032.	5134	395	2005-03-03T08:30	3	Cortisol-AM
7052.	5134	326	2005-04-18T09:18	3	Cortisol-AM
235.	5005	1	2004-10-29T00:00	1	Urinary Creatinine
264.	5005	1.77	2004-09-17T09:00	1	Urinary Creatinine
1642.	5033	1.1	2004-11-12T09:04	4	Urinary Creatinine
2638.	5052	1.5	2005-01-24T08:59	1	Urinary Creatinine
2651.	5052	1.1	2004-12-13T00:00	1	Urinary Creatinine
2919.	5058	2.8	2005-01-10T00:00	1	Urinary Creatinine
2971.	5058	1	2005-02-21T08:30	1	Urinary Creatinine
4409.	5087	1.2	2005-02-07T00:00	1	Urinary Creatinine
4438.	5087	.	2005-03-21T08:30	1	Urinary Creatinine
4707.	5092	1	2005-02-14T00:00	2	Urinary Creatinine
4731.	5092	2.5	2005-03-28T09:00	2	Urinary Creatinine
6038.	5117	.	2005-04-13T08:15	4	Urinary Creatinine
6087.	5117	.	2005-02-28T00:00	4	Urinary Creatinine
6265.	5121	1.6	2005-02-28T00:00	3	Urinary Creatinine
6274.	5121	2	2005-04-11T09:07	3	Urinary Creatinine
7040.	5134	9.3	2005-04-18T09:18	3	Urinary Creatinine
7044.	5134	1.1	2005-03-07T00:00	3	Urinary Creatinine
2612.	5052	12	2005-01-24T08:59	1	24 Hr Urine Cortisol
2649.	5052	9	2004-12-13T00:00	1	24 Hr Urine Cortisol
4694.	5092	15	2005-03-28T09:00	2	24 Hr Urine Cortisol
4708.	5092	5	2005-02-14T00:00	2	24 Hr Urine Cortisol
6262.	5121	37	2005-02-28T00:00	3	24 Hr Urine Cortisol
6290.	5121	21	2005-04-11T09:07	3	24 Hr Urine Cortisol
7017.	5134	11	2005-03-07T00:00	3	24 Hr Urine Cortisol
7042.	5134	20	2005-04-18T09:18	3	24 Hr Urine Cortisol

* tmtgp = treatment group: 1 = ciclesonide 100 mcg, 2 = 200 ciclesonide 200 mcg, 3 = ciclesonide 25 mg, and 4 = placebo

APPENDIX IV
Adverse Events in Study 401 (287/2004)

