CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-300

ADMINISTRATIVE DOCUMENTS

RECORD OF TELEPHONE CONVERSATION

On September 26, 2002, we contacted Altana Inc. (Altana) and made reference to their ANDA 76-300. We requested that Altana tighten the stability specification for ——— based on the Innovator data. Ms. Bialeski informed us that she will submit a proposal for the new specification. We informed Ms. Bialeski that we granting a —month expiry because Altana have provided only ——— data and the——— stability data ———. Ms. Bialeski acknowledged our comment. She inquired if Altana could provide updated stability data to extend the expiry to —month after tentative approval is granted. We informed Ms. Bialeski that that could be done as an amendment after tentative approval. In addition, we requested that Altana revise the stability tables to include the current specifications. Ms. Bialeski agreed to do so and submit all of the above as a telephone amendment. On October 8, 2002, I (Sarah Ho) contacted Ms. Carman and made reference to their ANDA 76-300 and to our teleconference on September 26, 2002. I requested for the innovator data to justify the stability specification for all the ——— Ms. Carman agreed to submit the data as a telephone amendment.	**DATE:** 9/26/02 & 10/8/02 **ANDA NUMBER** 76-300 **TELECON INITIATED BY AGENT** **PRODUCT NAME:** Fluticasone Propionate Oint, 0.005 % **FIRM NAME:** Altana Inc. **FIRM REPRESENTATIVES:** Audrey Bialeski, Regulatory Affiars Virginia Carman, Regulatory Affairs **TELEPHONE NUMBER:** 631-454-7677 ext. 3007 **FDA REPRESENTATIVES** Nashed Nashed James Fan Sarah Ho **SIGNATURES:** N.Nashed 10/17/02 J.Fan 10/17/02 S.Ho 10/17/02

Orig: ANDA 76-300
Cc: Division File
Chem. I Telecon Binder
V:\FIRMSAM\ALTANA\TELECONS\76300.02.09.26.doc

RECORD OF TELEPHONE CONVERSATION

On this date, I contacted Altana Inc. (Altana) and made reference to their ANDA 76-300. I requested that Altana tighten the [redacted] specification to [redacted] Ms. Zewelski agreed to submit the revised specification as a telephone amendment.	**DATE:** 11/4/02
	ANDA NUMBER 76-300
	TELECON INITIATED BY AGENT
	PRODUCT NAME: Fluticasone Propionate Oint, 0.005 %
	FIRM NAME: Altana Inc.
	FIRM REPRESENTATIVES: Audrey Zeweleski, Regulatory Affiars
	TELEPHONE NUMBER: 631-454-7677 ext. 3007
	FDA REPRESENTATIVES Sarah Ho
	SIGNATURES: S.Ho 11/4/02

Orig: ANDA 76-300
Cc: Division File
Chem. I Telecon Binder
V:\FIRMSAM\ALTANA\TELECONS\76300.02.11.04.doc

RECORD OF TELEPHONE CONVERSATION

Agency: We noticed that you only have — months stability data. Did you want only — months expiration dating. When we sent you the TA letter in 2003, you were TA for — months expiration dating. You should have more stability data now.

Firm: Yes, we have more data now and we do not want — months expiration dating. We will submit updated stability data as a t-amend.

DATE
4/14/04

ANDA NUMBER
76-300

IND NUMBER

TELECON

INITIATED BY

SPONSOR

FDA x

PRODUCT NAME
Fluticasone Propionate Ointment, 0.005%

FIRM NAME
Altana

NAME OF PERSON WITH WHOM CONVERSATION WAS HELD
Audrey Zaweski

TELEPHONE NUMBER
631-454-7677 ext3007

SIGNATURE
A. Vu 4/14/04

CC: 76-300
Chem Div I, T-con Notebook
V:\FIRMSAM\ALTANA\TELECONS\76300.14apr2004.doc

RECORD OF TELEPHONE CONVERSATION

Agency: In your April 15, 2004 amendment, you submitted — months stability data. You had a failed point data at 15 grams at — months, the ——— was out of spec.

Firm: I know, we will take 18 months.

Agency: You need to point out your failed point, its part of the cGMP requirements. We also do not understand the numbers in the parentheses.

Firm: they represent the range around the mean (top, middle, bottom).

Agency: It's confusing, you need to revise them. You need to request 18 months expiration dating for the 15 grams tube size. You also need to adjust the specification for top,middle, and bottom and also include the RSD. In the future, you need to clearly point out your failing data.

Firm: Agreed, we will send in your request as a t-amendment.

DATE
4/16/04

ANDA NUMBER
76-300

IND NUMBER

TELECON

INITIATED BY

SPONSOR

FDA x

PRODUCT NAME

Fluticasone propionate Ointment, 0.005%

FIRM NAME
Altana, Inc.

