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Approval Package for:

APPLICATION NUMBER:

ANDA 90-785

Name: Clindamycin Phosphate Foam, 1%

Sponsor: Cobrek Pharmaceuticals, Inc.

Approval Date: March 31, 2010

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APPLICATION NUMBER:

ANDA 90-785

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APPLICATION NUMBER:

ANDA 90-785

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 090785

Cobrek Pharmaceuticals, Inc.
Attention: James L. Kadow
Vice President, Regulatory Affairs
3315 Algonquin Road, Suite 310
Rolling Meadows, IL 60008

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated August 26, 2008, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Clindamycin Phosphate Foam, 1%.

Reference is also made to your amendments dated April 2, and June 15, 2009, and February 19, March 15 and March 17, 2010.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Clindamycin Phosphate Foam, 1%, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Evoclin Foam, 1%, of Stiefel Laboratories, Inc. (Stiefel)

The reference listed drug (RLD) upon which your ANDA is based, Stiefel's Evoclin Foam, 1%, is subject to periods of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent Nos. 7,141,237 (the '237 patent) and 7,374,747 (the '747 patent) are scheduled to expire on January 23, 2024, and August 9, 2026, respectively.

These two patents were listed after the submission of your ANDA. With respect to both patents, you amended your ANDA to contain paragraph IV certifications under section 505(j)(2)(A)(vii)(IV) of the Act stating that each patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Clindamycin Phosphate Foam, 1%, under this ANDA. You have notified the agency that Cobrek Pharmaceuticals, Inc. (Cobrek) complied with the requirements of section 505(j)(2)(B) of the Act.[1]

We note that the '237 and '747 patents were filed with the Secretary not later than 60 days after the enactment of the QI Supplemental Funding Act of 2008 (QI Act). The QI Act provides that with respect to patent information filed with the Secretary within the 60-day period after enactment –

> each applicant that, not later than [February 5, 2009], amends an application that is, on or before [October 8, 2008], a substantially complete application (as defined in paragraph (5)(B)(iv) of section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j))) to contain [a paragraph IV certification] with respect to that patent shall be deemed to be a first applicant (as defined in paragraph (5)(B)(iv) of such section 505(j).

Therefore, with this approval, Cobrek is eligible for 180 days of generic drug exclusivity for Clindamycin Phosphate Foam, 1%.[2] This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the Act, will begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA informing the agency of the date the exclusivity begins to run.

---

[1] For the reasons explained in the agency's March 17, 2009 response to a citizen petition submitted by Stiefel regarding your ANDA, regardless of whether litigation for infringement was initiated by Stiefel within 45 days of receipt of notification of the paragraph IV certification, your ANDA is not subject to a 30-month stay of approval. See Docket No. FDA-2009-P-0120.

[2] See part (b) of section 4 of the QI Supplemental Funding Act of 2008 (QI Act). These Transitional Rules provide that, with respect to patent information filed with the Secretary within the 60-day period after enactment of the QI Act --
"each applicant that, not later than 120 days after the date of the enactment of this Act, amends an application that is, on or before the enactment of this Act, a substantially complete application … to contain a [paragraph IV certification] with respect to that patent shall be deemed to be a first applicant (as defined in paragraph (5)(B)(iv) of such section 505(j)."

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

We note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

Postmarketing reporting requirements for this ANDA 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.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

Within 14 days of the date of this letter, submit updated content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling. Upon receipt and verification, we will transmit that

version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission as ***"Miscellaneous Correspondence – SPL for Approved ANDA 090785".***

Sincerely yours,

{See appended electronic signature page}

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-90785	ORIG-1	COBREK PHARMACEUTICALS INC	CLINDAMYCIN PHOSPHATE

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

/s/

ROBERT L WEST
03/31/2010
Deputy Director, for Gary Buehler

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-785

LABELING

9F0-000 ELS607-1 **ELS 607**

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Description: Clindamycin Phosphate Foam, 1% contains clindamycin phosphate, USP, at a concentration equivalent to 10 mg clindamycin per gram in a thermolabile hydroethanolic foam vehicle consisting of cetyl alcohol, ethanol (58%), polysorbate 60, propylene glycol, purified water, and stearyl alcohol pressurized with a hydrocarbon (propane/butane) propellant.

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ALLEGAN, MI 49010 Rev. 05/09

NDC 45802-660-32

Clindamycin Phosphate Foam, 1%

50 g

℞ Only

FOR TOPICAL USE ONLY. NOT FOR OPHTHALMIC, ORAL, OR INTRAVAGINAL USE.

Usual Dosage: Use only as prescribed by your physician. See package insert for full prescribing information.