Site 5202

	Adverse Event	id	Severity	Start Date	Stop Date	DSI Comment
68.	Lower respiratory tract infection NOS	1003	Mild	2004-02-02	2004-02-11	
69.	Urticaria NOS	1006	Mild	2004-01-06	2004-02-12	
70.	Gastroenteritis viral NOS	1006	Moderate	2004-02-10	2004-02-14	
71.	Headache	1009	Mild	2004-01-06	2004-01-06	
72.	Headache	1009	Mild	2004-01-13	2004-01-13	
73.	Anxiety	1009	Moderate	2004-01-29		
74.	Intraocular pressure	1017	Moderate	2004-01-09	2004-01-10	
75.	Skin chapped	1017	Moderate	2004-01-09	2004-01-09	
76.	Dry eye NOS	1017	Severe	2004-01-10	2004-01-13	
77.	Skin chapped	1017	Moderate	2004-01-21	2004-01-21	
78.	Dry eye NOS	1017	Moderate	2004-01-15	2004-01-15	
79.	Eye swelling	1024	Mild	2004-02-03	2004-02-07	
80.	Chapped lips	1030	Severe	2004-01-16	2004-02-12	
81.	Nasal dryness	1030	Mild	2004-01-21	2004-01-23	
82.	Contusion	1036	Mild	2004-01-18	2004-01-18	
83.	Nausea	1041	Severe	2004-01-09	2004-01-10	
84.	Hypersensitivity NOS	1041	Severe	2004-01-10	2004-01-21	
85.	Influenza like illness	1041	Severe	2004-01-18	2004-01-21	
86.	Nasopharyngitis	1044	Mild	2004-02-08	2004-02-09	
87.	Gastroenteritis viral NOS	1047	Moderate	2004-01-11	2004-01-11	
88.	Corneal infection NOS	1047	Severe	2004-02-08	2004-02-13	
89.	Dizziness	1389	Severe	2004-01-15	2004-01-15	
90.	Vomiting NOS	1391	Mild	2004-02-02	2004-02-02	
91.	Conjunctival hyperaemia	1406	Severe	2004-02-12	2004-02-19	
92.	Conjunctival hyperaemia	1407	Moderate	2004-02-17	2004-02-26	
93.	Headache	1418	Severe	2004-02-01	2004-02-18	
94.	Insomnia	1418	Severe	2004-02-02	2004-02-02	
95.	Nasopharyngitis	1421	Moderate	2004-01-17	2004-01-19	
96.	Post procedural pain	1421	Severe	2004-01-12	2004-01-16	
97.	Sinusitis NOS	1425	Moderate	2004-02-18	2004-03-03	
98.	Gastroenteritis viral NOS	1425	Severe	2004-02-13	2004-02-15	

99.	Limb injury NOS	1427	Moderate	2004-02-13	2004-02-18	
100.	Contusion	1427	Moderate	2004-02-13	2004-02-18	
101.	Nasopharyngitis	1479	Severe	2004-02-14	2004-02-17	
102.	Conjunctival hyperaemia	1479	Severe	2004-02-17	2004-02-24	
103.	Food poisoning NOS	1484	Moderate	2004-02-02	2004-02-03	

Site 5203

	Adverse Event	id	Severity	Start Date	Stop Date	DSI Comment
104.	Cough	1051	Moderate	2003-12-17	2003-12-24	
105.	Throat irritation	1051	Moderate	2003-12-17	2003-12-24	
106.	Cough	1051	Moderate	2003-12-28	2003-12-28	
107.	Limb injury NOS	1051	Moderate	2004-01-01	2004-01-08	
108.	Cough	1051	Moderate	2004-01-01	2004-01-26	
109.	Fatigue	1051	Moderate	2004-01-07	2004-01-09	
110.	Ear pain	1051	Moderate	2004-01-15	2004-01-16	
111.	Arthralgia	1051	Severe	2004-01-10		
112.	Pruritus	1051	Mild	2004-01-19	2004-01-19	
113.	Dysgeusia	1054	Mild	2003-12-24	2003-12-26	
114.	Headache	1054	Severe	2003-12-26	2004-01-09	
115.	Abdominal pain NOS	1054	Moderate	2004-01-02	2004-01-10	
116.	Nasal passage irritation	1054	Mild	2004-01-07	2004-01-14	
117.	Myalgia	1054	Moderate	2004-01-05	2004-01-05	
118.	Ear pain	1054	Moderate	2004-01-05	2004-01-05	
119.	Tympanic membrane disorder NOS	1054	Mild	2004-01-07		
120.	Nasal passage irritation	1055	Moderate	2003-12-24		
121.	Insomnia	1056	Mild	2004-01-01	2004-01-03	
122.	Headache	1057	Moderate	2004-01-14	2004-01-14	
123.	Tympanic membrane disorder NOS	1058	Mild	2004-01-06	2004-01-20	
124.	Pharyngitis	1060	Mild	2004-01-03	2004-02-10	
125.	Dizziness	1060	Moderate	2004-01-05	2004-02-10	
126.	Upper respiratory tract infection NOS	1060	Moderate	2004-01-21	2004-02-10	
127.	Cough	1061	Mild	2003-12-26	2003-12-26	
128.	Herpes simplex	1061	Mild	2004-01-09	2004-01-22	
129.	Tympanic membrane disorder NOS	1061	Mild	2004-01-27		
130.	Tympanic membrane disorder NOS	1066	Mild	2003-12-30	2004-02-03	
131.	Blood pressure increased	1066	Moderate	2004-01-27	2004-02-03	