NAME OF PERSON WITH WHOM CONVERSATION WAS HELD

Audrey Zaweski

TELEPHONE NUMBER
631-454-7677 ext3007

SIGNATURE
P. Schwartz PS 4/20/04
N. Nashed NN 4/20/04
A. Vu 4/21/04

CC: 76-300
Chem Div I, T-con Notebook
V:\FIRMSAM\ALTANA\TELECONS\76300.16apr2004.doc

RECORD OF TELEPHONE CONVERSATION

Agency: Why do you [redacted] your ointment before [redacted] ? What added value does this do?

Firm: We [redacted] our ointment to [redacted] It's easier to [redacted] the ointment [redacted].

Agency: But by [redacted] the ointment, what happened to the [redacted] of the ointment itself?

Firm: We are not changing the [redacted] of the product. [redacted] before measuring the viscosity.

Agency: What's your data on the viscosity?

Firm: We have [redacted] months data: [redacted] and our stability spec is: [redacted].

Agency: Could you do some developmental work? We want you to do a comparative study measuring the viscosity: [redacted] the ointment. Depending on the data, you may need to change your viscosity testing method and your specifications. We want you to commit to performing this study [redacted] 60 days after approval. We want a Post Approval Commitment.

Firm: Agreed, we will fax our commitment and the time frame for the study.

DATE
5/11/04

ANDA NUMBER
76-300

IND NUMBER

TELECON

INITIATED BY

SPONSOR

FDA x

PRODUCT NAME
Fluticasone ointment, .005%

FIRM NAME
Altana

NAME OF PERSON WITH WHOM CONVERSATION WAS HELD
Audrey Zaweski, Weldon Crowe, Daren Keans, Joe Check

TELEPHONE NUMBER
631-454-7677 ext 3007

SIGNATURE
P. Schwartz 5/13/04
J. Fan 5/13/04
A. Vu 5/13/04

CC: 76-300
Chem Div I, T-con Notebook
V:\FIRMSAM\ALTANA\TELECONS\76300.11may2004.doc

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-300

CORRESPONDENCE

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

December 17, 2001 *VIA FEDERAL EXPRESS*

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

505(j)(2)(A) OK
15-FEB-2002

Original Submission
Abbreviated New Drug Application
Fluticasone Propionate Ointment, 0.005%

Dear Sir or Madam:

Pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act and in accordance with the provisions under 21 CFR §314.94, Altana Inc. is submitting this Abbreviated New Drug Application to market a new drug, **Fluticasone Propionate Ointment, 0.005%**.

The Reference Listed Drug (RLD) that is the basis for this submission is **Cutivate ® Ointment, 0.005%** (fluticasone propionate ointment), Manufactured by Glaxo Wellcome Inc., NDA 19-957. The proposed drug, Fluticasone Propionate Ointment, 0.005% contains the same active ingredient and is identical in strength, dosage form and route of administration to the RLD. All inactive ingredient amounts conform to the ranges as listed in the Inactive Ingredient Guide (January 1996).

The exhibit batch, Batch #G280, included in this application was fully packaged utilizing the 15 gram, 30 gram and 60 gram presentations for which approval is currently requested. The number of units filled for these packaging sizes and the disposition of any remaining bulk product are reconciled in the exhibit batch record.

Included in this Five (5) volume submission, along with Form FDA 356h, is the required Patent Status and Exclusivity Statements; Draft Labeling; Bioequivalence Study; full Components and Composition statements; Raw Materials Controls, description of the Manufacturing Facilities, Manufacturing and Processing Instructions, In-Process Controls, Filling and Packaging procedures; Container/Closure System; controls for the Finished Dosage Form, Analytical Methods; Stability of the Finished Dosage Form; Environmental Assessment and Certification Requirements of the Generic Drug Enforcement Act of 1992.

A copy of the two bioequivalency data diskettes are located in the inside cover of Volume 1.1 of the Pharmacokinetics copy of the Abbreviated New Drug Application.

All regulatory correspondence related to this Abbreviated New Drug Application should be addressed to the following:

Ms. Virginia Carman
Associate Director, Regulatory Affairs
Altana, Inc.
60 Baylis Road
Melville, NY 11747
Telephone: (631) 454-7677
Facsimile: (631) 756-5114

A certified copy of the technical section and a copy of the Methods Validation package, are being sent to the New York District Office under separate cover.

Sincerely,
ALTANA INC.

Audrey Bialeski For

Robert J. Anderson. Esq.
Senior Director, Scientific Affairs

RJA/ap

Enclosures

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

February 13, 2002

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

VIA FEDERAL EXPRESS

NEW CORRESP
NC

ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
Telephone Amendment

Dear Sir or Madam:

Reference is made to the Altana Inc. Abbreviated New Drug Application dated December 17, 2001 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act and in accordance with the provisions under 21 CFR §314.94, for **Fluticasone Propionate Ointment, 0.005%**.

