CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

65-067

Generic Name: Clindamycin Phosphate Topical Suspension USP, 1% (base)

Sponsor: Altana Inc.

Approval Date: January 31, 2002

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 65-067

CONTENTS

Reviews / Information Included in this ANDA Review.	
Approval Letter	X
Tentative Approval Letter(s)	
Final Printed Labeling(s)	X
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Chemistry Review(s)	X
Microbiology Review(s)	
Bioequivalence Review(s)	X
Administrative Document(s)	X
Correspondence	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-067

APPROVAL LETTER

ANDA 65-067

JAN 31 2002

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

Dear Madam:

This is in reference to your abbreviated new drug application dated March 7, 2000, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Clindamycin Phosphate Lotion (Clindamycin Phosphate Topical Suspension USP), 1% (base).

Reference is also made to your amendments dated February 14, August 20, and December 13, 2001.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Clindamycin Phosphate Lotion (Clindamycin Phosphate Topical Suspension USP), 1% (base), to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Cleocin T® Topical Lotion, 1% (base) of Pharmacia and Upjohn Co.).

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print.

Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

/S/

Gary Buehler 1/31/02
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-067

FINAL PRINTED LABELING(S)

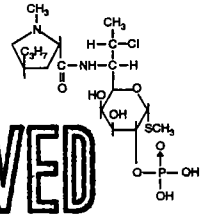
fougera®

CLINDAMYCIN PHOSPHATE
Topical Suspension USP, 1%

℞ only JAN 31 2002

FOR EXTERNAL USE ONLY

DESCRIPTION: Clindamycin Phosphate Topical Suspension contains clindamycin phosphate, USP, at a concentration equivalent to 10 mg clindamycin per milliliter.
Clindamycin phosphate is a water soluble ester of the semi-synthetic antibiotic produced by a 7(S)-chloro-substitution of the 7(R)-hydroxyl group of the parent antibiotic lincomycin.
The topical suspension contains cetostearyl alcohol (2.5%), glycerin, glyceryl stearate SE (with potassium monostearate), isostearyl alcohol (2.5%), methylparaben (0.3%), sodium lauroyl sarcosinate, stearic acid and purified water.
The structural formula is represented below:



APPROVED

Molecular Formula: $C_{18}H_{34}ClN_2O_8PS$ Molecular Weight: 504.97
The chemical name for clindamycin phosphate is Methyl 7-chloro-6,7,8-trideoxy-6-(1-methyl-*trans*-4-propyl-L-2-pyrrolidinecarboxamido)-1-thio-L-*threo*-α-D-*galacto*-octopyranoside 2-(dihydrogen phosphate).

CLINICAL PHARMACOLOGY: Although clindamycin phosphate is inactive *in vitro*, rapid *in vivo* hydrolysis converts this compound to the antibacterially active clindamycin.
Cross resistance has been demonstrated between clindamycin and lincomycin.
Antagonism has been demonstrated between clindamycin and erythromycin.
Following multiple topical applications of clindamycin phosphate at a concentration equivalent to 10 mg clindamycin per mL in an isopropyl alcohol and water solution, very low levels of clindamycin are present in the serum (0-3 ng/mL) and less than 0.2% of the dose is recovered in urine as clindamycin.
Clindamycin activity has been demonstrated in comedones from acne patients. The mean concentration of antibiotic activity in extracted comedones after application of Clindamycin Phosphate Topical Solution for 4 weeks was 597 mcg/g of comedonal material (range 0-1490). Clindamycin *in vitro* inhibits all *Propionibacterium acnes* cultures tested (MICs 0.4 mcg/mL). Free fatty acids on the skin surface have been decreased from approximately 14% to 2% following application of clindamycin.

INDICATIONS AND USAGE: Clindamycin Phosphate Topical Suspension is indicated in the treatment of acne vulgaris. In view of the potential for diarrhea, bloody diarrhea and pseudomembranous colitis, the physician should consider whether other agents are more appropriate. (See **CONTRAINDICATIONS, WARNINGS** and **ADVERSE REACTIONS**.)

CONTRAINDICATIONS: Clindamycin Phosphate Topical Suspension is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin, a history of regional enteritis or ulcerative colitis, or a history of antibiotic-associated colitis.

WARNINGS: Orally and parenterally administered clindamycin has been associated with severe colitis which may result in patient death. Use of the topical formulation of clindamycin results in absorption of the antibiotic from the skin surface. Diarrhea, bloody diarrhea, and colitis (including pseudomembranous colitis) have been reported with the use of topical and systemic clindamycin. Studies indicate a toxin(s) produced by clostridia is one primary cause of antibiotic-associated colitis. The colitis is usually characterized by severe persistent diarrhea and severe abdominal cramps and may be associated with the passage of blood and mucus. Endoscopic examination may reveal pseudomembranous colitis. Stool culture for *Clostridium difficile* and stool assay for *C. difficile* toxin may be helpful diagnostically.
When significant diarrhea occurs, the drug should be discontinued. Large bowel endoscopy should be considered to establish a definitive diagnosis in cases of severe diarrhea.

(OVER)

Antiperistaltic agents such as opiates and diphenoxylate with atropine may prolong and/or worsen the condition. Vancomycin has been found to be effective in the treatment of antibiotic-associated pseudomembranous colitis produced by *Clostridium difficile*. The usual adult dosage is 500 mg to 2 grams of vancomycin orally per day in three to four divided doses administered for 7 to 10 days. Cholestyramine or colestipol resins bind vancomycin *in vitro*. If both a resin and vancomycin are to be administered concurrently, it may be advisable to separate the time of administration of each drug.

Diarrhea, colitis, and pseudomembranous colitis have been observed to begin up to several weeks following cessation of oral and parenteral therapy with clindamycin.

PRECAUTIONS: General: Clindamycin phosphate topical suspension should be prescribed with caution in atopic individuals.

Drug Interactions: Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore it should be used with caution in patients receiving such agents.

Pregnancy: Teratogenic Effects: *Pregnancy Category B*: Reproduction studies have been performed in rats and mice using subcutaneous and oral doses of clindamycin ranging from 100 to 600 mg/kg/day and have revealed no evidence of impaired fertility or harm to the fetus due to clindamycin. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known whether clindamycin is excreted in human milk following use of Clindamycin Phosphate Topical Suspension. However, orally and parenterally administered clindamycin has been reported to appear in breast milk. Because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness in pediatric patients under the age of 12 have not been established.

ADVERSE REACTIONS: In 18 clinical studies of various formulations of topical clindamycin phosphate using placebo vehicle and/or active comparator drugs as controls, patients experienced a number of treatment emergent adverse dermatologic events [see table below].

Number of Patients Reporting Events

Treatment Emergent Adverse Event	Solution n= 553 (%)	Gel n= 148 (%)	Lotion n= 160 (%)
Burning	62 (11)	15 (10)	17 (11)
Itching	36 (7)	15 (10)	17 (11)
Burning/Itching	60 (11)	# (-)	# (-)
Dryness	105 (19)	34 (23)	29 (18)
Erythema	86 (16)	10 (7)	22 (14)
Oiliness/Oily Skin	8 (1)	26 (18)	12*(10)
Peeling	61 (11)	# (-)	11 (7)

not recorded
* of 126 subjects

Orally and parenterally administered clindamycin has been associated with severe colitis which may end fatally.

Cases of diarrhea, bloody diarrhea and colitis (including pseudomembranous colitis) have been reported as adverse reactions in patients treated with oral and parenteral formulations of clindamycin and rarely with topical clindamycin (see **WARNINGS**).

Abdominal pain and gastrointestinal disturbances as well as gram-negative folliculitis have also been reported in association with the use of topical formulations of clindamycin.

OVERDOSAGE: Topically applied clindamycin phosphate topical suspension can be absorbed in sufficient amounts to produce systemic effects. (See **WARNINGS**.)

DOSAGE AND ADMINISTRATION: Apply a thin film of Clindamycin Phosphate Topical Suspension twice daily to affected area.

Shake well immediately before using.

Keep in container and keep tightly closed.

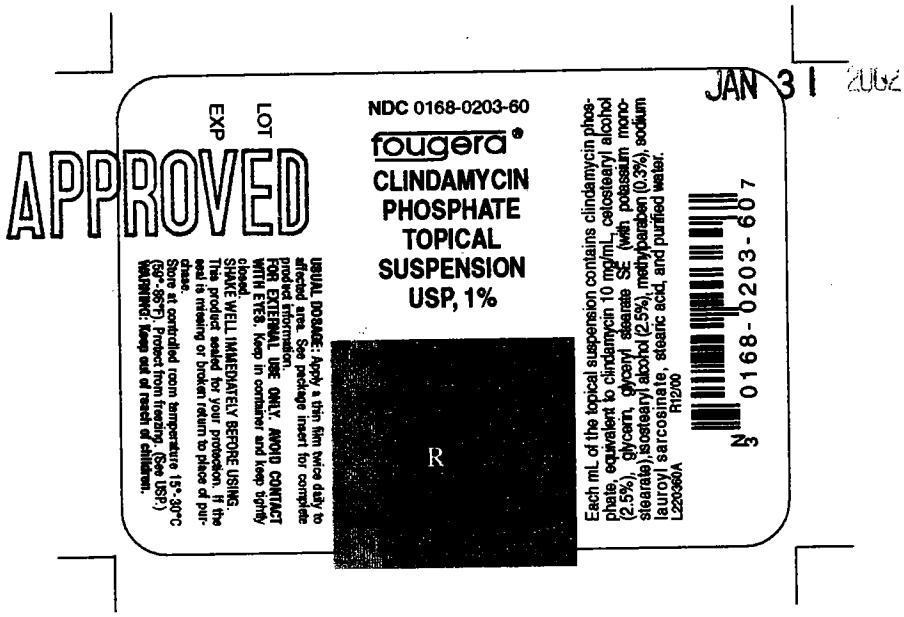
HOW SUPPLIED: Clindamycin Phosphate Topical Suspension USP, 1%, containing clindamycin phosphate equivalent to 10 mg clindamycin per mL, is supplied as follows:

NDC 0168-0203-60 60 mL bottle

Store at controlled room temperature 15° -30° C (59° -86°F). Protect from freezing. (See USP.)