132.	Nasal passage irritation	1067	Mild	2003-12-29	2003-12-29
133.	Nausea	1067	Moderate	2004-01-21	2004-01-22
134.	Nasal passage irritation	1073	Mild	2004-01-13	2004-01-28
135.	Tympanic membrane disorder NOS	1074	Moderate	2004-01-15	2004-01-29
136.	Rhinorrhoea	1076	Mild	2003-12-24	2003-12-24
137.	Bronchitis NOS	1076	Moderate	2004-01-05	2004-01-19
138.	Rhinorrhoea	1078	Mild	2004-01-07	2004-01-08
139.	Arthralgia	1078	Moderate	2004-01-24	2004-02-05
140.	Herpes simplex	1080	Moderate	2004-01-11	2004-01-15
141.	Nasal passage irritation	1080	Mild	2004-01-28	2004-02-04
142.	Pharyngeal erythema	1081	Mild	2003-12-30	2004-01-14
143.	Sneezing	1081	Moderate	2003-12-30	2004-01-27
144.	Skin test NOS positive	1083	Moderate	2003-12-23	2003-12-25
145.	Arthralgia	1083	Moderate	2004-01-07	2004-01-15
146.	Cough	1083	Moderate	2004-01-05	2004-01-06
147.	Pharyngitis	1083	Mild	2004-01-05	2004-01-06
148.	Musculoskeletal stiffness	1083	Mild	2004-01-26	2004-02-02
149.	Neck pain	1085	Moderate	2004-01-02	2004-01-02
150.	Ear pain	1085	Moderate	2004-01-04	2004-01-06
151.	Nausea	1085	Mild	2004-01-06	2004-01-06
152.	Nausea	1085	Mild	2004-01-25	2004-01-25
153.	Pain NOS	1086	Moderate	2004-01-02	2004-01-02
154.	Vomiting NOS	1086	Moderate	2004-01-02	2004-01-02
155.	Diarrhoea NOS	1086	Moderate	2004-01-02	2004-01-02
156.	Pruritus	1086	Moderate	2004-01-15	
157.	Cerumen impaction	1087	Mild	2003-12-31	
158.	Tympanic membrane disorder NOS	1088	Mild	2003-12-30	2004-01-27
159.	Nasal passage irritation	1091	Moderate	2003-12-30	2004-01-24
160.	Influenza	1092	Severe	2003-12-27	2003-12-30
161.	Ear pain	1095	Moderate	2004-01-13	2004-01-20
162.	Tympanic membrane disorder NOS	1095	Mild	2004-01-15	2004-01-29
163.	Upper respiratory tract infection NOS	1095	Severe	2004-01-30	2004-02-13
164.	Insomnia	1097	Moderate	2004-01-07	2004-01-08
165.	Back pain	1097	Severe	2004-01-11	2004-01-13
166.	Nasal passage irritation	1097	Moderate	2004-01-15	2004-01-29
167.	Insomnia	1097	Severe	2004-01-26	2004-01-27
168.	Hoarseness	1098	Moderate	2003-12-27	2003-12-29

APPENDIX V
Efficacy in Study 401 (287/2004)

Subjects to be included in Efficacy (Symptom Score) Audit from Study 5202

	id
75.	1416
582.	1390
588.	1044
595.	1413
602.	1014
644.	1406
663.	1030
686.	1421
759.	1394
841.	1028

Subjects to be included in Efficacy (Symptom Score) Audit from Study 5203

	id
82.	1098
544.	1306
640.	1313
784.	1095
873.	1306

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/s/

Colette Jackson
3/8/2006 11:21:14 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-004

ALTANA Pharma
210 Park Avenue
Florham Park, NJ 07932

Attention: Cheryl Czachorowski
Senior Manager, Regulatory Affairs

Dear Ms. Czachorowski:

Please refer to your December 22, 2005, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ciclesonide Nasal Spray.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on February 20, 2006, in accordance with 21 CFR 314.101(a).

