CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

76-453/S-001;S-002;S-003; S-004;S-005

Generic Name: Lidocaine and Prilocaine Cream 2.5%/2.5%

Sponsor: Altana Inc.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 76-453/S-001;S-002;S-003; S-004;S-005

CONTENTS

Reviews / Information Included in this ANDA Review.

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Tentative Approval Letter(s)	
Final Printed Labeling(s)	X
CSO Labeling Review(s)	X
Medical Officer Review(s)	
Chemistry Review(s)	X
Microbiology Review(s)	X
Bioequivalence Review(s)	
Administrative Document(s)	X
Correspondence	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76-453/S-001;S-002;S-003; S-004;S-005

APPROVAL LETTERS

ANDA 76-453/S-001

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

JUN 14 2004

Dear Madam:

This refers to your supplemental new drug application dated September 22, 2003, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act, regarding your abbreviated new drug application for Lidocaine and Prilocaine Cream 2.5%/2.5%.

Reference is also made to your amendment submitted March 31, 2004.

This supplemental application, submitted as a "Supplement - Changes Being Effected", provides for the following change:

> An automated method for the drug product microbial limit test.

We have completed the review of this supplemental application and it is approved.

We remind you that you must comply with the requirements for and approved abbreviated new drug application described in 21 CFR 314.80-81.

The material submitted is being retained in our files.

Sincerely yours,

Neal J Sweeney 6-10-04

Neal J. Sweeney, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 76-453/S-002

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

OCT 21 2004

Dear Madam:

This is in reference to your supplemental new drug application, dated December 3, 2003, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug application for Lidocaine and Prilocaine Cream, 2.5%/2.5%.

Reference is also made to your amendment dated July 1, 2004.

This supplemental application, submitted as a "Prior Approval Supplement", provides for the following change:

S-002: To obtain approval of an alternate

We have completed the review of this supplemental application and it is approved.

We remind you that you must comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.

The material submitted is being retained in our files.

Sincerely yours,

R.C. Adams for

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 76-453/S-003,S-004 and S-005

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

JUL 2 1 2004

Dear Madam:

This is in reference to your supplemental new drug application, dated December 19, 2003, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug application for Lidocaine and Prilocaine Cream, 2.5%/2.5%.

These supplemental applications, submitted as a "Changes Being Effected in 30 Days", provide for the following changes:

S-003 and S-004: To obtain approval of an additional 5 gram package size and a alternate Altana Inc. packaging site for Lidocaine and Prilocaine Cream 2.5%/2.5% finished product.

S-005: Associated Labeling

We have completed the review of these supplemental applications and they are approved.

We remind you that you must comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.

The material submitted is being retained in our files.

Sincerely yours,

R. C. Adams for

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76-453/S-001;S-002;S-003; S-004;S-005

FINAL PRINTED LABELING(S)

APPROVED

JUL 2 1 2004

#24

NDC 0168-0357-55 FOR HOSPITAL USE ONLY

fougera®

Rx only

NET WT 5 grams

LIDOCAINE and PRILOCAINE CREAM, 2.5%/2.5%

NOT FOR OPHTHALMIC USE FOR EXTERNAL USE ONLY

Each gram contains: lidocaine 25 mg, prilocaine 25 mg, polyoxyethylene fatty acid ester, carbomer 934, purified water, and sodium hydroxide to adjust pH to approximately 9. Contains no preservatives.

Apply to intact skin and cover with an occlusive dressing.

See package insert for full prescribing information.

WARNING: Keep out of reach of children.

Store at 20°-25°C (68°-77°F) (See USP Controlled Room Temperature).

See crimp of tube for Lot No. and Exp. Date

E. FOUGERA & CO.

a division of Altana Inc., MELVILLE, NY 11747

A5217
#24
R10/03

0168-0357-55

PMS

APPROVED

JUL 2 1 2004

indi

AL USE ONLY

5 mg, prilocaine 25 mg,
carbomer 934, purified water,
pH to approximately 9.

th an occlusive dressing.
ribing information.
children.
ee USP Controlled Room

d Exp. Date

LE, NY 11747

FOR HOSPITAL USE ONLY

NOTE: The proper application of lidocaine and prilocaine cream, 2.5%/2.5% requires use of an occlusive dressing.