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

IF2203
R12/00
#175

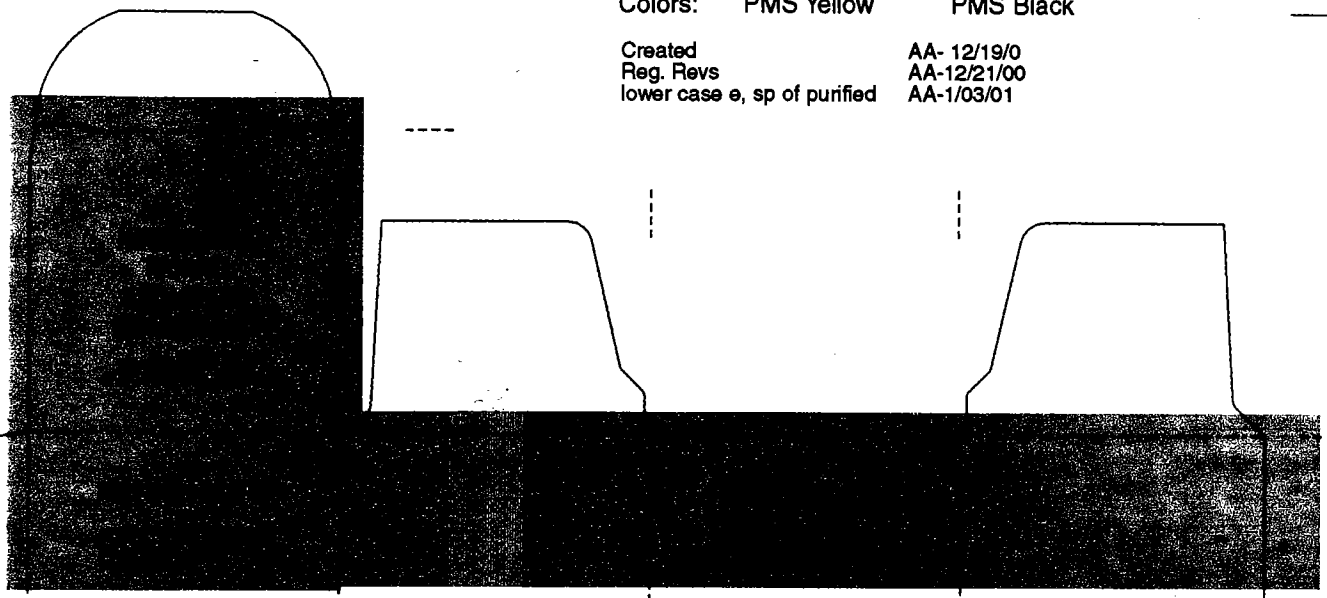


L220360A R12/00
Name: Clindamycin Phos. SUSPENSION 60mL
Size: 3.5 x 2.5
SSL-
STOCK:
NDC #: 0168-0203-60
Colors: PMS Yellow Black

FDA revisions - 12/19/00- AA

Name: Clindamycin SUSPENSION 60 mL Carton
Die Size: 1.625 x 1.625 x 5
UPC Code: 0168-0203-60
Pharma Code: #
Colors: PMS Yellow PMS Black

Created AA- 12/19/0
Reg. Revs AA-12/21/00
lower case e, sp of purified AA-1/03/01



CLINDAMYCIN PHOSPHATE TOPICAL SUSPENSION USP, 1%

(10 mg/mL) clindamycin

FOR TOPICAL USE ONLY

60 mL

℞only

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

USUAL DOSAGE: Apply a thin film twice daily to affected area.

See package insert for complete product information.

FOR EXTERNAL USE ONLY

AVOID CONTACT WITH EYES

Keep in container and keep tightly closed.

SHAKE WELL IMMEDIATELY BEFORE USING.

Store at controlled room temperature 15°-30°C (59°-86°F). Protect from freezing. (See USP.)

WARNING: Keep out of reach of children.

IP4833
R12/00
#175

CLINDAMYCIN PHOSPHATE TOPICAL SUSPENSION USP, 1%

(10 mg/mL) clindamycin

FOR TOPICAL USE ONLY

60 mL

℞only

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

APPROVED

JAN 31

Each mL of the topical suspension contains clindamycin phosphate, equivalent to clindamycin 10 mg/mL, cetostearyl alcohol (2.5%), glycerin, glyceryl stearate SE (with potassium monostearate), isostearyl alcohol (2.5%), methylparaben (0.3%), sodium lauroyl sarcosinate, stearic acid and purified water.

This product sealed for your protection. If the seal is missing or broken return to place of purchase.
See bottle for Lot No. and Expiration Date.

N 3 0168-0203-60 7

T6358

RINT SIDE SHOWN

158

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-067

CSO LABELING REVIEW(S)

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 65-067

Date of Submission: August 22, 2001

Applicant's Name: Altana Inc.

Established Name: Clindamycin Phosphate Topical Suspension USP, 1%

Labeling Deficiencies:

1. General Comment

   a. [redacted]

   b. We acknowledge your intentions to file your company website address to DDMAC for their review.

2. CONTAINER: 60 mL bottle

   In your "Each mL ...contains" statement, revise " — " to read " suspension".

3. CARTON: 1s

   a. See General Comments.

   b. See comments under CONTAINER.

4. INSERT

   See General Comments and revise the text or your insert labeling accordingly.

Please revise your container labels, carton and insert labeling, as instructed above, and submit in final print.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes, http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html.

To facilitate review of your next submission, and in accordance with 21 CFR 14.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

/S/

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

APPEARS THIS WAY
ON ORIGINAL

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 65-067

Date of Submission: March 7, 2000

Applicant's Name: Altana Inc.

Established Name: Clindamycin Phosphate Topical Suspension USP, 1%

Labeling Deficiencies:

1. CONTAINER: 60 mL bottle

   a. Increase the prominence of the "Shake well ..." statement.

   b. Revise to add "(See USP)" following your storage temperature statement.

   c. Delete [redacted] from your label.

2. CARTON: 1s

   See comments under CONTAINER.

3. INSERT

   a. ADVERSE REACTIONS

      Revise the first sentence to read, "... formulations of topical clindamycin phosphate ...".

   b. DOSAGE AND ADMINISTRATION

      Revise the last sentence to read, "Keep in container and keep tightly closed".

   c. HOW SUPPLIED

      See comment 1(b and c) under CONTAINER.

Please revise your container labels, carton and insert labeling, as instructed above, and submit in final print.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes, http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

/S/

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

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-067

CHEMISTRY REVIEW(S)

1. CHEMIST'S REVIEW NO. #1

2. ANDA #65-067

3. NAME AND ADDRESS OF APPLICANT

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

Telephone: 631-454-7677 ext. 2091
Fax: 631-756-5114

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Cleocin T® (Lotion; Topical)
Innovator Company: Pharmacia & Upjohn (NDA #50-600)

Signed certification is provided (page 11) stating that all listed patents in the U.S. have expired.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Clindamycin Phosphate Topical Suspension USP, 1%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:
Original Submission: 3/7/00 (Amendment 5/5/00)
Acknowledgment: 5/8/00

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
See DMF list under #37

13. DOSAGE FORM

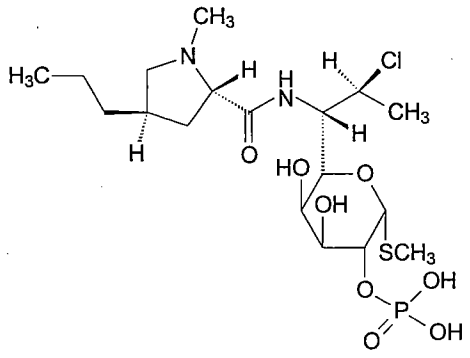
Topical lotion

14. POTENCY

1% (as clindamycin)

15. CHEMICAL NAME AND STRUCTURE

Clindamycin Phosphate. L-*threo*-α-*galacto*-Octopyranoside, methyl 7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl]-amino]-1-thio-, 2-(dihydrogen phosphate), (2*S*-*trans*)-. $C_{18}H_{34}ClN_2O_8PS$. 504.97. 24729-96-2.