At this time, we have not identified any potential filing review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

If you have any questions, call Colette Jackson, Regulatory Project Manager, at (301) 796-1230.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, MD, Ph.D.
Director
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Badrul Chowdhury
3/2/2006 11:43:07 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 22-004

ALTANA Pharma
210 Park Avenue
Florham Park, NJ 07932

Attention: Cheryl Czachorowski
Senior Manager, Regulatory Affairs

Dear Ms. Czachorowski:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Ciclesonide Nasal Spray

Review Priority Classification: Standard (S)

Date of Application: December 22, 2005

Date of Receipt: December 22, 2005

Our Reference Number: NDA 22-004

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on February 20, 2006, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be October 22, 2006.

Under 21 CFR 314.102(c), you may request a meeting with this Division (to be held approximately 90 days from the above receipt date) for a brief report on the status of the review but not on the ultimate approvability of the application. Alternatively, you may choose to receive a report by telephone.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirement. We acknowledge receipt of your request within this application for a partial waiver of pediatric studies. We have reviewed your partial waiver request and agree that a waiver is justified only for pediatric studies in patients zero to 6

months of age for ciclesonide since the disease does not exist or is difficult to diagnose in children of this age range.

We also acknowledge receipt of your request within this application for a deferral of pediatric studies. We are deferring submission of your pediatric studies for patients 6 months to 2 years of age until December 31, 2008.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the Guidance for Industry on Qualifying for Pediatric Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" in addition to your plans for pediatric drug development described above. Please note that satisfaction of the requirements in section 2 of PREA alone may not qualify you for pediatric exclusivity.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. Address all communications concerning this NDA as follows:

U.S. Postal Service/ Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Pulmonary and Allergy Drug Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call Colette Jackson, Project Manager, at (301) 796-1230.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, MD, Ph.D.
Director
Division of Pulmonary and Allergy Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Badrul Chowdhury
2/24/2006 04:19:42 PM

MEMO OF FILING MEETING

DATE: February 13, 2006

BACKGROUND:

NDA 22-004 is a new molecular entity. IND 65,488 is the referenced IND for ciclesonide.

ATTENDEES:

Eugene Sullivan, M.D., Ph.D., Deputy Division Director, DPADP
Lydia Gilbert-McClain, M.D., Acting Clinical Team Leader, DPADP
Carol Bosken, M.D., Clinical Reviewer, DPADP
Eugenia Nashed, Ph.D., Acting Pharmaceutical Assessment Lead
Art Shaw, Ph.D., Chemistry Reviewer
Huiqing Hao, Ph.D., Pharmacology/Toxicology Reviewer
Tim McGovern, Ph.D., Pharmacology/Toxicology Team Leader
Emmanuel Fadiran, Ph.D., Clinical Pharmacology/Biopharmaceutics Team Leader
Sayed Al Habet, Ph.D., Clinical Pharmacology/Biopharmaceutics
Amjad Iqbal, Pharm.D., Clinical Pharmacology/Biopharmaceutics Fellow
Feng Zhou, Ph.D., Statistical Reviewer
Ruthie Davi, Ph.D., Statistical Team Leader
Colette Jackson, Project Manager
Miranda Raggio, Project Manager

ASSIGNED REVIEWERS:

Discipline

Reviewer

Medical:

Carol Bosken

Secondary Medical:

Lydia Gilbert-McClain,

Statistical:

Feng Zhou

Pharmacology:

Huiqing Hao

Statistical Pharmacology:

Chemist:

Art Shaw

Environmental Assessment (if needed):

Biopharmaceutical:

Microbiology, sterility:

Microbiology, clinical (for antimicrobial products only):

DSI:

Regulatory Project Manager:

Colette Jackson

Other Consults:

Per reviewers, are all parts in English or English translation?