Reference is also made to the telephone conference held on February 11, 2002 between Paras Patel, FDA and Virginia Carman, *Associate Director*, Regulatory Affairs, Altana Inc.

Mr. Patel requested draft copies of the proposed container, carton and insert labeling for all presentations of the proposed drug. Included in **Attachment I** are the draft copies of the 15, 30 and 60 gram product presentations including the product package insert. In addition to the draft labeling, a current DMF authorization letter for the [redacted] is included in **Attachment II** and a cGMP Certification for the Altana Inc. Melville facility located at 60 Baylis Road, Melville, NY 11747 is included as **Attachment III**.

If you have any questions or require additional information please contact Virginia Carman at (631) 454-7677 extension 2091. FAX communications can be made to (631) 756-5114.

Sincerely,
ALTANA INC.

Virginia Carman for

Robert J. Anderson. Esq.
Senior Director, Scientific Affairs

RJA/jb

CENTER FOR DRUG EVALUATION AND RESEARCH
FEB 14 2002
DGD

ANDA 76-300

FEB 15 2002

Altana Inc.
Attention: Virginia Carman
60 Baylis Road
Melville, NY 11747

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the telephone conversation dated January 25, 2002 and to your correspondence dated February 13, 2002.

NAME OF DRUG: Fluticasone Propionate Ointment, 0.005%

DATE OF APPLICATION: December 17, 2001

DATE (RECEIVED) ACCEPTABLE FOR FILING: December 18, 2001

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Sarah Ho
Project Manager
(301) 827-5848

Sincerely yours,

Gregory S. Davis for

Wm Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

MINOR AMENDMENT

ANDA 76-300

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

APR 16 2002

TO: APPLICANT: Altana Inc.

TEL: 631-454-7677

ATTN: Virginia Carman

FAX: 631-756-5114

FROM: Sarah Ho

PROJECT MANAGER: 301-827-5754

Dear Madam:

This facsimile is in reference to your abbreviated new drug application dated December 17, 2001, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Fluticasone Propionate Ointment, 0.005%.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (4 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:
CMC comments provided. Please include in your response.

4/16/2002 fax

Redacted 4

Page(s) of trade secret and /or confidential commercial information

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

April 22, 2002

Office of Generic Drugs
Food and Drug Administration
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

NEW CORRESP

RE: ANDA 76-300
Fluticasone Propionate Ointment, 0.005%

Dear Sir or Madam:

Reference is made to the Altana Inc. Abbreviated New Drug Application dated December 17, 2002 submitted pursuant to Section 505 (j) of the Federal Food Drug and Cosmetic Act for Fluticasone Propionate Ointment, 0.005%. Reference is also made to several telephone conversations between representatives of the Division of Bioequivalence and Altana Inc.

The Division requested clarification as to whether the Fluticasone Ointment bioequivalence study was performed under occlusive dressing as stated in the final report. This was a concern as the labeling states that the product should not be used under occlusive dressings.

Altana Inc. verified with ——, the CRO that performed the study that the study was performed under occlusive dressings. —— explained that a previous attempt to perform a dose response study on Fluticasone Cream, which is ten times more potent than Fluticasone Ointment, was unsuccessful in obtaining any useful data.

When the study was redone using light occlusion (paper tape not cellophane) useful readings were obtained. As per the 1995 Guidance, occlusive dressings are allowed under certain conditions, i.e. low potency corticosteroids.

Due to the ten times lower potency of Fluticasone Ointment the occlusive dressing method was used for the pilot and pivotal studies.

RECEIVED

APR 2 4 2002

OGD / CDER

If you have any questions, or require additional information please contact me at (631) 454-7677 ext. 2091. Fax communication may be sent to (631) 756-5114.

Sincerely,

ALTANA Inc.

Virginia Carman
Associate Director, Regulatory Affairs

VC/cc

APPEARS THIS WAY
ON ORIGINAL

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

May 21, 2002

Office of Generic Drugs, Center for Drug Evaluation and Research, FDA
Metro Park North II
7500 Standish Place Rm. 150
Rockville, MD 20855-2773

B10

NEW CORRESP

RE: ANDA 76-300
Telephone Bioequivalence Amendment
Fluticasone Propionate Ointment, 0.005%

Dear Sir:

Reference is made to the Altana Inc. Abbreviated New Drug Application dated December 17, 2002 submitted pursuant to Section 505 (j) of the Federal Food Drug and Cosmetic Act for Fluticasone Propionate Ointment 0.005%. Reference is also made to Altana Inc.'s correspondence of April 22, 2002, as well as, several conversations between representatives of the Division of Bioequivalence and Altana Inc.

The Division requested Altana Inc. to provide them with the actual data refered to in the April 22, 2002 letter. As per a telephone conversation between Altana and the Division it was agreed that, as the referenced information was not generated on Altana's behalf, the CRO who performed the study ——— would provide the data directly to the Division. Altana Inc. will provide the cover letter and Form FDA 653H.