This box does not include occlusive dressings.

NOT FOR OPHTHALMIC USE FOR EXTERNAL USE ONLY

FOR HOSPITAL USE ONLY

NDC 0168-0357-55 ℞only

fougera®

LIDOCAINE and PRILOCAINE CREAM, 2.5%/2.5%

NOT FOR OPHTHALMIC USE FOR EXTERNAL USE ONLY

CONTAINS 5 - 5 gram tubes

NOT FOR OPHTHALMIC USE FOR EXTERNAL USE ONLY

N 3 0168-0357-55 3

FOR HOSPIT

NDC 0168-0357-55

fougera®

LIDOCAINE a
PRILOCAINE
2.5%/2.5%

NOT FOR OPHTHALMIC USE

CONTAINS 5 - 5 gram

FOR HOSPITAL USE ONLY

NDC 0168-0357-55

fougera®

Rx only

LIDOCAINE and PRILOCAINE CREAM, 2.5%/2.5%

NOT FOR OPHTHALMIC USE FOR EXTERNAL USE ONLY

CONTAINS 5 - 5 gram tubes

FOR HOSPITAL USE ONLY

Each gram contains: lidocaine 25 mg, prilocaine 25 mg, polyoxyethylene fatty acid ester, carbomer 934, purified water, and sodium hydroxide to adjust pH to approximately 9.
Contains no preservatives.
Apply to intact skin and cover with an occlusive dressing.
See package insert for full prescribing information.
WARNING: Keep out of reach of children.
Store at 20°-25°C (68°-77°F) (See USP Controlled Room Temperature).
See crimp of tube for Lot No. and Exp. Date

E. FOUGERA & CO.
a division of Altana Inc., MELVILLE, NY 11747

IP5217
R11/03

FOR HOSPITAL USE ONLY

NOTE: The proper application of lidocaine and prilocaine cream, 2.5%/2.5% requires use of an occlusive dressing.

This box does not include occlusive dressings.

NOT FOR OPHTHALMIC USE FOR EXTERNAL USE ONLY

FOR HOSPITAL USE ONLY

NDC 0168-0357-55

Rx only

fougera®

LIDOCAINE and PRILOCAINE CREAM, 2.5%/2.5%

NOT FOR OPHTHALMIC USE FOR EXTERNAL USE ONLY

CONTAINS 5 - 5 gram tubes

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76-453/S-001;S-002;S-003; S-004;S-005

CSO LABELING REVIEW(S)

REVIEW OF PROFESSIONAL LABELING # 1

Supplement (FPL)

DATE OF REVIEW: May 26, 2004

ANDA: 76-453/S-005

NAME OF FIRM: Altana Inc.

NAME OF DRUG: Lidocaine and Prilocaine Cream, 2.5%/2/5 %

DATE OF SUBMISSION: December 19, 2003

COMMENTS

1. CONTAINER - 5 gm

   Satisfactory in FPL as of 12/19/03 submission (vol. 3.1)

2. CARTON - 5 x 5 gm Tubes

   Satisfactory in FPL as of 12/19/03 submission (vol. 3.1)

RECOMMENDATIONS:

From the viewpoint of the labeling, this supplement may be approved.

FOR THE RECORD:

1. This supplement was submitted in conjunction with chemistry for a new packaging size of 5 gm/tube.

2. The review was done using the sponsor's approved labeling, approved August 18, 2003. No labeling supplement was approved subsequent to the approval of this drug product.

3. No new innovator's labeling was approved after the approval of this application.

4. The sponsor did not include the revised insert labeling reflecting addition of this new packaging size. They will submit this in an annual report. Refer to the T-con prepared by Chan Park on May 26, 2004.

5. It was confirmed that his new size is only for hospital use, as declared on the container and carton labeling and confirmed via a T-con. The sponsor claimed that the innovator's 5 gm is also for hospital use only and packaged in a Non-CRC system.

6. The packaging system for this 5 gm is not CRC, as confirmed with the sponsor via a T-con on May 26, 04. Any product containing more than 5 mg of lidocaine in a single package needs CRC. This 5 gm product contains 125 mg of lidocaine. However, according to the FR Notice published in 1995 on special packaging, which also makes a reference to the original Poison Prevention Packaging Act of 1997 (PPPA), it appears that this special packaging regulation (such as CRC) applies only to the **household substances**. Since this 5 gm tube is only for hospital use, it appears all right in non-CRC packaging. Consequently, the sponsor did not include direction specific to the opening and closing of the CRC cap, which appears on the container and carton for the 30 gm tube.