XYES

NO

If no, explain:

CLINICAL FILE REFUSE TO FILE _____

- Clinical site inspection needed: YES NO
- Advisory Committee Meeting needed? YES, date if known _____ NO
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

XN/A YES NO

CLINICAL MICROBIOLOGY FILE _____ REFUSE TO FILE _____ XN/A

STATISTICS FILE REFUSE TO FILE _____

BIOPHARMACEUTICS FILE REFUSE TO FILE _____

- Biopharm. inspection needed: YES
 NO

PHARMACOLOGY FILE REFUSE TO FILE _____

- GLP inspection needed: YES
 NO

CHEMISTRY FILE REFUSE TO FILE _____

- Establishment(s) ready for inspection? YES NO
- Microbiology YES NO N/A

ELECTRONIC SUBMISSION:

Any comments:

REGULATORY CONCLUSIONS/DEFICIENCIES:

- _____ The application is unsuitable for filing. Explain why:
- The application, on its face, appears to be well organized and indexed. The application appears to be suitable for filing.
- No filing issues have been identified.
- _____ Filing issues to be communicated by Day 74.

ACTION ITEMS:

1. Document no filing issues conveyed to applicant by Day 74.

Colette Jackson
Regulatory Project Manager, HFD-570

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/s/

Colette Jackson
2/24/2006 02:54:11 PM
CSO

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): Division of Drug, Marketing, Advertising and Communication (DDMAC) WO Bldg 22 Rm. 1400		FROM: Colette Jackson Project Manager Division of Pulmonary and Allergy Products		
DATE January 25, 2006	IND NO.	NDA NO. 22-004	TYPE OF DOCUMENT N	DATE OF DOCUMENT December 21, 2005
NAME OF DRUG Ciclesonide	PRIORITY CONSIDERATION Standard		CLASSIFICATION OF DRUG Pro-corticosteroid	DESIRED COMPLETION DATE August 31, 2006
NAME OF FIRM: ALTANA Pharma				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Labeling Review				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:				
This is a request for an evaluation and review of the package insert, carton, and container labeling for Ciclesonide. This submission is electronic only and is located in the EDR in the submission dated December 21, 2005.				
PDUFA DATE: October 22, 2006				
CC: Archival NDA 22-004 HFD-570/Division File HFD-570/Jackson				
SIGNATURE OF REQUESTER		METHOD OF DELIVERY (Check one) X MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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/s/

Colette Jackson
1/25/2006 06:04:22 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): Director, Division of Medication Errors and Technical Support (DMETS), HFD-420 WO Rm 4414		FROM: Colette Jackson Project Manager Division of Pulmonary and Allergy Drug Products, HFD-570		
DATE January 25, 2006	IND NO.	NDA NO. 22-004	TYPE OF DOCUMENT N	DATE OF DOCUMENT December 21, 2005
NAME OF DRUG Ciclesonide	PRIORITY CONSIDERATION Standard		CLASSIFICATION OF DRUG Pro-corticosteroid	DESIRED COMPLETION DATE August 31, 2006
NAME OF FIRM: AstraZeneca				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE-NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): Trade name review				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:				
<p>This is a request for a consult on ALTANA Pharma's NDA 22-004 for Ciclesonide. This submission is electronic only and is located on the EDR under the submission dated December 21, 2005. DMETS has completed 2 prior tradename reviews for ciclesonide under IND 65,488.</p> <p>PDUFA DATE: October 22, 2006 ATTACHMENTS: CC: Archival NDA 22-004 HFD-570/Division File HFD-570/Jackson</p>				
SIGNATURE OF REQUESTER		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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/s/

Colette Jackson
1/25/2006 06:02:31 PM

DSI CONSULT: Request for Clinical Inspections

Date:

To: Leslie Ball, M.D., Branch Chief, GCP2, HFD-47

From: Colette Jackson, Regulatory Health Project Manager, HFD-570
Division of Pulmonary and Allergy Products

Subject: **Request for Clinical Site Inspections**
NDA 22-004
Altana Inc.
Ciclesonide Nasal Spray

Protocol/Site Identification:

As discussed with you, the following protocols/sites essential for approval have been identified for inspection. These sites are listed in order of priority.