16. RECORDS AND REPORTS

N/A

17. COMMENTS

Status Summary:

DMF:	DMF ——— adequate
Labeling:	Not satisfactory (6/29/00)
EER:	Pending

Sample: Not requested (USP drug)
Bio: Under review

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable (MAJOR AMENDMENT)

19. REVIEWER: Maria C. Shih
DATE COMPLETED: 7/25/00

APPEARS THIS WAY
ON ORIGINAL

Redacted 36

pages of trade secret and /or confidential commercial information

1. CHEMIST'S REVIEW NO. #2

2. ANDA #65-067

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

Telephone: 631-454-7677 ext. 2091
Fax: 631-756-5114

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Cleocin T® (Lotion; Topical)
Innovator Company: Pharmacia & Upjohn (NDA #50-600)

Signed certification is provided (page 11) stating that all listed patents in the U.S. have expired.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Clindamycin Phosphate Topical Suspension USP, 1%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:
Original Submission: 3/7/00 (Amendment 5/5/00)
Acknowledgment: 5/8/00
Amendment 2/9/01 to N/A (MAJOR) 8/7/00
Telephone Amendment 6/20/01

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. Rx or OTC
Rx

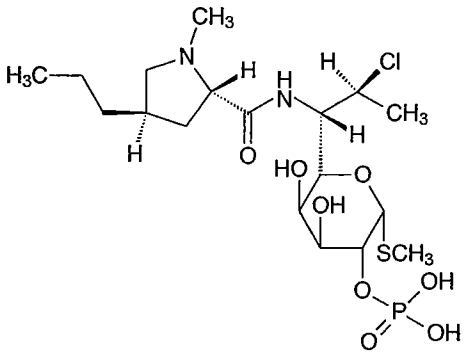
12. RELATED IND/NDA/DMF(s)
See DMF list under #37

13. DOSAGE FORM
Topical lotion

14. POTENCY 1% (as clindamycin)

15. CHEMICAL NAME AND STRUCTURE

Clindamycin Phosphate. L-*threo*-α-*galacto*-Octopyranoside, methyl 7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl]-amino]-1-thio-, 2-(dihydrogen phosphate), (2*S*-*trans*)-. $C_{18}H_{34}ClN_2O_8PS$. 504.97. 24729-96-2.



16. RECORDS AND REPORTS N/A

17. COMMENTS

A. **This is a first generic application for this dosage form.**

(The current USP monograph uses "Clindamycin Phosphate Topical Suspension", rather than "lotion", see E-mail dated 4/11/00 from C. Hoppes).

[redacted]

B. See Memo dated 5/1/01 from Div. Of Scientific Investigations (HFD-48) stating the non-compliance situation of Altana's Bio studies.

In MAJOR Amendment 2/9/01, Altana responds as follows:

(All are acceptable except #Q6, [redacted] and [redacted])

Q1. In the composition statement (page 2887), please change the last column to "[redacted]" instead of "[redacted]"

A1. Firm revises the composition statement (Attachment I).

Chem Rec 2 a

Redacted 3

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

(Attachment VIII). Included in Attachment IX is the

[redacted]

A12. See under A8.

Comments:

Regarding stability data included in this submission:

1. Under Attachment IX (the updated accelerated, RT and cycling stability data for lot E254, manufactured using

[redacted]

2. [redacted]

3. Ask Altana for long-term stability data for lot E254.

Status Summary for #65-067:

DMF:	DMF [redacted] adequate
Labeling:	Under review
EER:	Pending
Sample:	Not requested (USP drug)
Bio:	Under review

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable (FAX AMENDMENT)

19. REVIEWER: Maria C. Shih — DATE COMPLETED: 6/25/01

Chem Rec #2

Redacted 13

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

1. CHEMIST'S REVIEW NO. #3

2. ANDA #65-067

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

Telephone: 631-454-7677 ext. 2091
Fax: 631-756-5114

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Cleocin T® (Lotion; Topical)
Innovator Company: Pharmacia & Upjohn (NDA #50-600)

Signed certification is provided (page 11) stating that all listed patents in the U.S. have expired.

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Clindamycin Phosphate Topical Suspension USP, 1%

8. SUPPLEMENT(s) PROVIDE(s) FOR:
N/A

9. AMENDMENTS AND OTHER DATES:
Original Submission: 3/7/00 (Amendment 5/5/00)
Acknowledgment: 5/8/00
Amendment 2/9/01 to N/A (MAJOR) 8/7/00
Telephone Amendment 6/20/01
FAX Amendment 8/22/01

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. Rx or OTC
Rx

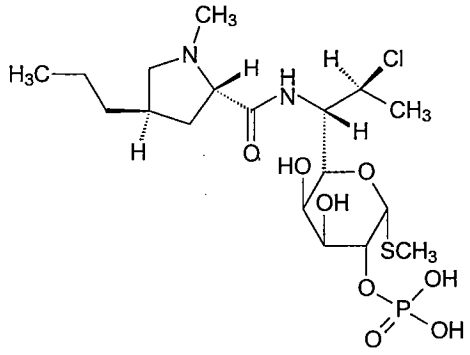
12. RELATED IND/NDA/DMF(s)
See DMF list under #37

13. DOSAGE FORM
Topical Suspension

14. POTENCY 1% (as clindamycin)

15. CHEMICAL NAME AND STRUCTURE

Clindamycin Phosphate. L-*threo*-α-*galacto*-Octopyranoside, methyl 7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl]-amino]-1-thio-, 2-(dihydrogen phosphate), (2*S*-*trans*)-. $C_{18}H_{34}ClN_2O_8PS$. 504.97. 24729-96-2.



16. RECORDS AND REPORTS N/A

17. COMMENTS

This is a first generic application for this dosage form.

Redacted 4

pages of trade secret and /or confidential commercial information

Q7

A7

Comments:

Ask Altana what are the correction/precaution procedures to prevent the ~~reference~~ recurrence of such happenings.

Status Summary for #65-067:

DMF:	DMF ~~——~~ ~~——~~ adequate
Labeling:	Not satisfactory 9/26/01
EER:	Pending
Sample:	Not requested (USP drug)
Bio:	Not satisfactory 7/6/01

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable (~~MINOR~~ AMENDMENT)

JAY

19. REVIEWER: Maria C. Shih — DATE COMPLETED: 9/27/01

Redacted 14

pages of trade secret and /or confidential commercial information

1. CHEMIST'S REVIEW NO. #4

2. ANDA #65-067

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

Telephone: 631-454-7677 ext. 2091
Fax: 631-756-5114

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Cleocin T® (Lotion; Topical)
Innovator Company: Pharmacia & Upjohn (NDA #50-600)

Signed certification is provided (page 11) stating that all listed patents in the U.S. have expired.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME N/A

7. NONPROPRIETARY NAME
Clindamycin Phosphate Topical Suspension USP, 1%

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:
Original Submission: 3/7/00 (Amendment 5/5/00)
Acknowledgment: 5/8/00
Amendment 2/9/01 to N/A (MAJOR) 8/7/00
Telephone Amendment 6/20/01
FAX Amendment 8/22/01
FAX Amendment 11/2/01

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. Rx or OTC
Rx

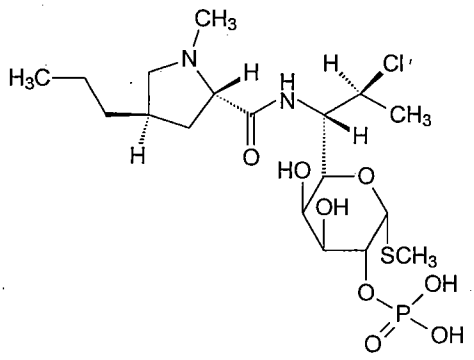
12. RELATED IND/NDA/DMF(s)
See DMF list under #37

13. DOSAGE FORM
Topical Suspension

14. POTENCY 1% (as clindamycin)

15. CHEMICAL NAME AND STRUCTURE

Clindamycin Phosphate. L-*threo*-α-*galacto*-Octopyranoside, methyl 7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl]-amino]-1-thio-, 2-(dihydrogen phosphate), (2*S*-*trans*)-. $C_{18}H_{34}ClN_2O_8PS$. 504.97. 24729-96-2.



16. RECORDS AND REPORTS N/A

17. COMMENTS

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Status Summary for #65-067:

DMF:	DMF [redacted] adequate
Labeling:	Pending
EER:	Pending
Sample:	Not requested (USP drug)
Bio:	Not satisfactory 7/6/01

18. CONCLUSIONS AND RECOMMENDATIONS
Not approvable (FAX Amendment)

19. REVIEWER: Maria C. Shih
DATE COMPLETED: 12/3/01

APPEARS THIS WAY
ON ORIGINAL

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1. CHEMIST'S REVIEW NO. 5

2. ANDA #65-067

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

Telephone: 631-454-7677 ext. 2091
Fax: 631-756-5114

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: Cleocin T® (Lotion; Topical)
Innovator Company: Pharmacia & Upjohn (NDA #50-600)

Signed certification is provided (page 11) stating that all listed patents in the U.S. have expired.