7. Post-approval revision:

Revise the net quantity statement to read " 5 x 5 gm tubes" rather than ——————

cc: ANDA 76-453/S-005
Dup/Division File
HFD-613/CPark/LGibson(no cc:)
V:\FIRMSAM\ALTANA\LTRS&REV\76453S05AP.LABELING.doc
Review

7/9/04 7/9/04 — orig signed 6/3/04. Review misplaced? yes

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76-453/S-001;S-002;S-003; S-004;S-005

CHEMISTRY REVIEW(S)

ANDA # 76-453/S-002

NAME AND ADDRESS OF APPLICANT:
Altana, Inc.
Attention: Virginia Carman
60 Baylis Road
Melville, NY 11747

PURPOSE OF AMENDMENT/SUPPLEMENT
S-02 To obtain approval of an alternate

DATE(S) OF SUBMISSION(S)
December 3, 2003

PHARMACOLOGICAL CATEGORY	TRADE NAME	NONPROPRIETARY NAME
Topical Anesthetic	N/A	Lidocaine and Prilocaine

DOSAGE FORM	POTENCY	RX OR OTC
Cream	2.5% / 2.5%	RX

SAMPLES	RELATED IND/NDA/DMF	STERILIZATION
N/A	N/A	N/A

LABELING
N/A

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION
N/A

APPEARS THIS WAY
ON ORIGINAL

5-002
CAIC

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

ANDA # 76-453/S-003 and S-004

NAME AND ADDRESS OF APPLICANT:
Altana, Inc.
Attention: Virginia Carman
60 Baylis Road
Melville, NY 11747

PURPOSE OF AMENDMENT/SUPPLEMENT
S-003 and 004 - These supplements are being submitted to obtain approval of an additional 5 gram package size and a alternate Altana Inc. packaging site for Lidocaine and Prilocaine Cream 2.5%/2.5% finished product.

DATE(S) OF SUBMISSION(S)
December 19, 2003

PHARMACOLOGICAL CATEGORY	TRADE NAME	NONPROPRIETARY NAME
Topical Anesthetic	N/A	Lidocaine and Prilocaine

DOSAGE FORM	POTENCY	RX OR OTC
Cream	2.5% / 2.5%	RX

SAMPLES	RELATED IND/NDA/DMF	STERILIZATION
N/A	N/A	N/A

LABELING
N/A

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION
December 29, 2003 - Acceptable

APPEARS THIS WAY
ON ORIGINAL

5-002
CMC

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

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76-453/S-001;S-002;S-003; S-004;S-005

MICROBIOLOGY REVIEW(S)

Product Quality Microbiology Review
Review for HFD-645

March 18, 2004

ANDA: 76-453/SS-001

Drug Product Names
Proprietary: n/a
Non-proprietary: Lidocaine and Prilocaine Cream 2.5%/2.5%

Drug Product Classification: n/a

Review Number: 1

Subject of this Review
Submission Date: September 22, 2003
Receipt Date: September 23, 2003
Consult Date: n/a
Date Assigned for Review: March 12, 2004

Submission History (for amendments only)
Date(s) of Previous Submission(s): none
Date(s) of Previous Micro Review(s): none

Applicant/Sponsor
Name: Altana Inc.
Address: 60 Baylis Road
Melville, NY 11747
Representative: Virginia Carman
Telephone: 631-454-7677

Name of Reviewer: Neal J. Sweeney, Ph. D.

Conclusion: Not recommended for approval

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** CBE-0

2. **SUPPLEMENT PROVIDES FOR:** an automated method for drug product microbial limit test

3. **MANUFACTURING SITE:** Unchanged

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Lidocaine and Prilocaine Cream 2.5%/2.5% topical cream

5. **METHOD(S) OF STERILIZATION:** ———

6. **PHARMACOLOGICAL CATEGORY:** topical anesthetic

B. **SUPPORTING/RELATED DOCUMENTS:** 76-065/SS-001 (global lead)

C. **REMARKS:** The applicant previously submitted a supplement (76-065/SS-001) for the same automated microbial limits method. Approval of supplement 76-065/SS-001 is currently pending resolution of deficiencies regarding microbial limits release criteria for the drug products affected by the proposed automated microbial limits method.