Therefore, included with this cover letter are the signed Form FDA 356h, explanation from the CRO ———, and the requested data.

If you have any questions or require additional information please contact me at (631) 454-7677 ext. 2091. Fax communication can be made to (631) 756-5114.

Sincerely,

Altana Inc.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

VC/cc

RECEIVED
MAY 2 3 2002
OGD / CDER

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

July 29, 2002

William Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

VIA FEDERAL EXPRESS

ORIG AMENDMENT
N/AF

ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
Labeling Amendment

Dear Mr. Rickman:

Reference is made to the Altana Inc. Abbreviated New Drug Application dated December 17, 2001 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for **Fluticasone Propionate Ointment, 0.005%**.

Reference is also made to the FDA correspondence dated July 2, 2002 which contained the following labeling deficiencies. All items have been addressed in **Comment**/Response format.

1. **CONTAINER (15 g, 30 g, 60 g)**

   Revise the name to read "Fluticasone Propionate Ointment, 0.005%"

   The 15, 30 and 60 gram container labeling has been revised to read "Fluticasone Propionate Ointment, 0.005%.

2. **CARTON (15 g, 30 g, 60 g)**

   See the comment under container

   The 15, 30 and 60 gram carton labeling has been revised to read "Fluticasone Propionate Ointment, 0.005%.

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3. INSERT

a. GENERAL

i. Please note that the following comments are based on the last approved insert labeling for Cutivate® Ointment (approved December 9, 2001). Refer to the website listed at the end of this letter

ii. Replace "Fluticasone Propionate Ointment" with "fluticasone propionate ointment" throughout the text. Please note that USAN names are common nouns and should be treated as such in the text of labeling (i.e., lower case). Upper case may be used when USAN names stand alone as on labels or in the title of the package insert.

"Fluticasone Propionate Ointment" has been replaced with "fluticasone propionate ointment" throughout the text of the insert, where necessary.

b. CLINICAL PHARMACOLOGY

i. Please add the following paragraph as the new second paragraph:

Fluticasone propionate is lipophilic and has a strong affinity for the glucocorticoid receptor. It has weak affinity for the progesterone receptor, and virtually no affinity for the mineralocortocoid, estrogen, or androgen receptors. The therapeutic potency of glucocorticoids is related to the half-life of the glucocorticoid-receptor complex. The half-life of the fluticasone propionate-glucocorticoid receptor complex is approximately 10 hours.

The following paragraph has been added as the new second paragraph.

> Fluticasone propionate is lipophilic and has a strong affinity for the glucocorticoid receptor. It has weak affinity for the progesterone receptor, and virtually no affinity for the mineralocortocoid, estrogen, or androgen receptors. The therapeutic potency of glucocorticoids is related to the half-life of the glucocorticoid-receptor complex. The half-life of the fluticasone propionate-glucocorticoid receptor complex is approximately 10 hours.

ii. **Please refer to the Cutivate® Ointment insert labeling approved December 9, 2001, for the pharmacokinetics subsection and add the following sections; Absorption, Distribution, Metabolism and Excretion.**

The following sections have been added to the pharmacokinetics subsection: Absorption, Distribution, Metabolism and Excretion.

c. **PRECAUTIONS**

i. **Third paragraph**

Please change this paragraph to be the same as the innovator's.

The third paragraph in the PRECAUTIONS section has been revised to be the same as the innovator's.

ii. **Fourth paragraph**

Please relocate the fourth paragraph "If HPA axis suppression..." to appear immediately after the second paragraph.

The fourth paragraph "If HPA axis suppression..." has been relocated to appear immediately after the second paragraph.

iii. **Fourth paragraph, sixth sentence**

Please make editorial changes (move sentence to one line).

We have made the revision to move sentence to one line.

iv. **Fifth paragraph**

Replace ——— with "pediatric patients"...

——— has been replaced with "pediatric patients"... in the fifth paragraph.

v. **Sixth paragraph**

Please add the following paragraph as the new sixth paragraph, "Fluticasone propionate ointment, 0.005% may cause local cutaneous adverse reactions (see ADVERSE REACTIONS)."

The following paragraph has been added as the new sixth paragraph.

"Fluticasone propionate ointment, 0.005% may cause local cutaneous adverse reactions (see ADVERSE REACTIONS)."

vi. **Last paragraph, first sentence:**

Replace ———— with "presence".

The last paragraph, first sentence has been revised to replace ———— with "presence".

vii. **Information for patients**

Please add the following statements;

5. **This medication should not be used on the face, underarms, or groin areas unless directed by a physician**

6. **As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, contact the physician.**

The following statements have been added to the "Information for Patients" section:

5. This medication should not be used on the face, underarms, or groin areas unless directed by a physician

6. As with other corticosteroids, therapy should be discontinued when control is achieved. If no improvement is seen within 2 weeks, contact the physician.

viii. **Geriatric Use**

Please include this subsection to appear immediately after the Pediatric Use subsection:

A limited number of patients above 65 years of age (n=203) have been treated with fluticasone propionate ointment in US and non-US clinical trials. While the number of patients is too small to permit separate analysis of efficacy and safety, the adverse reactions reported in this population were similar to those reported by younger patients. Based on available data, no adjustment of dosage of fluticasone in geriatric patients is warranted.