5. SUPPLEMENT(s) N/A

6. PROPRIETARY NAME N/A

7. NONPROPRIETARY NAME
Clindamycin Phosphate Topical Suspension USP, 1%

8. SUPPLEMENT(s) PROVIDE(s) FOR: N/A

9. AMENDMENTS AND OTHER DATES:
Original Submission: 3/7/00 (Amendment 5/5/00)
Acknowledgment: 5/8/00
Amendment 2/9/01 to N/A (MAJOR) 8/7/00
Telephone Amendment 6/20/01
[Amendment 7/27/00]
FAX Amendment 8/22/01
FAX Amendment 11/2/01
FAX Amendment 12/13/01

10. PHARMACOLOGICAL CATEGORY
Antibacterial

11. Rx or OTC
Rx

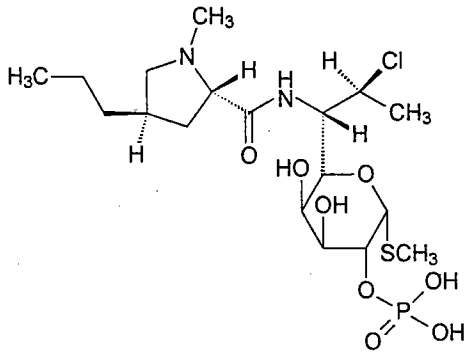
12. RELATED IND/NDA/DMF(s)
See DMF list under #37

13. DOSAGE FORM
Topical Suspension

14. POTENCY 1% (as clindamycin)

15. CHEMICAL NAME AND STRUCTURE

Clindamycin Phosphate. L-*threo*-α-*galacto*-Octopyranoside, methyl 7-chloro-6,7,8-trideoxy-6-[[(1-methyl-4-propyl-2-pyrrolidinyl)carbonyl]-amino]-1-thio-, 2-(dihydrogen phosphate), (2*S*-*trans*)-. $C_{18}H_{34}ClN_2O_8PS$. 504.97. 24729-96-2.



16. RECORDS AND REPORTS N/A

17. COMMENTS

NOTE:

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Review of Amendment 7/27/00: (Acceptable)
New exhibit batches Lot #E254 ([redacted] size) is produced

[redacted]

[redacted]

Status Summary for #65-067:

DMF:	DMF [redacted] adequate
Labeling:	Acceptable (1/23/02)
EER:	Acceptable (12/20/01)
Sample:	Not requested (USP drug)
Bio:	Acceptable (12/12/01)

18. CONCLUSIONS AND RECOMMENDATIONS
Approval recommended

19. REVIEWER: Maria C. Shih

DATE COMPLETED: 1/10/02; 1/23/02 (as revised)

APPEARS THIS WAY
ON ORIGINAL

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-067

BIOEQUIVALENCE REVIEW(S)

OCT 13 200

BIOEQUIVALENCY DEFICIENCIES

ANDA: 65-067 APPLICANT: Altana Inc.

DRUG PRODUCT: Clindamycin Phosphate Topical Suspension USP 1%

The Division of Bioequivalence has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiencies have been identified:

1. The data listing categories for exclusions from the Per Protocol population include:

   a.)Outside visit window for Day 84 visit
   b.)Non-compliance
   c.)Use of prohibited medication after start of study.

   The following categories are listed for the Per Protocol population in your application:

   a.)Failed to return
   b.)Protocol violation
   c.)Other

   Because you include exclusions from the MITT population in the total exclusions from the Per Protocol population, it is difficult to decipher what these categories correspond to in the data listings. In addition, the criteria for non-compliance were not defined in either the protocol or the study report. Please clarify the reasons for exclusion from the study and define non-compliance.

2. The Case Report Forms for the following study subjects need to be submitted for review:

305	317	244	075	079	081	097	326	492	499	393	436
178	402	208	364	369	452	235	239	037	313	489	066
267	269	100	324	330	120	442	129	134	437	438	145
148	165	179	009	404	206	217	365	370	454	232	036
487	247	265	095	322	327	336	491	128	397	008	193
403	361	429	244	223	210	213	319	119	435	384	390
431											

3. CRF #341 was supplied but several pages of the CRF are missing. Please provide another copy of the CRF.

4. CRF #229 was supplied but the Study Summary Sheet is missing. Please provide a copy of this page.

Sincerely yours,

/S/

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

CC: ANDA 65-067
ANDA DUPLICATE
DIVISION FILE
FIELD COPY
DRUG FILE

Endorsements:
HFD-600/Mary Fanning
HFD-600/Lizzie Sanchez
HFD-652/Krista M. Scardina
HFD-650/Dale Conner

/S/ 9/27/00
/S/ 9/27/00

V: firmsam/altana/ltrs&rev/65-067.DEF.BIO

BIOEQUIVALENCY - DEFICIENCIES Submission Date: 07 March 2000

1. **BIO STUDY** (STU) Strengths: 1%

Clinical: [redacted] **Outcome: IC**

Outcome Decisions:
AC - Acceptable
NC - No Action
UN - Unacceptable
IC - Incomplete

WinBio Comments

The Bio Study is incomplete

[redacted]

APPEARS THIS WAY
ON ORIGINAL

LI, Huaxiang 4.1

JUL 20 2001

BIOEQUIVALENCY DEFICIENCIES

ANDA: 65-067 APPLICANT: Altana Inc.

DRUG PRODUCT: Clindamycin Phosphate Topical Suspension USP 1%

The Division of Bioequivalence has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiencies have been identified:

1. Please provide an exact definition for compliance, including the acceptable number of missed applications, the evaluation of returned study medication tubes, and any other criteria that went into an evaluation of study compliance. You did not give any data on compliance or the number of subjects who needed repeat instruction on the application of the test product at the post-baseline visits. Also, please provide any available data and clarify the use of the term in these two contexts.

2. Please submit an electronic copy of the data set.

3. Please clarify why patient #244 did not meet inclusion criteria as the case report form does not contain information that makes this clear.

4. During a routine inspection of the clinical sites used to conduct the bioequivalence study, the Division of Scientific Investigation (DSI) found that based on the non-compliance of the regulation with regard to the retention of reserve samples (21 CFR 320.63), the authenticity of the test and reference drug products used in the study cannot be assured. The final rule for retention of reserve samples (Federal Register of April 28, 1993; 80 FR 25918) states that the testing facility, not the sponsor, should separate out the study drugs to be retained as reserve samples for blinded bioequivalence studies. Please provide an explanation for failure to retain reserve samples at the clinical sites.

Sincerely yours,

/S/

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA # :65-067 SPONSOR : Altana, Inc.

DRUG AND DOSAGE FORM : **Clindamycin Phosphate Topical Suspension USP**

STRENGTH(S) : **1%**

TYPES OF STUDIES : Bio Study

CLINICAL STUDY SITE(S) : N/A

ANALYTICAL SITE(S) : **N/A**

STUDY SUMMARY :
The study meets the bioequivalence criteria and therefore demonstrates the bioequivalence between the test and reference product.
DISSOLUTION : N/A

DSI INSPECTION STATUS

Inspection needed: NO	Inspection status:	Inspection results:
First Generic _____	Inspection requested: (date)	
New facility _____	Inspection completed: (date)	
For cause _____		
Other _____		

PRIMARY REVIEWER : Mary Fanning

INITIAL : /S/ DATE : 12/12/01

SECONDARY REVIEWER : Rabi Patnaik

INITIAL : /S/ DATE : 12/12/2001

DIRECTOR, DIVISION OF BIOEQUIVALENCE : DALE P. CONNER, Pharm. D.

INITIAL : /S/ DATE : 12/12/01

8-2-01 6.1

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA:65-067 APPLICANT: Altana, Inc.

DRUG PRODUCT:Clindamycin Phosphate Topical Suspension USP, 1%

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

/S/

Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-067

ADMINISTRATIVE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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

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

Form Approved: OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on page 2.

FOR FDA USE ONLY
APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Altana Inc.	04/10/01
TELEPHONE NO. (Include Area Code)	**FACSIMILE (FAX) Number (Include Area Code)**
(631) 454-7677	(631) 756-5114
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE
60 Baylis Road Melville, NY 11747	

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 65-067

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Clindamycin Phosphate Topical Suspension USP	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*	**CODE NAME** *(If any)*

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Lotion (Suspension)	1%	Topical

(PROPOSED) INDICATION(S) FOR USE:
Indicated for the treatment of acne vulgaris.

APPLICATION INFORMATION

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

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

IF AN ANDA, or 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

Name of Drug	Holder of Approved Application
Cleocin T	Pharmacia & Upjohn

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

IF A SUBMISSION OR PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION DUPLICATE COPY - Response to deficiency letter dated 08/07/00, received on 11/22/00.

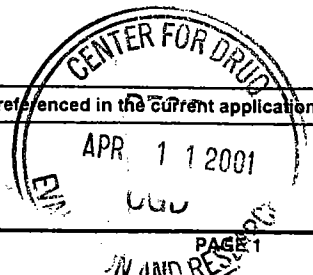
PROPOSED MARKETING STATUS *(check one)* ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED ~~One~~ THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

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

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

DMF —
DMF —
DMF —



CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

65-067

CORRESPONDENCE

ALTANA

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

December 13, 2001

Florence S. 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, MD 20855-2773

VIA Telefax (301-827-4337)
and FEDERAL EXPRESS

65-067
Clindamycin Phosphate Topical Suspension USP 1%
FAX AMENDMENT - Chemistry

NEW CORRESP

Dear Ms. Fang:

Reference is made to Altana's Abbreviated New Drug Application submitted on March 7, 2000 pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Clindamycin Phosphate Topical Suspension USP.

Reference is also made to the FDA facsimile correspondence received December 12, 2001 for Chemistry comments in response to the Altana Inc. Amendment dated November 2, 2001. As requested, this response has been appropriately identified as a "FAX AMENDMENT" and addresses all chemistry comments provided.