WARNING: FLAMMABLE. AVOID FIRE, FLAME, OR SMOKING DURING AND IMMEDIATELY FOLLOWING APPLICATION.

This package is not child resistant. Keep out of reach of children. Avoid contact with eyes.

Contents under pressure. Do not puncture or incinerate container. Do not expose to heat or store at temperatures above 120°F (49°C).

Store at 20 – 25°C (68 – 77°F) [see USP Controlled Room Temperature].

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E-mail: (b) (6) @perrigo.com

DESIGNER

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50 g

Clindamycin Phosphate Foam, 1%

NDC 45802-660-32

EFA 1339

000-000 EFA1339-#

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NDC 45802-660-32

Clindamycin Phosphate Foam, 1%

NDC 45802-660-32

Clindamycin Phosphate Foam, 1%

NDC 45802-660-32

Clindamycin Phosphate Foam, 1%

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DESIGNER

ART INFORMATION

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ARTIST (b) (6)

DATE: 5-27-09 L.S. 4T5.CON

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100 g

Clindamycin Phosphate Foam, 1%

NDC 45802-660-33

EFA 1340

000-000 EFA1340-#

PERRIGO

NDC 45802-660-33

Clindamycin Phosphate Foam, 1%

FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC, ORAL, OR INTRAVAGINAL USE.

Description: Clindamycin Phosphate Foam, 1%, contains clindamycin phosphate, USP at a concentration equivalent to 10 mg clindamycin per gram in a thermolabile hydroethanolic foam vehicle consisting of cetyl alcohol, ethanol (58%), polysorbate 60, propylene glycol, purified water, and stearyl alcohol pressurized with a hydrocarbon (propane/butane) propellant.

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Rev. 05/09

100 g Rx Only

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Esko-Graphics BarX
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Select correct rotation
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FRONT

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FPO 1000

CLINDAMYCIN PHOSPHATE FOAM, 1%

℞ Only

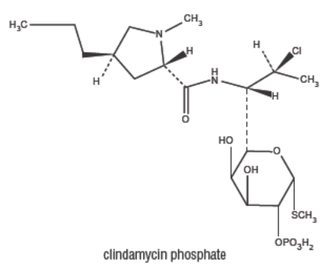
FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC, ORAL, OR INTRAVAGINAL USE.

DESCRIPTION

Clindamycin Phosphate Foam, 1% contains clindamycin phosphate, USP, a topical antibiotic for topical dermatologic use.

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 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), with the empirical formula $C_{18}H_{34}ClN_2O_8PS$, a molecular weight of 504.97. The following is the chemical structure:



clindamycin phosphate

Clindamycin Phosphate Foam, 1% contains clindamycin phosphate, USP, at a concentration equivalent to 10 mg clindamycin per gram in a thermolabile hydroethanolic foam vehicle consisting of cetyl alcohol, ethanol (58%), polysorbate 60, propylene glycol, purified water, and stearyl alcohol pressurized with a hydrocarbon (propane/butane) propellant.

CLINICAL PHARMACOLOGY

Pharmacokinetics - In an open label, parallel group study in 24 patients with acne vulgaris, 12 patients (3 male and 9 female) applied 4 grams of clindamycin phosphate foam, 1%, once-daily for five days, and 12 patients (7 male and 5 female) applied 4 grams of clindamycin phosphate topical gel, 1%, once daily for five days. On Day 5, the mean C_{max} and AUC(0-12) were 23% and 9% lower, respectively, for clindamycin phosphate foam than for clindamycin phosphate topical gel.

Following multiple applications of clindamycin phosphate foam, 1% less than 0.024% of the total dose was excreted unchanged in the urine over 12 hours on Day 5.

Microbiology - The clindamycin component has been shown to have *in vitro* activity against *Propionibacterium acnes*, an organism which is associated with acne vulgaris; however, the clinical significance of this activity against *P. acnes* was not examined in clinical trials with this product. Cross-resistance between clindamycin and erythromycin has been demonstrated.

CLINICAL STUDIES

In one multicenter, randomized, double-blind, vehicle-controlled clinical trial patients with mild to moderate acne vulgaris used clindamycin phosphate foam, 1% or the vehicle foam once daily for twelve weeks. Treatment response, defined as the proportion of patients clear or almost clear, based on the Investigator Static Global Assessment (ISGA), and the mean percent reductions in lesion counts at the end of treatment in this study are shown in the following table:

Efficacy Parameters	Clindamycin Phosphate Foam, 1% n=386	Vehicle Foam n=127
Treatment response (ISGA)	31%	18%*
Percent reduction in lesion counts		
Inflammatory Lesions	49%	35%*
Noninflammatory Lesions	38%	27%*
Total Lesions	43%	31%*

* P< 0.05

INDICATIONS AND USAGE

Clindamycin Phosphate Foam, 1% is indicated for topical application 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 Foam, 1% 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. Antiperistaltic agents, such as opiates and diphenoxylate with atropine, may prolong and/or worsen the condition.