The following subsection has been added immediately after the Pediatric Use subsection.

A limited number of patients above 65 years of age (n=203) have been treated with fluticasone propionate ointment in US and non-US clinical trials. While the number of patients is too small to permit separate analysis of efficacy and safety, the adverse reactions reported in this population were similar to those reported by younger patients. Based on available data, no adjustment of dosage of fluticasone in geriatric patients is warranted.

d. **DOSAGE AND ADMINISTRATION**

Please include the subsection, Geriatric Use, with the following statement:

"In studies where geriatric patients (65 years of age or older, see PRECAUTIONS) have been treated with fluticaosne propionate ointment, safety did not differ from that in younger patients; therefore, no dosage adjustment is recommended.

The subsection, Geriatric Use, with the following statement "In studies where geriatric patients (65 years of age or older, see PRECAUTIONS) have been treated with fluticaosne propionate ointment, safety did not differ from that in younger patients; therefore, no dosage adjustment is recommended" has been included in the Dosage and Administration section.

Altana is submitting 12 copies of the container, carton and insert labeling in final print as instructed. These copies are included in **Attachment I.**

Altana acknowledges, that prior to approval it may be necessary to further revise the labeling subsequent to approved changes for the Reference Listed Drug. Altana will routinely monitor the following website for any approved changes.

http://www.fda.gov/cder/ogd/rld/labelingreviewbranch.html

To facilitate the review of this Amendment and in accordance with 21 CFR 314.94(a)(8)(iv), Altana has provided a side by side comparison of the proposed labeling with the last submitted labeling with all the differences annotated and explained. Please refer to **Attachment II.**

If you have any questions or require additional information, please contact Ms. Audrey Bialeski, *Manager*, Regulatory Affairs at (631) 454-7677 extension 3007. Fax communications can be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Audrey Bialeski for

Robert J. Anderson, Esq.
Sr. Director, Scientific Affairs

RJA/jb

ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

July 30, 2002

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

ORIG AMENDMENT

VIA FEDERAL EXPRESS

ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
Minor Amendment

Dear Sir or Madam:

Reference is made to the Altana Inc. Abbreviated New Drug Application dated December 17, 2001 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act and in accordance with the provisions under 21 CFR §314.94, for **Fluticasone Propionate Ointment, 0.005%**.

Reference is also made to the FDA correspondence dated April 16, 2002 wherein the following CMC comments were provided. All items have been answered in **Comment**/Response format.

A. Deficiency

1.

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7/30/2002 ALTANA LTR

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Page(s) of trade secret and /or confidential commercial information

Pharma

ALTANA

September 30, 2002

ALTANA Inc
60 Baylis Road
Melville, NY 11747
USA
T +1 (631) 454-7677
www.altanainc.com

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, Maryland 20855

VIA TELEFAX (301) 594-0180
AND FEDERAL EXPRESS

ORIG AMENDMENT
N/A m

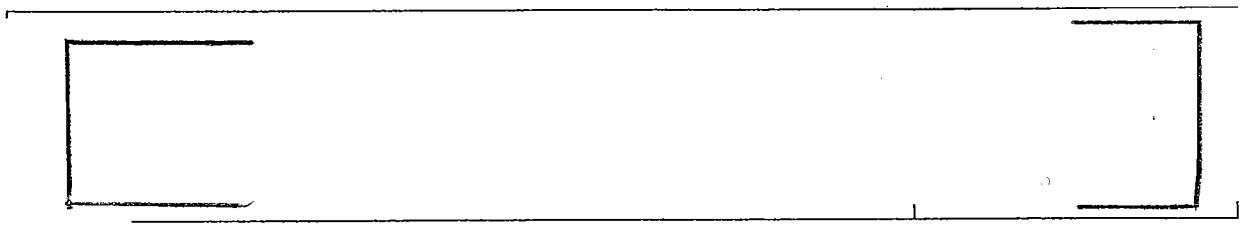
ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
Telephone Amendment

Dear Dr. Patel:

Reference is made to the Altana Inc. Abbreviated New Drug Application dated December 17, 2001 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for **Fluticasone Propionate Ointment, 0.005%**

Reference is also made to the September 26, 2002 teleconference held between Altana and FDA representatives. Altana has prepared this correspondence to address the items discussed during the conference call.

The Stability Specifications for Fluticasone Propionate Ointment, 0.005% have been revised as follows:



As requested, the stability report forms for the exhibit batch G280 have been updated to reflect the current proposed specifications. Copies of the Stability Specifications and the Stability Report Forms have been included for review.