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APPEARS THIS WAY
ON ORIGINAL

Executive Summary

I. Recommendations

A. Recommendation on Approvability – not recommended

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – n/a

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The non-sterile product is to be tested for microbial limits using the proposed automated method.

B. Brief Description of Microbiology Deficiencies – Revised microbial limits acceptance criteria for product release should be provided.

C. Assessment of Risk Due to Microbiology Deficiencies – minor

III. Administrative

A. Reviewer's Signature Neal J Sweeney 3-18-04

Neal J. Sweeney, Ph. D.

B. Endorsement Block

N. Sweeney N Sweeney 3-18-04

C. CC Block

cc:
Original ANDA
Division File
Field Copy

APPEARS THIS WAY
ON ORIGINAL

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

Product Quality Microbiology Review
Review for HFD-645

May 28, 2004

ANDA: 76-453/SS-001

Drug Product Names
Proprietary: n/a
Non-proprietary: Lidocaine and Prilocaine Cream 2.5%/2.5%

Drug Product Classification: n/a

Review Number: 2

Subject of this Review
Submission Date: March 31, 2004
Receipt Date: April 1, 2004
Consult Date: n/a
Date Assigned for Review: April 1, 2004

Submission History (for amendments only)
Date(s) of Previous Submission(s): September 22, 2003
Date(s) of Previous Micro Review(s): September 23, 2003

Applicant/Sponsor
Name: Altana Inc.
Address: 60 Baylis Road
Melville, NY 11747
Representative: Virginia Carman
Telephone: 631-454-7677

Name of Reviewer: Neal J. Sweeney, Ph. D.

Conclusion: Recommended for approval

Product Quality Microbiology Data Sheet

A. 1. **TYPE OF SUPPLEMENT:** CBE-0

2. **SUPPLEMENT PROVIDES FOR:** an automated method for drug product microbial limit test

3. **MANUFACTURING SITE:** Unchanged

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Lidocaine and Prilocaine Cream 2.5%/2.5% topical cream

5. **METHOD(S) OF STERILIZATION:** ———

6. **PHARMACOLOGICAL CATEGORY:** topical anesthetic

B. **SUPPORTING/RELATED DOCUMENTS:** 76-065/SS-001 (global lead)

C. **REMARKS:** The applicant previously submitted a supplement (76-065/SS-001) for the same automated microbial limits method.

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APPEARS THIS WAY
ON ORIGINAL

Executive Summary

I. Recommendations

A. Recommendation on Approvability –recommended for approval

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – n/a

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – The non-sterile product is to be tested for microbial limits using the proposed automated method.

B. Brief Description of Microbiology Deficiencies – None.

C. Assessment of Risk Due to Microbiology Deficiencies – No Microbiology deficiencies were noted. The safety risk associated with use of the alternate automated Microbial Limits test for the drug product is minimal.

III. Administrative

A. Reviewer's Signature Neal J. Sweeney 5-28-04
Neal J. Sweeney, Ph. D.

B. Endorsement Block
N. Sweeney NS 5-28-04

C. CC Block
cc:
Original ANDA
Division File
Field Copy

APPEARS THIS WAY
ON ORIGINAL

Product Quality Microbiology Assessment

Note: Only the sections of the 'Product Quality Microbiology Assessment' that are applicable to the supplemental change proposed are included below.

The subject supplement amendment provides a response to the microbiology deficiency conveyed to the applicant in the Agency's March 19, 2004 deficiency letter. The original deficiency is italicized below:

> *Revised drug product release specifications, including microbial limits acceptance criteria for the proposed automated test, should be provided.*

Response: Revised Finished Product and Stability specifications are provided. Both finished product and stability specifications for the automated microbial limits test, using the [redacted] method proposed, state the following:

"Microbial Limits:

[redacted]

Comment: The proposed automated [redacted] test method has more stringent acceptance criteria for the finished product and stability samples versus the currently approved method (USP <61). The applicant's currently approved specification for the microbial limits test method (USP <61>), used to test finished product and stability samples, allows for [redacted] for total aerobic microbial count.