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

Chemistry

Regarding the data analysis issue of "Others" for API degradation determination:

1. **Is there a limit for "Others"?**

   The specification has been revised to include a limit for "Others" at each NMT Included as **Attachment I** is the revised specification.

2. **Please establish direction/procedures for data analysis and presentation in order to maintain consistency.**

   The specifications have been re-formatted to a two page document to provide additional space to record results, please refer to **Attachment I**. The Analytical Procedure has also been revised to include procedures for the recording of results onto the specification sheets in order to maintain consistency. The approximate relative retention times for the known impurities have been updated to reflect the actual data obtained. **Attachment II** contains the revised Analytical Procedure.

Regarding your stability data and proposed expiration dating of 24 months:

3. **The data submitted in the new container/closure system does not justify 24 months expiration dating. Until such time as a 3-month accelerated study with acceptable results is performed and submitted, the expiration dating is limited to the length of time supported by the long term studies.**

   Three month accelerated stability studies (Lot E254) have been performed in the new container/closure system and submitted as an Amendment to the ANDA on July 27, 2000 (pages 283-290). An additional three month accelerated stability study (Lot F270) was completed in November 2000. Both lots demonstrate satisfactory results after three months storage at accelerated temperatures and fully support the proposed expiration dating of 24 months for the drug product. Copies of the accelerated stability reports for the new container/closure system in both lots have been included as **Attachment III.**

4. [redacted]

   On July 27, 2000 Altana Inc. filed an Amendment to this ANDA for a change of the active [redacted] and a new label adhesive. Included in this Amendment was an executed batch record (Lot E254), finished product test results, accelerated and room temperature stability data, componentry information and additional regulatory information to support the proposed changes.

   In addition Altana's November 2001 Amendment included stability data for an additional batch (F270) manufactured using the [redacted]

   Please refer to the July 27, 2000, specifically pages 328-334 and November 2, 2001 Amendments.

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

VC/jb

TELEFAX DATED: December 13, 2001

ALTANA

Altana Inc. 60 Baylis Road, Melville, NY 11747 631-454-7677 Fax: 631-756-5114

BYK GULDEN PHARMA GROUP

TO: Mark Anderson FAX NO: 301-827-4337

FROM: Virginia Carman

OF PAGES (including this page): 42

65-067
Clindamycin Phosphate Topical Suspension USP 1%
FAX AMENDMENT - Chemistry

ORIG AMENDMENT FA

Dear Mr. Anderson:

Please find the FAX Amendment dated December 13, 2001 is response to the FDA correspondence dated December 12, 2001.

As requested this response is being faxed directly to the document control room at 301-827-4337.

A hard copy will also be sent Via Federal Express to the following address.

Office of Generic Drugs, CDER, FDA
Document Control Room, MPN II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

If you have any questions or require additional information please contact me at 631-454-7677 extension 2091.

Sincerely,

ALTANA INC.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

ALTANA

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

November 2, 2001

Noted & Changed 11/17/01
IS!

NDA
DRUG AMENDMENT

Florence S. 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, MD 20855-2773

VIA FEDERAL EXPRESS

65-067
Clindamycin Phosphate Topical Suspension USP 1%
FAX AMENDMENT - Chemistry and Labeling

Dear Ms. Fang:

Reference is made to Altana's Abbreviated New Drug Application submitted on March 7, 2000 pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Clindamycin Phosphate Topical Suspension USP.

Reference is also made to the FDA facsimile correspondence received October 24, 2001 for Chemistry and Labeling comments in response to the Altana Inc. Amendment dated August 22, 2001. As requested this response has been appropriately identified as a "FAX AMENDMENT" and addresses the chemistry and labeling deficiencies.

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

Chemistry

1. **We note that there are two — methods validated for the determination of impurities and related substances for the API (Part A and Part B). Please clarify which method you use for routine in-house testing of the API impurities and related substances.**

   Altana uses an — method for analysis of the impurities and related substances for the API (Part A and Part B). Altana uses both (Part A and Part B) for the analysis of impurities and related substances to capture total impurities as explained below.

   CENTER FOR DRUG EVALUATION AND RESEARCH
   NOV 06 2001

   Part A (used for analysis of the following)

   [ ]

   Part B (used for the analysis of the following)

Redacted 4

pages of trade secret and/or confidential commercial information

name is unacceptable. Please delete the proposed proprietary name for all labels and labeling or submit another name for our review and comment.

Altana has included two sets of container, carton and insert labeling. **Attachment IV** contains the trade name "Fougera® Clindamycin Phosphate Lotion" in addition to the USP established name. This labeling remains unchanged from that which was previously submitted on August 22, 2001.

Altana has also prepared labeling which is identical to the labeling cited above, except that it contains the USP established name "Clindamycin Phosphate Topical Suspension USP, 1%". See **Attachment V**.

Altana Inc. is prepared to use the USP designated name, so as not to delay approval of this application. However, we have asked our legal counsel to address the use of the trade name in separate correspondence to the Division of Labeling and Program Support. Our legal counsel has explained to us that they believe we have the right to use a trade name as long as we also comply with the requirement to include the USP-designated established name of the drug.

b. **We acknowledge your intentions to file your company website address to DDMAC for their review.**

Altana Inc. has filed the company website to DDMAC, along with a Form FDA 2253 to a single application as required.

Labeling with revisions to include the web address will be submitted after the approval of this application as a Prior Approval Supplement in accordance with 21 CFR 314.70(b).

2. **CONTAINER: 60 mL bottle**

In your "Each mL...contains" statement, revise [redacted] to read "suspension".

The Fougera Labeling states "[redacted]". The USP labeling states "Each mL of the suspension contains...".

3. **CARTON: 1s**

a. **See General Comments.**
See response above.

b. **See comments under CONTAINER.**
See response above.

4. INSERT

See General Comments and revise the text on your insert labeling accordingly.

The Fougera Labeling has remained unchanged from the August 22, 2001 Amendment. The USP labeling has been revised to read Clindamycin Phosphate Topical Suspension USP, 1% throughout the package insert. Minor editorial changes have been made accordingly.

Included as **Attachment IV** are twelve copies of the Final Printed container, carton and insert labeling for the Fougera® Clindamycin Phosphate Lotion, 1% (Clindamycin Phosphate Topical Suspension USP, 1%). Altana has revised the USP container, carton and insert labeling as stated above. Included as **Attachment V** are twelve copies of the Final Printed container, carton and insert labeling for Clindamycin Phosphate Topical Suspension USP, 1%.

To facilitate the review and in accordance with 21 CFR 314.94 (a)(8)(iv), a side-by-side comparison has been provided of the proposed labeling with all differences annotated and explained see **Attachment VI**.

Altana Inc. will monitor the FDA website, http://www.fda.gov/cder/ogd/rld/labeling for the latest approved labeling supplements for NDA 50-537 (Cleocin T®, manufactured by Pharmacia and Upjohn) on a routine basis.

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

VC/jb

ALTANA

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

August 22, 2001

Noted: To Marion Shah /S/ 8/29/01

Florence S. 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, MD 20855-2773

VIA FEDERAL EXPRESS

Clindamycin Phosphate Topical Suspension USP 1%
65-067
FAX AMENDMENT - Chemistry and Labeling

FPL
ORIG AMENDMENT
N/FA

1 g/100 mL
1000 mg/100 mL
10 mg/mL

Dear Ms. Fang:

Reference is made to Altana's Abbreviated New Drug Application submitted on March 7, 2000 pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Clindamycin Phosphate Topical Suspension USP.

Reference is also made to the Agency facsimile correspondences received August 3 and August 9, 2001 for Chemistry and Labeling comments in response to the Altana Inc. Amendments dated February 9, 2001 and June 20, 2001. As requested this response has been appropriately identified as a "FAX AMENDMENT" and addresses the chemistry and labeling deficiencies as requested in the facsimile correspondence dated August 9, 2001.

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

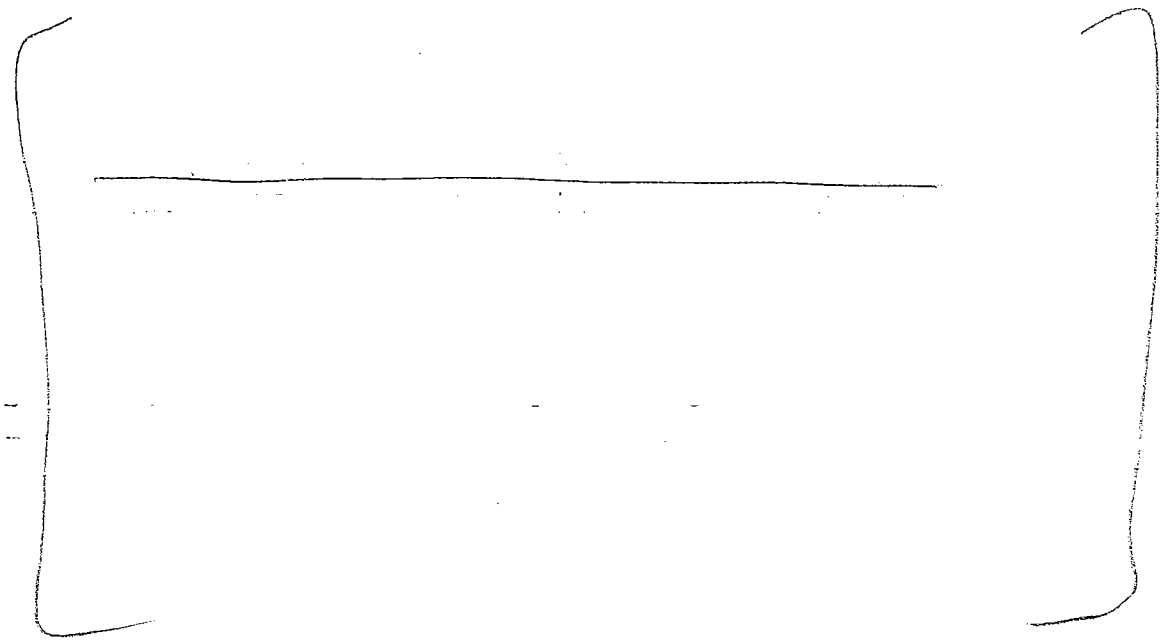
Chemistry

1. **Do you use the same — method for assay and impurities? Do you use the same — method for the drug substance as well as the drug product? The validation package for the — method(s) should be provided.**