Site # (Name and Address)	Protocol #	Number of Subjects	Indication
Perennial Rhinitis	144/2005	Arkansas Research Medical Testing 1207 Rebamen Park Road Little Rock, AR 72202	
Seasonal Rhinitis	287/2004	Daniel V. Freeland, MD 8501 North Mopac Expressway, Suite 200 Austin, Texas 78759	
Seasonal Rhinitis	287/2004	Central Texas Health Research 705 A Landa Street New Braunfels, Texas 78130	

Goal Date for Completion:

We request that the inspections be performed and the Inspection Summary Results be provided by (inspection summary goal date) August 1, 2006. We intend to issue an action letter on this

application by (division action goal date) September 22, 2006. The PDUFA due date for this application is October 22, 2006.

Should you require any additional information, please contact Colette Jackson.

If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?

YES NO

Is the application affected by the Application Integrity Policy (AIP)?
If yes, explain.

YES xNO

If yes, has OC/DMPQ been notified of the submission?

YES NO

• Does the submission contain an accurate comprehensive index? xYES NO

• Was form 356h included with an authorized signature? xYES NO
If foreign applicant, both the applicant and the U.S. agent must sign.

• Submission complete as required under 21 CFR 314.50?
If no, explain: xYES NO

• If an electronic NDA, does it follow the Guidance? xYES NO
If an electronic NDA, all certifications must be in paper and require a signature.
Which parts of the application were submitted in electronic format?

Modules 1 through 5 were submitted electronically.

Additional comments:

Module 1 provided also in paper.

• If in Common Technical Document format, does it follow the guidance? xYES NO

• Is it an electronic CTD?(eCTD not currently available) xYES NO
If an electronic CTD, all certifications must be in paper and require a signature.
Which parts of the application were submitted in electronic format?

Modules 1 through 5 were submitted in electronic format.

Additional comments:

Module 1 was also provided in paper.

• Patent information included with authorized signature? xYES NO

• Exclusivity requested? xYES, 5 years NO
Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

• Correctly worded Debarment Certification included with authorized signature? xYES NO
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

NOTE: Debarment Certification must have correct wording, e.g.: "I, the undersigned, hereby certify that _____ Co. did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug and Cosmetic Act in connection with the studies listed in Appendix ____." Applicant may not use wording such as "To the best of my knowledge"

- Financial Disclosure information included with authorized signature? xYES NO
(Forms 3454 and/or 3455 must be used and must be signed by the APPLICANT.)
- Field Copy Certification (that it is a true copy of the CMC technical section)? xYES NO

Refer to 21 CFR 314.101(d) for Filing Requirements

- PDUFA and Action Goal dates correct in COMIS? xYES NO
 If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name/Applicant name correct in COMIS? If not, have the Document Room make the corrections.
- List referenced IND numbers: IND 65,488
- End-of-Phase 2 Meeting(s)? Date(s) 10/1/05
 If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) 8/29/05 (CMC); 6/7/05
 If yes, distribute minutes before filing meeting.

Project Management

- Package insert consulted to DDMAC? xYES NO
- Trade name (plus PI and all labels and labeling) consulted to ODS/Div. of Medication Errors and Technical Support? xYES NO
- MedGuide and/or PPI (plus PI) consulted to ODS/Div. of Surveillance, Research and Communication Support? xN/A YES NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? xN/A YES NO

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/ Div. of Surveillance, Research and Communication Support? xN/A YES NO
- Has DOTCDP been notified of the OTC switch application? YES NO

Clinical

was notified the NDA was filed [21 CFR 314.52(b)]. Subsequently, the applicant must submit documentation that the patent holder(s) received the notification ([21 CFR 314.52(e)].