Acceptable

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76-453/S-001;S-002;S-003; S-004;S-005

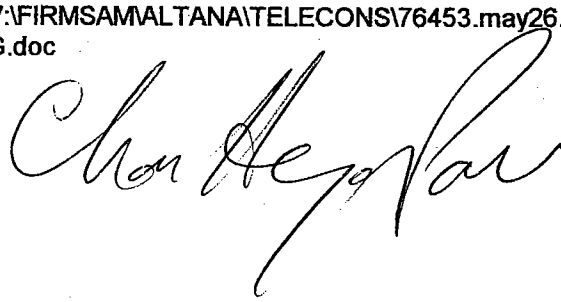
ADMINISTRATIVE DOCUMENTS

RECORD OF TELEPHONE CONVERSATION

The sponsor submitted a supplement for a new packaging size of 5 gm/Tube. The sponsor submitted only container labels and carton labeling, but not the insert labeling revised to reflect this new packaging size. They stated that no other change was made to the insert labeling. The sponsor stated that they will submit the revised insert labeling in an annual report, which is acceptable. The sponsor confirmed that this new packaging size is for the institution use only as declared on the container and carton.

Chan

V:\FIRMSAM\ALTANA\TELECONS\76453.may26.04.LABELING.doc



DATE May 26, 2004

ANDA 76-453/S-005

IND NUMBER

TELECON

INITIATED BY MADE
_ APPLICANT/ X BY
SPONSOR TELE.

X FDA _ IN
PERSON

FPRODUCT NAME
Lidocaine and Prilocaine Cream, 2.5 %/2.5 %

FIRM NAME
Altana

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Cindy Dye

TELEPHONE NUMBER
631-454-7677

SIGNATURE

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76-453/S-001;S-002;S-003; S-004;S-005

CORRESPONDENCE

Pharma

ALTANA

SUPPL AMENDEMENT
SCC-002/AM

NAI
7/12/04

July 1, 2004

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

Florence F. Fang
Director
Division of Chemistry II
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

ANDA 76-453/S-002
Lidocaine and Prilocaine Cream 2.5%/2.5%
MINOR Amendment

Dear Sir or Madam:

Reference is made to the Abbreviated New Drug Application dated July 1, 2002 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 Lidocaine and Prilocaine Cream, 2.5%/2.5% and approved August 18, 2003.

Reference is also made to Altana Inc.'s supplemental application of December 3, 2003, and the Agency's correspondence of June 16, 2004. This correspondence is designated as a **MINOR amendment** and appears prominently in this cover letter.

Each item has been addressed in **comment**/response format.

Please revise your drug substance specifications to include a specification of NMT ——— for ——— per your July 14, 2003 amendment to your original application and water per your supplier's CoA.

The drug substance specifications have been revised to include a specification of NMT ——— for ——— and NMT ——— for ——— A copy of the revised specification is included as **Attachment I**.

RECEIVED
JUL 0 2 2004
OGD / CDER

ANDA 76-453/S-002

JUN 16 2004

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

Dear Madam:

This is in reference to your supplemental new drug application, dated December 3, 2003, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug application for Lidocaine and Prilocaine Cream, 2.5%/2.5%.

This supplemental application, submitted as a "Prior Approval Supplement", provides for the following change:

S-002: To obtain approval of an alternate manufacturer of the Lidocaine active drug substance

The supplemental application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

Please revise your drug substance specifications to include a specification of NMT [redacted] for [redacted] per your July 14, 2003 amendment to your original application and [redacted] per your [redacted] CoA.

The file on these supplemental applications is now closed. You are required to take an action described under 21 CFR 314.120, which will either amend or withdraw these supplemental applications. Your amendments should respond to the deficiency listed. Partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The responses to this letter will be considered MINOR amendments and should be so designated in your cover letter.

If you have substantial disagreement with our reasons for not approving these supplemental applications, you may request an opportunity for a hearing.

The material submitted is being retained in our files.