   The drug substance assay is performed according to the current USP method for Clindamycin Phosphate. Altana uses an — method for analysis of the impurities and related substances. **Attachment I** contains a copy of the report entitled *Verification of the — Assays for Impurities and Related Substances in Clindamycin Phosphate Raw Material*

   The drug product assay and impurities analysis is performed using a single — method. This validated method was submitted on pages 3812 –3878 of the original ANDA for product

CENTER FOR DRUG EVALUATION AND RESEARCH
AUG 24 2001



b. **We acknowledge your intent to include a web address on your labeling after the approval of this application. Please note that section 502(a) of the Federal Food, Drug and Cosmetic Act states that your product will be deemed to be misbranded if its false or misleading. In particular, prior to approval of labeling bearing your web address, please provide communication from the FDA's Division of Drug Marketing, Advertising and Communications (DDMAC), that your website is neither false or misleading. Labeling with revisions to include your web address may be submitted after the approval of this application as a prior approval supplement in accord with 21 CFR 314.70(b).**

Altana Inc. will file the company website to DDMAC, along with a Form FDA 2253 to a single application as required.

Labeling with revisions to include the web address will be submitted after the approval of this application as a Prior Approval Supplement in accordance with 21 CFR 314.70(b).

CONTAINER: 60 mL

a. **See General Comments.**

See response to General Comments: a, as stated above.

b. In your "Each mL ...contains" statement, revise ' [redacted] **to read "suspension."**

Altana has revised [redacted] .." to read "Each mL contains...."
Any reference to [redacted] has been omitted.

CARTON:

a. See General Comments.

See response to General Comments: a, as stated above.

b. See comments under CONTAINER.

Altana has revised "' [redacted] ..." to read "Each mL contains..."
Any reference to [redacted] has been omitted.

INSERT:

See General Comments and revise the text of your insert labeling accordingly.

See response to General Comments: a, as stated above.

Altana has revised the container and carton labeling as stated above. The insert has remained unchanged from the February 21, 2001 Major Amendment submission. Included as **Attachment IX** are twelve copies of the Final Printed container, carton and insert labeling.

To facilitate the review and in accordance with 21 CFR 314.94 (a)(8)(iv), a side-by-side comparison has been provided of the proposed labeling with all differences annotated and explained see **Attachment X**.

Altana Inc. has monitored the FDA website, http://www.fda.gov/cder/ogd/rld/labeling and the latest approved labeling supplements for NDA 50-537 (Cleocin T, manufactured by Pharmacia and Upjohn) is March 15, 1989. A copy of the electronic page is included as **Attachment XI**. Altana Inc. will monitor the site on a routine basis.

If you have any questions or require additional information, please contact me at (631) 454-7677 extension 3007. FAX communications can be made to (631) 756-5114.

Sincerely,

ALTANA, INC.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

VC/jb

C:\Jackie\Clindamycin Phosphate\ANDA65067.DLR.Fax.Chem&Lab.Aug2001.doc

ALTANA

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

August 20, 2001

Mr. Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
(301) 594-0320

VIA FEDERAL EXPRESS

BIOAVAILABILITY
ORIG AMENDMENT
N/A B

ANDA 65-067
Clindamycin Phosphate Topical Suspension USP, 1%
BIOEQUIVALENCY AMENDMENT

Dear Mr. Conner:

Reference is made to the Altana Inc. Abbreviated New Drug Application for Clindamycin Phosphate Topical Suspension USP, 1%, submitted on March 7, 2000 in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act and to the Bioequivalency Amendment submitted on February 14, 2001. Reference is also made to the FDA correspondence dated July 20, 2001, outlining Bioequivalency Deficiencies in the February 14, 2001 submission. (A copy of the correspondence is included in **Attachment I.**)

As required, Altana has responded to all of the items listed. This response has been appropriately identified as a "BIOEQUIVALENCY AMENDMENT."

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

1. **Please provide an exact definition for compliance, including the acceptable number of missed applications, the evaluation of returned study medication tubes, and any other criteria that went into an evaluation of study compliance. You did not give any data on compliance of the number of subjects who needed repeat instruction on the application of the test product at the post-baseline visits. Also, please provide any available data and clarify the use of the term in these two contexts.**

   In the clinical study ALT 03/97, study subjects were considered compliant with the study medication regimen if they missed no more than six (6) consecutive applications or no more than twelve (12) total applications, based on the subjects' verbal responses when questioned by the coordinator. The number of applications reported missed by each subject is provided in Data Listing 8 in Appendix D of the study report in the original application.

CENTER FOR DRUG EVALUATION AND RESEARCH
AUG 21 2001
OGD

The returned medication bottles were examined visually to determine if the subjects had used an amount of lotion that was appropriate for the extent of their acne. Due to the inter-subject differences in the severity and surface area involved in the disease, it was not considered possible to objectively measure usage of the medication.

There is no way to determine at this point the number of subjects who needed repeat instruction in application of study medication at a follow-up visit.

Non-compliance was the reason for exclusion from the Per Protocol analysis population of five (5) subjects in the generic clindamycin group, four (4) subjects assigned to Cleocin® T, and five (5) vehicle subjects. They are accounted for in Table 2, "Patient Distributions in Analysis Populations-Numbers Included and Excluded with Reasons for Exclusion" in the numbers excluded for protocol violations.

2. **Please submit an electronic copy of the data set.**

An electronic copy of the data set is included in **Attachment II**.

3. **Please clarify why patient #244 did not meet inclusion criteria as the case report form does not contain information that makes this clear.**

Subject #244 was excluded because of the use at entry and during the study of an inhaled corticosteroid, Nasacort AQ®.

4. **During a routine inspection of the clinical sites used to conduct the bioequivalence study, the Division of Scientific Investigation (DSI) found that based on the non-compliance of the regulation (21 CFR 320.63), the authenticity of the test and reference drug products used in the study cannot be assured. The final rule for retention of reserve samples (Federal Register of April 28, 1993; 80 FR 25918) states that the testing facility, not the sponsor, should separate out the study drugs to be retained as reserve samples for blinded bioequivalence studies. Please provide an explanation for failure to retain reserve samples at the clinical sites.**

The clinical study ALT 03/97 complies with 21 CFR 320.63 "Retention of bioequivalence samples". This section of the CFR provides that either the applicant or the contract research organization (CRO) may store the retain samples for a bioequivalence study in accordance with, and for the period specified in, §320.38 and shall release the reserve samples to FDA upon request in accordance with §320.38. In turn, 21 CFR 320.38(h) explicitly provides that an independent third party may be used to perform this function. The authenticity of the test and reference drug products used in this study can be assured as appropriate quantities of retained samples are being stored at an independent third party in compliance with the requirements of §320.63 and §320.38.

Altana's Standard Operating Procedure No. 710 for the "Sampling and Retention of Bioequivalence Samples" specifies that all of the randomized clinical supplies will be shipped to an independent third party. A designee at this third party site is responsible for inventorying and verifying the randomized clinical supplies. This designee is also responsible for choosing two blocks of randomized patient supplies for retention bioequivalence samples. This amount should be equivalent to 5 times the amount required to perform complete analytical testing. Each retention sample is clearly identified as a retention sample that has come directly from the same sample population as is being used in the specific bioequivalence study. The remaining blocks of randomized clinical supplies are returned to inventory for use in the bioequivalence study. The third party site is also responsible for shipping randomized clinical supplies to each investigative site.

If FDA intends to impose that the individual investigative site must maintain the retain samples; it should be clearly stated in the regulation. Altana Inc. anxiously awaits publication of FDA's interpretation of §320.63 as currently no Federal Register Notice, comment period or proposed rule has been published by FDA.

However, in order to improve and better explicate selection and storage of reserve samples, Altana Inc. has recently revised the reserve sample policy. The clinical supplies are shipped directly to each investigative site and upon receipt, each investigator will select the samples to be retained. Each site will then maintain the retain samples or contract with an independent third party, selected by the CRO, to the retain samples.

This concludes E. Fougera & Co.'s response to the Bioequivalency Amendment. 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.