Altana understands the Fluticasone Propionate Ointment, 0.005% will be tentatively approved with an expiration date of — months. As agreed to in the September 26, 2002 teleconference, Altana will submit updated Controlled Room Temperature Stability data for the exhibit batch G280 in order to extend the expiration period prior to receiving full approval of this Abbreviated New Drug Application.

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OGD / CDER

If you have any questions or require additional information, please contact Ms. Audrey Bialeski, *Manager*, Regulatory Affairs at (631) 454-7677 extension 3007. Fax communications can be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Virginia Carman for

Robert J. Anderson, Esq.
Sr. Director, Scientific Affairs

RJA/ab

APPEARS THIS WAY
ON ORIGINAL

Pharma

ALTANA

October 18, 2002

ORIG AMENDMENT

N/Am

ALTANA Inc
60 Baylis Road
Melville, NY 11747
USA
T +1 (631) 454-7677
www.altanainc.com

Rashmikant M. Patel, Ph.D.
Director, Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

VIA TELEFAX (301) 594-0180
& FEDERAL EXPRESS

ANDA 76-300
FLUTICASONE PROPIONATE OINTMENT, 0.005%
TELEPHONE AMENDENT

Dear Dr. Patel:
Reference is made to the Altana Inc. Abbreviated New Drug Application dated December 17, 2001 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Fluticasone Propionate Ointment, 0.005%.

Reference is also made to the October 8, 2002 teleconference held between Altana and FDA representatives. Altana has prepared this correspondence to address the items discussed during this call.

As requested, analytical results for the RLD Cutivate Ointment have been included.

No additional stability data has been generated to date on the Altana product. However, it appears that our submission of September 30, 2002 may not have included all of the updated data. This information has been included as well.

As noted in the September 30, 2002 submission, we understand that the Fluticasone Propionate Ointment, 0.005% will be tentatively approved with an expiration date of ~ months. Altana will submit updated stability data for exhibit batch G280 in order to extend the expiry period prior to receiving full approval of the Abbreviated New Drug Application.

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ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
Telephone Amendment

If you have any questions or require additional information please contact Ms. Audrey Zaweski, Manager, Regulatory Affairs, at (631) 454-7677 ext. 3007. Fax communications may be made to (631) 756-5114.

Sincerely

ALTANA INC.

Virginia Cannon for

Robert J. Anderson, Esq.
Associate Director, Regulatory Affairs

RJA:vc

APPEARS THIS WAY
ON ORIGINAL

Pharma

ALTANA

November 4, 2002

ORIG AMENDMENT
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Rockville, Maryland 20855

VIA TELEFAX (301) 594-0180
AND FEDERAL EXPRESS

ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
Telephone Amendment

Dear Dr. Patel:

Reference is made to the Altana Inc. Abbreviated New Drug Application dated December 17, 2001 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for **Fluticasone Propionate Ointment, 0.005%**

Reference is also made to the November 4, 2002 teleconference held between Altana and FDA representatives. Altana has prepared this correspondence to address the items discussed during the conference call.

Altana has revised the Finished Product and Stability Specifications for [redacted]. Copies of the proposed specifications have been included for review.

If you have any questions or require additional information, please contact Ms. Audrey Zaweski, *Manager*, Regulatory Affairs at (631) 454-7677 extension 3007. Fax communications can be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Audrey Zaweski for

Robert J. Anderson, Esq.
Sr. Director, Scientific Affairs

RJA/az

2.1

Pharma

ALTANA

November 5, 2002

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ORIG AMENDMENT
NAM

VIA TELEFAX (301) 594-0180
AND FEDERAL EXPRESS

ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
Telephone Amendment

Dear Dr. Patel:

Reference is made to the Altana Inc. Abbreviated New Drug Application dated December 17, 2001 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for **Fluticasone Propionate Ointment, 0.005%**

Reference is also made to the November 5, 2002 teleconference held between Altana and FDA representatives. Altana has prepared this correspondence to address the items discussed during the conference call.

Altana has updated the ———— Specification on the Stability Report Forms for the Exhibit batch G280. The Stability Report Forms were updated to reflect the proposed specifications of ———— submitted in the November 4, 2002 Telephone Amendment. Copies of the Stability Report Forms have been included for review.

If you have any questions or require additional information, please contact Ms. Audrey Zaweski, *Manager*, Regulatory Affairs at (631) 454-7677 extension 3007. Fax communications can be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Audrey Zaweski for

Robert J. Anderson, Esq.
Sr. Director, Scientific Affairs

RJA/az

Pharma

ALTANA

November 19, 2002

ORIG AMENDMENT

N/Amn

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VIA FEDERAL EXPRESS

ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
Telephone Amendment - Response to Request for Information

Dear Sir or Madam:

Reference is made to the Altana Inc. Abbreviated New Drug Application dated December 17, 2001 submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act and in accordance with the provisions under 21 CFR §314.94, for **Fluticasone Propionate Ointment, 0.005%**.