Sincerely yours,

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

Pharma

ALTANA

March 31, 2004

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

Gary. J. Buehler, Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North I
7500 Standish Place
Rockville, MD 20855

SUPPLEMENT AMENDMENT
VIA FEDERAL EXPRESS
S3001 AS

ANDA 76-453/S-001
Lidocaine and Prilocaine Cream 2.5%/2.5%
RESPONSE TO MICROBIOLOGY DEFICIENCIES

Dear Mr. Buehler:

Reference is made to Altana Inc.'s original Abbreviated New Drug Application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for ANDA 76-453, Lidocaine and Prilocaine Cream 2.5%/2.5% and approved August 18, 2003.

Reference is also made to the supplemental application submitted on September 22, 2003 to provide for an automated method for the USP Microbial Limit Tests <61> and to the FDA correspondence dated March 19, 2004 citing microbiology deficiencies.

This submission has been formatted in **comment**/response format.

Revised drug product release specifications, including microbial limits acceptance criteria for the proposed automated test, should be provided.

Revised drug product release specifications, including microbial limits acceptance criteria for the proposed automated test, are attached.

RECEIVED
APR 0 1 2004
OGD/CDER

ANDA 76-453/S-001
Lidocaine and Prilocaine Cream, 2.5%/2.5%
RESPONSE TO MICROBIOLOGY DEFICIENCIES

If any additional information is required, or if you have any questions, please contact me at (631) 454-7677, ext. 2091. Facsimile communications may be made to (631) 756-5114.

Sincerely,
ALTANA INC.

Virginia Carman
Associate Director, Regulatory Affairs

/cd

Enclosure

APPEARS THIS WAY
ON ORIGINAL

ANDA 76-453/S-001

MAR 19 2004

Altana Inc.
Attention: Robert J. Anderson
60 Baylis Road
Melville, NY 11747

Dear Sir:

This refers to your supplemental new drug application dated September 22, 2003, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act, regarding your abbreviated new drug application for Lidocaine and Prilocaine Cream, 2.5%/2.5%.

This supplemental application, submitted as a "Supplement - Changes Being Effected", provides for the following change:

An automated method for the drug product microbial limit test.

The supplemental application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

LIST OF MICROBIOLOGY DEFICIENCIES

Revised drug product release specifications, including microbial limits acceptance criteria for the proposed automated test, should be provided.

Please clearly identify your amendment to this letter as a RESPONSE TO MICROBIOLOGY DEFICIENCIES. The RESPONSE TO MICROBIOLOGY DEFICIENCIES should also be noted in your cover page/letter.

The file on this supplemental application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the supplemental application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter

will be considered a MINOR amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this supplemental application, you may request an opportunity for a hearing.

Sincerely yours,

Neal J. Sweeney 3-19-04

Neal J. Sweeney, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 76-453/SS-001
Division File
Field Copy

Endorsements:
HFD-600/Neal J. Sweeney/3-19-04/N. Sweeney 3-19-04
HFD-617/Bonnie McNeal/3-19-04/B. McNeal 3/19/04

Final typed by: B. McNeal 3/19/04

Filename: V:FIRMSAM/Altana/LTRS&REV/76453SS001NA.doc

SUPPLEMENT Deficiency Letter - Minor

APPEARS THIS WAY
ON ORIGINAL

Pharma

NDA NO. 76-453 REF NO. SCA-003-AT
NDA SUPPL FOR Packaging Addn.

EER Subm. Rec'd 12/29/03 on

ALTANA

December 19, 2003

NDA NO. 76-453 REF NO. SCD-004-AT
NDA SUPPL FOR Packaser Addition

ORIGINAL

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Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room, MPN II
7500 Standish Place, Room 150
Rockville, MD 20855

VIA FEDERAL EXPRESS

NDA NO. 76-453 REF NO. SLE 006 AT
NDA SUPPL FOR Labeling Revision

ANDA 76-453
Lidocaine and Prilocaine Cream, 2.5%/2.5%
Special Supplement – Changes Being Effected – 30 Day Implementation

Dear Sir or Madam:

Reference is made to Altana Inc. Abbreviated New Drug Application for Lidocaine and Prilocaine Cream, 2.5%/2.5% submitted in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act and approved on August 18, 2003.

Reference is made to the guidance for industry *Changes to an Approved NDA or ANDA*, dated November 1999 wherein the addition of a new container size requires a Special Supplement – Changes Being Effected.