___ 21 CFR 314.50(i)(1)(ii): No relevant patents.

___ 21 CFR 314.50(i)(1)(iii): The patent on the listed drug is a method of use patent and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications.

___ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above.)

___ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

• Did the applicant:

• Identify which parts of the application rely on information the applicant does not own or to which the applicant does not have a right of reference?

YES NO

• Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?

YES NO

• Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?

N/A YES NO

• Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).?

N/A YES NO

• If the (b)(2) applicant is requesting exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

• Certification that each of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).

YES NO

• A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.

YES NO

• EITHER

The number of the applicant's IND under which the studies essential to approval were conducted.

YES, IND # _____ NO

OR

A certification that it provided substantial support of the clinical investigation(s) essential to approval if it was not the sponsor of the IND under which those clinical studies were conducted?

N/A YES NO

- Has the Director, Div. of Regulatory Policy II, HFD-007, been notified of the existence of the (b)(2) application?
YES NO

ATTACHMENT

R E V I E W

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: March 13, 2006
From: Arthur B. Shaw, Ph.D., Chemist, Division of Pharmaceutical Assessment 1,
Branch 2, ONDQA
To: NDA 22004
Subject: Filing Review and Preliminary CMC issues to be communicated to
applicant

The CMC section of this NDA is acceptable for filing.

I. Drug Substance

The drug substance synthesis in DMF [redacted] was extensively reviewed to support the ciclesonide [redacted] and the DMF was found ACCEPTABLE but an IR letter was sent. The holder has responded. The same situation is true for DMF [redacted] for the intermediate used to prepare the ciclesonide. There are no significant issues to be resolved regarding the [redacted]

[redacted]

ACCEPTABLE for filing.

II. Drug Product

A. Components and Composition

Ingredient	Amount				Function
	mg/actuation	mg/mL	Wt %2	mg/bottle	
				120 puff presentation	
Ciclesonide, _____	0.050				Active ingredient
Microcrystalline Cellulose (MMC) and Carboxymethylcellulose Sodium (CMCNa) NF _____					
Potassium Sorbate NF					
Edetate Disodium USP					
Hydrochloric Acid NF q.s. ad			pH 4.5 ± 0.2		pH adjustment
Purified Water USP q.s. ad					

MCC/CMCNa is a premix of MCC and CMCNa and is found in the NF. Its _____

The choices of the excipients are discussed in the Pharmaceutical Development Report (PDR).

ACCEPTABLE for filing.

B. Manufacturing Sites

Manufacture, in-process testing, release testing, packaging, and labeling are performed by: _____

ALTANA Pharma AG
Robert-Bosch-Strasse
8 D-78224 Singen Germany

[Redacted]

ACCEPTABLE for filing.

C. Manufacturing Process

Preparation of the formulation was studied in the PDR and it was found that the order of the addition of ingredients is important to achieving a product that display the correct [Redacted] properties and suspendability.

ACCEPTABLE for filing.

D. In-process Controls

[Redacted]

ACCEPTABLE for filing.

E. Specifications

The specifications have been set based on the Nasal Spray Guidance (NSG) and discussions with the Agency at meetings that occurred during the development process.

[Redacted]

1

ACCEPTABLE for filing.

4 Page(s) Withheld

 ✓ § 552(b)(4) Trade Secret / Confidential

 § 552(b)(5) Deliberative Process

 § 552(b)(5) Draft Labeling

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/s/

Arthur B. Shaw
3/13/2006 12:42:54 PM
CHEMIST
CMC Filing Review

Blair Fraser
3/20/2006 07:50:31 AM
CHEMIST

1 Page(s) Withheld

 § 552(b)(4) Trade Secret / Confidential

 § 552(b)(5) Deliberative Process

 § 552(b)(5) Draft Labeling

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/s/

Arthur B. Shaw
3/13/2006 06:07:21 PM
CHEMIST
Addendum to filing review
This is an additional quesiton about the DMFs.