Audrey Bialeski for

Virginia Carman
Associate Director, Regulatory Affairs

VC: jfa
Attachment

ALTANA

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

June 20, 2001

NEW CORRESP
NC/B10

Mr. Dale Conner, RPh
Director, Division of Bioequivalence
Office of Generic Drugs (HFD-650)
7500 Standish Place, RM E130
Rockville, MD 20855

RE: ANDA 65-067 TELEPHONE BIOEQUIVALENCE AMENDMENT
Clindamycin Phosphate Topical Suspension USP, 1%

Dear Mr. Conner:

Reference is made to the Altana Abbreviated New Drug Application submitted on March 7, 2001 pursuant to Section 505(j) of the Federal, Food, Drug and Cosmetic Act for Clindamycin Phosphate Topical Suspension, USP.

Reference is also made to the telephone conversation of June 18, 2001 between Ms. Krista Scardina of the Division and Ms. Virginia Carman of Altana Inc. Altana was requested to provide information on the number of visits a patient could miss during the study and still be considered evaluable.

There was no stated limit on the number of visits a subject could miss and remain evaluable for the (PP) population. The only requirement was the final visit evaluations be completed, which would occur at the Day 84 visit for most subjects, or the last completed visit for subject dropped due to insufficient therapeutic response or intolerable adverse events. The Day 84 visit was the primary time point for comparison of results in the 3 treatment groups.

In the analysis of results in the PP population, missed visits were represented in the database by missing values. The Last Observed Carried Forward method of replacing missing values was not used in that population. Therefore, the values of N at each visit could vary slightly.

If any further information is necessary, please contact me at (631) 454-7677 ext. 2091. Fax communication may be made to (631) 756-5114.

Sincerely,

ALTANA INC.

Virginia Carman

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

ORIG AMENDMENT

N/AB

February 14, 2001

Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs (HFD-600)
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20855

VIA FEDERAL EXPRESS

ANDA 65-067
Clindamycin Phosphate Topical Suspension USP, 1%
Bioequivalency Amendment

Dear Dr. Conner:

Reference is made to the bioequivalency data submitted on March 7, 2000 for Clindamycin Phosphate Topical Suspension USP, 1% in accordance with Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the FDA facsimile received by Altana Inc. on January 8, 2001 (dated October 13, 2000) containing bioequivalency deficiencies from the Office of Generic Drug's Division of Bioequivalence. Each comment has been addressed in **comment**/ response format.

1. **The data listing categories for exclusions from the Per Protocol population include:**
   a. **Outside visit window for Day 84 visit**
   b. **Non-compliance**
   c. **Use of prohibited medication after start of study.**

   The following categories are listed for the Per Protocol population in your application:
   a. **Failed to return**
   b. **Protocol violation**
   c. **Other**

   Because you include exclusions from the MITT population in the total exclusions from the Per Protocol population, it is difficult to decipher what these categories correspond to in the data listings. In addition, the criteria for non-compliance were not defined in either the protocol or the study report. Please clarify the reasons for exclusion from the study and define non-compliance.

   A listing of the number of subjects excluded from the efficacy analysis populations, by category of exclusion, has been provided as Attachment I. This listing was compiled from Table 1 in Appendix B of the study report.

   All subjects excluded for "Non-Compliance" had missed more than the maximum allowed number of applications of study medication. When multiple invalidating events occurred in one subject, the listed reason for exclusion was the earliest of those events.

2. **The Case Report Forms for the following study subjects need to be submitted for review:**

305	**317**	**244**	**075**	**079**	**081**	**097**	**326**	**492**	**499**	**393**	**436**
178	**402**	**208**	**364**	**369**	**452**	**235**	**239**	**037**	**313**	**489**	**066**
267	**269**	**100**	**324**	**330**	**120**	**442**	**129**	**134**	**437**	**438**	**145**
148	**165**	**179**	**009**	**404**	**206**	**217**	**365**	**370**	**454**	**232**	**036**
487	**247**	**265**	**095**	**322**	**327**	**336**	**491**	**128**	**397**	**008**	**193**
403	**361**	**429**	**244**	**223**	**210**	**213**	**319**	**119**	**435**	**384**	**390**
431											

Please see Attachment II for the Case Report Forms for the study subjects listed above.

3. **CRF #341 was supplied but several pages of the CRF are missing. Please provide another copy of the CRF.**

Another copy of CRF #341 has been provided as Attachment III.

4. **CRF #229 was supplied but the Study Summary Sheet is missing. Please provide a copy of this page.**

A copy of the Study Summary Sheet for CRF #229 has been included as Attachment IV.

This concludes the Altana Inc. response to this Bioequivalency Amendment.

In addition, Altana Inc. is providing the following information regarding the Clindamycin Phosphate USP drug substance.

The initial [redacted] has ceased production of Clindamycin Phosphate. This material was used to manufacture the exhibit batch provided to demonstrate bioequivalency to the Reference Listed Drug. In July 2000 Altana Inc. filed an Amendment to this pending application to provide for [redacted] of Clindamycin Phosphate USP manufactured by [redacted] This submission was prepared in accordance with the FDA Guidance for Industry entitled "Alternate Source of the Active Pharmaceutical Ingredient in Pending ANDAs". As provided for in this Guidance document, the original API source was withdrawn solely because of [redacted] decision to cease production of the material. There were no deficiencies specifically relating to that API such as: lack of adequate controls, evidence of adulteration or evidence of falsification of data in the application or identified in the pre-approval inspection. The previous bioequivalence batch and the bioequivalence study were acceptable except for the cGMP issues that were specific to the original API. The specifications for the alternate source API are essentially the same as the original source API.

The Amendment for the [redacted] included analytical test results for the [redacted] an exhibit batch record for the drug product and appropriate accelerated and controlled room temperature data. Copies of the Certificates of Analysis and associated analytical data for the [redacted] lot of [redacted] used in the bioequivalence study and the lot of [redacted] material submitted in the July Amendment are enclosed as Attachment V. Altana Inc. has compared the analytical test results for the [redacted] and [redacted] Both manufacturers' drug substance complies with the USP specifications for Clindamycin Phosphate USP.

Altana Inc. has also performed Particle Size Analysis on the [redacted] material sources and obtained the following results:

Clindamycin Phosphate USP		
Particle Size Results	[redacted] Lab Control #9701000079	[redacted] Lab Control #9903000191
[redacted]		
Observations	[redacted]	

Examination of the results generated for each of these materials finds them to be sufficiently similar to be considered therapeutically equivalent.

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

Sincerely,

ALTANA INC.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

VC/ab

ALTANA

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

February 9, 2001

Florence S. 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, MD 20855-2773

N/AC
ORIG AMENDMENT

VIA FEDERAL EXPRESS

Clindamycin Phosphate Topical Suspension USP 1%
65-067
MAJOR AMENDMENT

Dear Ms. Fang:

Reference is made to Altana's Abbreviated New Drug Application submitted on March 7, 2000 pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act for Clindamycin Phosphate Topical Suspension USP.

Reference is also made to the Agency facsimile received November 22, 2000 (dated August 7, 2000). As requested this response has been appropriately identified as "MAJOR AMENDMENT."

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

Chemistry

1. **In the composition statement (page 2887), please change the last column to "——" instead of "——"**
   In the composition statement, Altana Inc. has changed the last column to "——" instead of "——". **Attachment I** contains the corrected page 2887.

2. **It is suggested that you develop an —— method for determining drug substance impurities/degradants. Please provide the methodology and analytical data including the —— Specifications and appropriate limits for impurities/degradants need to be established.**
   Altana Inc. currently uses an ——method for the drug substance impurities/degradants. The specifications are established and in place for the new drug substance material manufactured by —— (please see deficiency #3 below). Included as

Attachment II are the specifications and updated analytical procedure including the [redacted] methodology for the [redacted]
For reference a copy of the BP monograph for Clindamycin Phosphate is also included. Analytical data and [redacted] for the [redacted] material are included as **Attachment III.** [redacted]

3. [redacted]

Included as **Attachment IV** is a copy of the [redacted]) letter amending their DMF #[redacted] in response to a deficiency letter received on November 12, 2000.

4. **We note that the COAs from both in-house and manufacturer, [redacted] for [redacted], are about two years old. Please clarify the retest day for this ingredient.**

[redacted]

Laboratory Raw Material Specification/Analysis Report for Approval of the 12 month extension.

Regarding the exhibit batch records:

5. **It is not clear how you obtained the bulk yield on page 3353 for batch lot #A344. Please clarify.**
The actual batch size was [redacted] (the weight of the drum and the validation samples). The theoretical batch size was [redacted] The bulk yield is obtained by using the following calculation.

$$\frac{\text{actual bulk size}}{\text{theoretical batch size}} \times 100 = \text{bulk yield \%}$$

[redacted]

Redacted 2

pages of trade secret and/or confidential commercial information

Labeling

1. **CONTAINER: 60 mL bottle**

   a. **Increase the prominence of the "Shake well..." statement.**
   b. **Revise to add "(See USP)" following your storage temperature statement.**
   c. **Delete [redacted] from your label.**

   Altana Inc. has increased the prominence of the "Shake well..." by capitalizing the statement.

   The storage statement has been revised to add (See USP).

   The [redacted] has been deleted from the label. Altana Inc. considers this part of the address and wishes to revise the labeling after approval to include the [redacted] address.

2. **CARTON: 1s**

   See comments under CONTAINER.
   Altana Inc. has increased the prominence of the "Shake well..." by capitalizing the statement.

   The storage statement has been revised to add (See USP).