In accordance with Section 506A(c)(1) of the Act, this supplement is being submitted with the referenced supportive documentation to obtain approval of an additional 5 gram package size as well as an alternate Altana Inc. packaging site for Lidocaine and Prilocaine Cream 2.5%/2.5% finished product.

Changes in size of Container

This Supplement is being submitted with the appropriate supportive documentation to obtain approval of a 5 gram tube presentation. The container/closure component materials including tube, cap, resins and colorants remain unchanged from the currently approved 30 gram container/closure system.

Alternate Packaging Site

This proposed 5 gram presentation, as well as the currently approved 30 gram presentation, will be packaged in Altana Inc.'s Melville facility. The Melville facility is a FDA registered establishment, approved for the manufacture and packaging of semi-solid and liquid topical dosage forms. The drug product will continue to be manufactured at the Altana Hicksville facility with a portion to be shipped to Altana's Melville facility. The Melville site is

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approximately 12 miles from the Hicksville site. Product will be shipped in double [redacted] bags within [redacted] drums.

Supporting Documentation

The exhibit batch being submitted was manufactured in accordance with the currently approved formulation and manufacturing instructions for Lidocaine and Prilocaine Cream, 2.5%/2.5%. The exhibit batch was split filled into the currently approved 30 gram container size and the 5 gram container size included in this Supplement. The 5 gram container size was packaged at the Melville site.

All In-process and Finished Product testing was performed using currently approved specifications and analytical procedures. Samples of the 5 gram container size packaged at the Melville site was placed on stability at accelerated and controlled room temperature conditions in accordance with the approved stability protocol. Based on satisfactory test results from the stability studies, Altana is proposing an expiration date of 24 months for the 5 gram tube.

The following documentation has been included in this submission in support of this new container package size and manufacturing site.

- Bottle and cap specifications and DMF Authorization Letter are included in **Attachment I.**
- Incoming Test Reports for the bottle and cap are included in **Attachment II.**
- A copy of the executed batch record (M600) is included in **Attachment III.**
- In-process and Finished Product Test Results are included in **Attachment IV.**
- Twelve copies of final printed container and carton labeling for the 5 gram tube are included in **Attachment V.** Please note the labeling states "**FOR HOSPITAL USE ONLY**".
- Stability Reports for Lot M600 containing 3 months accelerated temperature data are included in **Attachment VI.**

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

Sincerely,

ALTANA INC.

Virginia Carman
Associate Director, Regulatory Affairs

VC:jb

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EER Submitted 12/29/03 amr

Pharma

ALTANA

December 3, 2003

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NDA NO. 76-453 REF NO. SCC-002
NDA SUPPL FOR SUPP. ADD.

ANDA 76-453
Lidocaine and Prilocaine Cream, 2.5%/2.5%
Prior Approval Supplement

Dear Sir or Madam:

Reference is made to Altana Inc. Abbreviated New Drug Application for Lidocaine and Prilocaine Cream, 2.5%/2.5% submitted in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act and approved on August 18, 2003.

Reference is made to the guidance for industry *Changes to an Approved NDA or ANDA*, dated November 1999 wherein the addition of a new Active Pharmaceutical Ingredient (API) requires a Prior Approval Supplement.

In accordance with Section 506A(c)(1) of the Act, this supplement is being submitted with the referenced supportive documentation to obtain approval of an alternate [redacted] The new [redacted] is:

[redacted]

[redacted] was [redacted] for use in an exhibit batch using the currently approved specifications and analytical procedures. The exhibit batch was [redacted] in accordance with the currently approved [redacted] instructions for Lidocaine and Prilocaine Cream. All componentry remain unchanged from that which was approved in the original application.

All In-Process and Finished Product testing was performed using the currently approved specifications and analytical procedures. Samples were placed on stability at accelerated and controlled room temperature conditions in accordance with the approved stability protocol.

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The following documentation has been included in this submission in support of this alternate

- DMF Authorization Letter
- Representative Certificate of Analysis from the raw material manufacturer
- A copy of the executed batch record for the exhibit batch M312
- Copies of the In-Process and Finished Product Testing for batch M312
- Stability Reports containing accelerated data

All results are within established specifications for all parameters tested.

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

Sincerely,

ALTANA INC.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

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