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

Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

Avoid contact of clindamycin phosphate foam with eyes. If contact occurs, rinse eyes thoroughly with water.

PRECAUTIONS

General - Clindamycin Phosphate Foam, 1% 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.

Carinogenesis, Mutagenesis, Impairment of Fertility - The carcinogenicity of a 1% clindamycin phosphate gel similar to clindamycin phosphate foam was evaluated by daily application to mice for two years. The daily doses used in this study were approximately 3 to 15 times higher than the human dose of clindamycin phosphate from 5 milliliters of clindamycin phosphate foam, assuming complete absorption and based on a body surface area comparison. No significant increase in tumors was noted in the treated animals.

A 1% clindamycin phosphate gel similar to clinamycin phosphate foam caused a statistically significant shortening of the median time to tumor onset in a study in hairless mice in which tumors were induced by exposure to simulated sunlight.

Genotoxicity tests performed included a rat micronucleus test and an Ames Salmonella reversion test. Both tests were negative.

Reproduction studies in rats using oral doses of clindamycin hydrochloride and clindamycin palmitate hydrochloride have revealed no evidence of impaired fertility.

Pregnancy: Teratogenic effects: Pregnancy Category B - Reproduction studies have been performed in rats and mice using subcutaneous and oral doses of clindamycin phosphate, clindamycin hydrochloride and clindamycin palmitate hydrochloride. These studies revealed no evidence of fetal harm. The highest dose used in the rat and mouse teratogenicity studies was equivalent to a clindamycin phosphate dose of 432 mg/kg. For a rat, this dose is 84 fold higher, and for a mouse 42 fold higher, than the anticipated human dose of clindamycin phosphate from clindamycin phosphate based on a mg/m² comparison. 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.

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Nursing Mothers - It is not known whether clinamycin is excreted in human milk following use of Clindamycin Phosphate Foam, 1%. 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 of clindamycin phosphate foam in children under the age of 12 have not been studied.

Geriatric Use - The clinical study with clindamycin phosphate foam did not include sufficient numbers of patients aged 65 and over to determine if they respond differently than younger patients.

ADVERSE REACTIONS

The incidence of adverse events occurring in ≥ 1% of the patients in clinical studies comparing clindamycin phosphate foam and its vehicle is presented below:

Selected Adverse Events Occurring in ≥ 1% of Subjects

Adverse Event	Number (%) of Subjects	
	Clindamycin Phosphate Foam, 1% N = 439	Vehicle Foam N = 154
Headache	12 (3%)	1 (1%)
Application site burning	27 (6%)	14 (9%)
Application site pruritus	5 (1%)	5 (3%)
Application site dryness	4 (1%)	5 (3%)
Application site reaction, not otherwise specified	3 (1%)	4 (3%)

In a contact sensitization study, none of the 203 subjects developed evidence of allergic contact sensitization to clindamycin phosphate foam, 1%.

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 Foam, 1% may be absorbed in sufficient amounts to produce systemic effects (see WARNINGS).

DOSAGE AND ADMINISTRATION

Apply Clindamycin Phosphate Foam, 1% once daily to affected areas after the skin is washed with mild soap and allowed to fully dry. Use enough to cover the entire affected area.

To Use Clindamycin Phosphate Foam, 1%:

1. Do not dispense Clindamycin Phosphate Foam, 1% directly onto your hands or face, because the foam will begin to melt on contact with warm skin.
2. Remove the clear cap.
3. Hold the can at an upright angle and then press firmly to dispense. Dispense an amount directly into the cap or onto a cool surface. Dispense an amount of Clindamycin Phosphate Foam, 1% that will cover the affected area(s). If the can seems warm or the foam seems runny, run the can under cold water.
4. Pick up small amounts of Clindamycin Phosphate Foam, 1% with your fingertips and gently massage into the affected areas until the foam disappears.

Throw away any of the unused medicine that you dispensed out of the can.

Avoid contact of Clindamycin Phosphate Foam, 1% with eyes. If contact occurs, rinse eyes thoroughly with water.

HOW SUPPLIED

Clindamycin Phosphate Foam, 1%, containing clindamycin phosphate equivalent to 10 mg clindamycin per gram, is available as follows:
100 gram can (NDC 45802-**660**-33)
50 gram can (NDC 45802-**660**-32)

STORAGE AND HANDLING

Store at 20 – 25°C (68 – 77°F) [see USP Controlled Room Temperature].