Reference is also made to the November 5, 2002 Telephone Amendment and November 19, 2002 teleconference held between Altana and FDA representative Ms. Sarah Ho. Altana has prepared this correspondence to address the item discussed during the conference call.

Ms. Ho requested we submit updated controlled room temperature stability reports for the exhibit batch G280. Inadvertently there were pages missing from the report in the November 5, 2002 Telephone Amendment.

If you have any questions or require additional information, please contact Ms. Audrey Zaweski, *Manager*, Regulatory Affairs at (631) 454-7677 extension 3007. Fax communications can be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Audrey Zaweski for

Robert J. Anderson, Esq.
Sr. Director, Scientific Affairs

RJA/jb

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ALTANA

November 20, 2002

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Facsimile 301-594-0180 and
VIA FEDERAL EXPRESS

ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
Telephone Amendment

Dear Dr. Patel:

Reference is made to the Altana Inc. Abbreviated New Drug Application for Fluticasone Propionate Ointment, 0.005% submitted on December 17, 2001 in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the November 20, 2002 teleconference held between Altana and FDA representatives. Altana has prepared this correspondence to address the item discussed during the conference call.

FDA requested that the Stability Specifications for [redacted] be revised based on the Controlled Room Temperature Stability Data previously submitted. Altana has revised the Stability Specifications as agreed with FDA and they are included in **Attachment I**. The following revisions were made.

[redacted]

The stability reports have also been updated to reflect these changes, see **Attachment II**. The In-Process and Finished Product Specifications did not require any revisions.

If you have any questions or require additional information, please contact Ms. Audrey Zaweski, *Manager*, Regulatory Affairs at (631) 454-7677 extension 3007. Fax communications can be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Audrey Zaweski for

Robert J. Anderson, Esq.
Sr. Director, Scientific Affairs

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February 5, 2003

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VIA TELEFAX (301) 594-0183
& FEDERAL EXPRESS

ANDA 76-300
FLUTICASONE PROPIONATE OINTMENT, 0.005%
TELEPHONE AMENDENT

ORIG AMENDMENT
N/AM

Dear Dr. Patel:

Reference is made to the Altana Inc. Abbreviated New Drug Application for Fluticasone Propionate Ointment, 0.005% submitted December 17, 2001 in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the February 4, 2002 teleconference held between Altana and FDA representatives. Altana has prepared this correspondence to address the item discussed during the conference call.

FDA has requested that the specifications for [redacted] be revised.

[redacted]

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If you have any questions or require additional information please contact Ms. Audrey Zaweski, Associate Director, Regulatory Affairs, at (631) 454-7677 ext. 3007. Fax communications may be made to (631) 756-5114.

Sincerely,

ALTANA INC.

for Audrey Zaweski

Robert J. Anderson, Esq.
Sr. Director, Scientific Affairs

RJA:az

Attachments

APPEARS THIS WAY
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Pharma

ALTANA

March 15, 2004

Gary Buehler
Director
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ORIG AMENDMENT
N/AM

VIA FEDERAL EXPRESS

ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
MINOR AMENDMENT – FINAL APPROVAL REQUESTED

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on April 22, 2002 for Fluticasone Propionate Ointment, 0.005% in accordance with Section 505 (j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the FDA correspondence dated February 27, 2003 granting Tentative Approval of the above referenced application. As requested, Altana Inc. is submitting this Minor Amendment-Final Approval Requested in order to reactivate the Fluticasone Propionate Ointment, 0.005% application for final approval consideration.

The Reference Listed Drug product (RLD) upon which the Altana application is based, Cutivate Ointment, 0.005% of GlaxoSmithKline, is currently subject to a period of patent protection. As noted in Approved Drug Products with Therapeutic Equivalence Evaluations, the Orange Book, U.S. Patent 4,335,121 (the `121 patent) is due to expire on May 14, 2004. In the application, Altana Inc. included a paragraph III certification to the `121 patent under Section 505 (j) (2) (A) (vii) (III) of the Act. The certification states that Altana Inc. will not market Fluticasone Propionate Ointment, 0.005% prior to the expiration of the patent. Altana Inc. also acknowledges that final approval of this application may not be made effective pursuant to 21 U.S.C. 355 (j) (5) (B) (ii) of the Act until the `121 patent has expired, i.e., currently May 14, 2004.

CHEMISTRY, MANUFACTURING AND CONTROLS

The following changes have been made to the Chemistry, Manufacturing and Controls since receipt of the tentative approval on February 27, 2003.

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CHEMISTRY

Specifications – Minor formatting changes were made to the specifications in addition to the following revisions:

- The In-Process, Finished Product and Stability Specifications were revised to include limits for [redacted] of fluticasone. The limits for [redacted] were also tightened.