Blair Fraser
3/20/2006 07:56:02 AM
CHEMIST

NDA Pharmacology Fileability Check List

NDA No: 22-004

Date of submission: December 21, 2005

Date of Fileability meeting: February 13, 2006

Information to Sponsor Yes () No (X)

Date of check list: February 10, 2006

(1) On its face, is the Pharm/Tox section of the NDA organized in a manner to allow substantive review? Yes (X) No () NA ()

(2) On its face, is the Pharm/Tox section of the NDA legible for review?
Yes (X) No () NA ()

(3) Are final reports of all required and requested preclinical studies submitted in this NDA? Yes (X) No () NA ()

	Yes	No	NA
Pharmacology	(X)	()	()
ADME	(X)	()	()
Toxicology (duration, route of administration and species specified)			
acute	(X)	()	()
subchronic and chronic studies	(X)	()	()
reproductive studies	(X)	()	()
carcinogenicity studies	(X)	()	()
mutagenicity studies	(X)	()	()
special studies	()	()	(X)
others	(X)	()	()

(4) If the formulation to be marketed is different from the formulation used in the toxicology studies, is repeating or bridging the studies necessary? Yes (X) No () NA ()

If no, state why not?

If yes, has the applicant made an appropriate effort to repeat the studies using the to be marketed product, to bridge the studies or to explain why such repetition or bridging should not be required? Yes (X) No () NA ()

A 4-week Intranasal studies in rats and a 4-week and a 6-month intranasal studies in dogs were completed.

(5) Are the proposed preclinical labeling sections (carcinogenesis, mutagenesis and impairment of fertility, pregnancy category and overdosage) appropriate (including human dose multiples expressed in either mg/m² or comparative systemic exposure levels) and in accordance with 201.57? Yes (X) No ().

(6) Has the applicant submitted all special studies/data requested by the Division prior to the submission including but not limited to pre-NDA discussion? Yes (X) No () NA ()

(7) On its face, does the route of administration used in the pivotal toxicity studies appear to be the same as the intended clinical route? Yes (X) No () NA ()

If not, has the applicant submitted a rationale to justify the alternative route?
Yes () No () NA ()

(8) Has the applicant submitted a statement(s) that all of the toxicity studies have been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations? Yes (X) No () NA ()

(9) Has the applicant submitted any studies or data to address any impurity or extractable issues (if any)? Yes () No (X) NA ()

(10) Are there any outstanding preclinical issues? Yes () No (X)
If yes, identify those below.

(11) From a preclinical perspective, is this NDA fileable? Yes (X) No ()

If no, state below why it is not.

(12) Should any additional information/data be requested? Yes () No (X)

NDA Planning Timeline

NDA No.: 22-004

Date of planning timeline:

PDUFA Due Date: October 20, 2006

Projected review completion date: August 22, 2006

Pharmacology and ADME
Toxicology

Milestone Dates
July 12, 2006

General toxicity studies
Carcinogenicity studies and mutagenicity studies
Reproductive studies
Special studies and Others

Completed
Completed
Completed
July 12, 2006

Labeling

August 12, 2006

Signatures (optional):

Reviewer Signature _____
Huiqing Hao, Ph.D.

Supervisor Signature _____
Tim MCGovern, Ph.D.

Concurrence Yes ___ No ___

cc:
NDA 22,004, HFD-570 Division Files
JacksonC, DPAP
BoskenC, DPAP
MCGovernT, DPAP
HaoH, DPAP

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/s/

Huiqing Hao
2/14/2006 10:17:35 AM
PHARMACOLOGIST

Timothy McGovern
2/14/2006 11:43:43 AM
PHARMACOLOGIST
I concur.