   The [redacted] has been deleted from the label. Altana Inc. considers this part of the address and wishes to revise the labeling after approval to include the [redacted] address.

3. **INSERT**

   a. **ADVERSE REACTIONS**
   Revise the first sentence to read, "...formulations of topical clindamycin phosphate...".
   The first sentence has been revised to read, "...formulations of topical clindamycin phosphate..."

   b. **DOSAGE AND ADMINISTRATION**
   Revise the last sentence to read, "Keep in container and keep tightly closed".
   The last sentence has been revised to read, "Keep in container and keep tightly closed".

c. **HOW SUPPLIED**
See comment 1 (b and c) under CONTAINER.
The storage statement has been revised to add (See USP).

The [redacted] has been deleted from the label. Altana Inc. considers this part of the address and wishes to revise the labeling after approval to include the [redacted] address.

As instructed and according to 21 CFR 314.94 (a)(8)(ii) included in Attachment XII are twelve copies of revised final printed container, carton and insert labeling. The product name for container, carton and insert labeling have all been revised to Clindamycin Phosphate Lotion (Clindamycin Phosphate Topical Suspension USP) to reflect the Reference Listed Drug's product name and USP nomenclature for the product name.

Altana Inc. notes that FDA reserves the right to request further changes in the labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

Altana Inc. has monitored the FDA website, http://www.fda.gov/cder/ogd/rld/labeling and the latest approved labeling supplements for NDA 50-537 (Cleocin T, manufactured by Pharmacia and Upjohn) is March 15, 1989. A copy of the electronic page is included as **Attachment XIII**. Altana Inc. will monitor the site on a routine basis.

To facilitate the review and in accordance with 21 CFR 314.94 (a)(8)(iv), a side-by-side comparison has been provided of the proposed labeling with all differences annotated and explained see **Attachment XIV**.

If you have any questions or require additional information, please contact me at (631) 454-7677 extension 3007. FAX communications can be made to (631) 756-5114.

Sincerely,

ALTANA, INC.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

VC/jb

ALTANA

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

July 27, 2000

EER requested 12/17/01

ORIG AMENDMENT

N/AC

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place
Rockville, Maryland 20855-2773

VIA FEDERAL EXPRESS

Re: ANDA 65-067
Clindamycin Phosphate Topical Suspension USP, 1% (base)
Amendment

Dear Sir or Madam:

Reference is made to the Altana Inc. original Abbreviated New Drug Application for Clindamycin Phosphate Topical USP, 1% (base) submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act on March 7, 2000.

In accordance with the provisions set forth in 21 CFR 314.96 Altana Inc., is hereby amending our application with the required supportive documentation to obtain approval of a new manufacturer of the active drug substance, Clindamycin Phosphate USP.

CENTER FOR DRUG EVALUATION AND RESEARCH RECD JUL 28 2000 OGD

The

Altana has tested the proposed new material and used it to manufacture an exhibit batch. In-process and finished product testing was conducted using the previously submitted specifications and procedures.

A DMF Referral letter authorizing FDA review of the DMF has been included in this submission along with a copy of the executed batch record, all active raw material and drug product test results and stability data acquired to date.

Concurrent with the evaluation of the new source for the active drug substance Altana Inc. also evaluated a ——— for the bottles and a new adhesive for the drug product label. Information such as the specifications for the ——— physicochemical testing performed on the cap and information regarding the new adhesive have been included as part of this submission.

If you require additional information or clarification, please contact me at (631) 454-7677, extension 2091. FAX communications may be made to (631) 756-5114.

Sincerely,
Altana Inc.

Virginia Carman

Virginia Carman
Associate Director, Regulatory Affairs

VC/et

ANDA 65-067

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

MAY 8 2000

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 made to the telephone conversation dated April 12, 2000 and your correspondence dated May 5, 2000.

NAME OF DRUG: Clindamycin Phosphate Topical Suspension USP, 1%

DATE OF APPLICATION: March 7, 2000

DATE (RECEIVED) ACCEPTABLE FOR FILING: March 9, 2000

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:

Mark Anderson
Project Manager
(301) 827-5849

Sincerely yours,

/S/

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

ALTANA

Itana Inc. 60 Baylis Road, Melville, N.Y. 11747 516-454-7677 Fax: 516-756-5114 BYK GULDEN PHARMA GROUP

Federal Express

March 7, 2000

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

65-067

RE: ANDA ~~64-178~~ RE-SUBMISSION
Abbreviated New Drug Application
Clindamycin Phosphate Topical Suspension USP, 1%

was withdrawn. This application 65-067 represents a brand new submissio

/S/ 4/10/0

/S/

Dear Sir or Madam:

Reference is made to an Abbreviated New Drug Application originally filed April 18, 1996 by the E. Fougera & Co. division of Altana Inc.

Reference is also made to the Agency' Refusal to File (RTF) letter of May 13, 1996. The reason for the RTF letter was a lack of a complete *in vivo* bioequivalence study.

We also refer to a Bioequivalence IND filed 12/31/97 and the Agency's comments of April 21, 1999.

At this time Altana Inc., pursuant to the regulations contained in 21CFR 314.94 is re-submitting an Abbreviated New Drug Application for Clindamycin Phosphate Topical Suspension USP, 1% (base). This is a complete revision. No data found in the original 1996 application are pertinent to this submission.

The reference listed drug that is the basis for this submission is CLEOCIN T® (NDA 50-537), manufactured by THE UPJOHN CO. The proposed drug, Clindamycin Phosphate Topical Suspension USP, 1%, contains the same active ingredient in the same strength and dosage form, has the same indications and usage, and route of administration as the reference listed drug.

The exhibit batch (#A344) included in this application was fully packaged utilizing the 60 mL presentation for which approval is currently requested. The number of units filled and the disposition of any remaining bulk product are reconciled in the exhibit batch record.

Included in this ten (10) volume submission, along with Form FDA 356h, is the required Patent Status and Exclusivity Statements; Draft Labeling; Bioequivalence Study; Components and Composition; Facilities; Raw Material, In-Process, and Finished Product Controls; Manufacturing and Processing; Filling and Packaging; Container/Closure System; Analytical Methods; Stability; Environmental Impact Analysis; Certification Requirements of the Generic Drug Enforcement Act of 1992; Clinical Investigator Certification and Field Copy Certification.

Additionally in this correspondence we wish to address the issues outlined in your April 21, 1999 correspondence to the IND. (Copy enclosed.) The Chemistry issues are addressed in this correspondence. Bioequivalence issues are addressed in Section 6 of the application. The observations are addressed in a "**comment**/response" format.

1. **The product names are not indicated in several COA's provided by the manufacturers for the inactive ingredients.**

   In some cases the inactive ingredients are marketed under trade names. In these cases we have indicated the trade name of the inactive at the bottom of the specification. We have additionally included a copy of the USAN or International Cosmetic Ingredient Dictionary & Handbook page for each inactive substance with the Trade name indicated (underlined).

2. **A detailed description section (or flow chart) for the manufacturing process is needed for the actual ANDA.**

   The flow chart can be found in Volume 11.8, Section 11.2.2, Manufacturing Flow Chart, pg. 3327-3329.

3. **In the actual ANDA the section regarding in-process controls has to be expanded and clarified.**

   Section 12 In-Process Controls has been expanded to include manufacturing and analytical procedures and controls.

4. **Please identify some of the degradation products and related substances listed under "Others" for specifications.**

   The Specifications have been expanded to include identification of the Relative Retention Times for the more pronounced peaks.

5. [redacted]

   Analytical results and up to 24 month stability data are located in Volume 1.10, Section 16, Stability pgs. 3929 to 3933.

6. **We have concerns regarding the [redacted] (NMT [redacted]). Please explain.**

Based upon generated stability data the [redacted] specification has been reduced to [redacted]. Please see Stability specification found in Volume 1.10, pgs. 3924 - 3926 as well as individual stability sheets.

All regulatory correspondences related to this Abbreviated New Drug Application should be addressed to:

Virginia Carman
Associate Director,
Regulatory Affairs
60 Baylis Road
Melville, NY 11747
(631) 454-7677 ext. 2091
FAX (631) 756-5114

A certified copy of Volumes 1.1, 1.8, 1.9 and 1.10 of this application are being sent to the New York District Office under separate cover.

We trust that this submission will meet your approval. Please advise if you require any additional information.

Sincerely,

Virginia Carman

Virginia Carman
Associate Director,
Regulatory Affairs

VC/ps

Enclosures

Altana Inc.
60 Baylis Road
Melville, New York 11747
(631) 454-7677
(631) 756-5114 (fax)

facsimile transmittal

NEW CORRESP
NC

To:	Lt. Greg Davis	**Fax:**	(301) 594-1174
From:	Virginia Carman Associate Director, Regulatory Affairs	**Date:**	May 5, 2000
Re:	ANDA 64-176 Clindamycin Phosphate Suspension USP, 1%	**Pages:**	70
CC:			

■ Urgent ■ For Review ☐ Please Comment ■ Please Reply ■ Please Recycle

Comments:

Dear Greg,

As per conversation, please find included with this cover sheet, our complete printed response to the Agency's request of April 12, 2000.

The full package including data diskette is being hand carried to the OGD today.

If you have any questions, please call me at (631) 454-7677, extenstion 2091.

Sincerely,

Virginia

Virginia

APPEARS THIS WAY
ON ORIGINAL