- The [redacted] test was revised for the Finished Product and Stability Specifications to specify [redacted]. The [redacted] was tightened and a specification for [redacted] was added.

- The [redacted], limit was revised for the Stability Specifications.

Analytical Procedures

- [redacted]

Attachment I contains copies of the revised documents.

Attachment II contains a copy of the Addendum to the Validation for Fluticasone Propionate Ointment that describes the extraction efficiency study.

MANUFACTURING

- [redacted]
- [redacted]

Attachment III contains copies of the revised documents.

LABELING

- No changes have been made to the text of the Fluticasone Propionate labeling since receiving tentative approval on February 27, 2003.

Altana respectively requests that this application be reactivated, as it is eligible for final approval.

An identical copy of this Amendment has been provided to the New York District Office. A document certification is attached.

If you have any questions or require additional information, please contact Ms. Audrey Zaweski at (631) 454-7677 Ext. 3007. Fax communications can be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Audrey Zaweski for

Robert J. Anderson, Esq.
Senior Director, Scientific Affairs

RJA/ap

Pharma

ALTANA

April 15, 2004

ORIG AMENDMENT
N/am

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VIA TELEFAX (301) 594-0180 and FEDERAL EXPRESS

ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
TELEPHONE AMENDMENT – REQUEST FOR UPDATED STABILITY

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on April 22, 2002 for Fluticasone Propionate Ointment, 0.005% in accordance with Section 505 (j) of the Federal Food, Drug and Cosmetic Act and Tentatively Approved on February 27, 2003.

Reference is also made to the Altana Inc. **MINOR AMENDMENT – FINAL APPROVAL REQUESTED** dated March 15, 2004. On April 14, 2004 FDA requested updated Controlled Room Temperature Stability Data for Fluticasone Propionate Ointment 0.005%

As requested, Altana Inc. is submitting this Telephone Amendment containing updated stability data to complete the information needed to reactivate the Fluticasone Propionate Ointment, 0.005% application for final approval consideration.

If you have any questions or require additional information, please contact Ms. Audrey Zaweski at (631) 454-7677 Ext. 3007. Fax communications can be made to (631) 756-5114.

Sincerely,

ALTANA INC.

for
Audrey Zaweski

Robert J. Anderson, Esq.
Senior Director, Scientific Affairs

RJA/ap

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April 16, 2004

Gary Buehler
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VIA TELEFAX (301) 594-0180 and FEDERAL EXPRESS

ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
TELEPHONE AMENDMENT

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on April 22, 2002 for Fluticasone Propionate Ointment, 0.005% in accordance with Section 505 (j) of the Federal Food, Drug and Cosmetic Act and Tentatively Approved on February 27, 2003.

Reference is also made to the Altana Inc. April 14, 2004 Telephone Amendment and April 16, 2004 teleconference between FDA and Altana representatives.

As requested, Altana Inc. is submitting revised finished product and stability specifications for the drug product. The ———— specification has been updated to include a Relative Standard Deviation (RSD) specification for the values obtained for the beginning, middle and end samples. The ———— specification now reads: ———————————————————— ———— have a relative standard deviation of ———————————————— mean of the three values. The mean of the three values falls within ———— % of the labeled content for fluticasone propionate."

Attachment I contains copies of the proposed finished product and stability specifications.

In addition, Altana Inc. commits to assigning an 18-month expiration period to the 15 gram tube size based on a review of the stability gathered to date. Any proposal to extend the expiration date will be submitted to FDA in accordance with the Post Approval Stability Commitment.

If you have any questions or require additional information, please contact Ms. Audrey Zaweski at (631) 454-7677 Ext. 3007. Fax communications can be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Audrey Zaweski for

Robert J. Anderson, Esq.
Senior Director, Scientific Affairs

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ALTANA

May 12, 2004

NDAM

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VIA TELEFAX (301) 594-0180 and FEDERAL EXPRESS

ANDA 76-300
Fluticasone Propionate Ointment, 0.005%
TELEPHONE AMENDMENT

Dear Mr. Buehler:

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on April 22, 2002 for Fluticasone Propionate Ointment, 0.005% in accordance with Section 505 (j) of the Federal Food, Drug and Cosmetic Act and Tentatively Approved on February 27, 2003 with Final Approval expected on May 14, 2004.

Reference is also made to the teleconference held on May 11, 2004 between FDA and Altana representatives.

As requested, Altana Inc. is submitting this Telephone Amendment to confirm the time line for the Post Approval Commitment discussed during the teleconference. Altana will submit a Post Approval Supplement within 60 days of final approval with additional information and data regarding the Viscosity testing procedure for Fluticasone Propionate Ointment, 0.005%.

If you have any questions or require additional information, please contact Ms. Audrey Zaweski at (631) 454-7677 Ext. 3007. Fax communications can be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Audrey Zaweski for

Robert J. Anderson, Esq.
Senior Director, Scientific Affairs

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