FLAMMABLE. AVOID FIRE, FLAME OR SMOKING DURING AND IMMEDIATELY FOLLOWING APPLICATION.

Contents under pressure. Do not puncture or incinerate. Do not expose to heat or store at temperature above 120°F (49°C).

Keep out of reach of children.

MADE IN ISRAEL

MANUFACTURED BY
PERRIGO
YERUHAM 80500, ISRAEL

DISTRIBUTED BY
PERRIGO®
ALLEGAN, MI 49010

Rev. 05/09

FPO

: 4T500 RC J1

FPO 1000

PLEASE RETURN ART TO:
PERRIGO®
ART DEPARTMENT
502 E. BELTLINE PLANT #6
ALLEGAN, MI 49010

(b) (6)

E-mail: (b) (6) @perrigo.com

GCPM ADMINISTRATOR (b) (6) PHONE:

RA ADMINISTRATOR

DATE 05-27-09

ART INFORMATION

CO.# RC PROD.# 475 00

ARTIST (b) (6)

PH. # (269) 686- 2736

DATE: 6-10-09 L.C.L. 4T5.CON

APPROVALS

GTP AS IS:

GTP WITH CHANGES:

NOT APPROVED:

ENGINEERING

FOIL VENDOR

RA AUDITOR

MARKETING

COPY AND DESIGN AREAS

Black

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-785

LABELING REVIEWS

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

ANDA Number:	90-785
Date of Submission:	August 26, 2008
Applicant's Name:	Clindamycin Phosphate Foam 1%
Established Name:	Cobrek Pharmaceuticals, Inc.
Proprietary Name:	None

LABELING DEFICIENCIES:

1. **CONTAINER:** (50 gram and 100 gram can)
   a. Please revise "Dosage…" to "Usual Dosage…"
   b. Add the statement "This package is not child resistant."
   c. Please enhance the prominence of the net quantity statement

2. **CONTAINER CARTON:** (50 gram and 100 gram can)
   See container comments 1.a. and 1.b.

3. **PROFESSIONAL INSERT:**
   In the DOSAGE AND ADMINISTRATION section – To Use Clindamycin Phosphate Foam, 1%, Number 2: The instructions direct the patient to "Align the black mark with the nozzle of the actuator." Please confirm whether your container includes a black mark and whether that mark can be aligned properly with the actuator.

Revise your labeling, as instructed above, and submit final printed labeling electronically. In addition, please review the guidance for industry titled "Providing Regulatory Submissions in Electronic Format-Content of Labeling". Please provide the labeling in the Structured Product Labeling (SPL) format.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -
http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

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.

NOTE TO THE CHEMIST:

- I am reviewing the labeling for Clindamycin Phosphate FOM 1% and I have a question. The container states that the product is CFC free. Is the propellant used in this product CFC free? [Chemist Response: Yes]

From: Farahani, Mahnaz
Sent: Thursday, April 23, 2009 2:32 PM
To: Stewart, Kendra
Subject: RE: Labeling question for ANDA 90785

Yes,

From: Stewart, Kendra
Sent: Thursday, April 23, 2009 11:24 AM
To: Farahani, Mahnaz
Cc: Stewart, Kendra
Subject: Labeling question for ANDA 90785

Good Morning,

I am reviewing the labeling for Clindamycin Phosphate FOM 1% and I have a question. The container states that the product is CFC free. Is the propellant used in this product CFC free?

Thanks,
Kendra Stewart

FOR THE RECORD:

1. MODEL LABELING:
   The reference listed drug for this product is Evoclin NDA 50-801 by Connetics. The model labeling used for this review is 50-851/S-006 approved July 11, 2006.

2. MEDWATCH: (Checked on 4/21/09)

3. PATENT AND EXCLUSIVITY: (Checked on 4/21/09)

PATENT DATA – NDA 50-801					
Patent No	**Expiration**	**Use Code**	**Use**	**Patent Certification**	**Labeling Impact**
7141237	Jan 23, 2024			IV	None
7374747	Aug 9, 2026	U-921	TREATMENT OF ACNE VULGARIS	IV	None

EXCLUSIVITY DATA – NDA 50-801			
Code	**Reference**	**Expiration**	**Labeling Impact**
There is no unexpired exclusivity for this product.			

4. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM: 2.3.P.3
   Perrigo Israel Pharmaceuticals Ltd.
   Industrial Zone
   Yeruham, 80500
   Israel

5. USP: (Checked on 4/21/09)
   Not USP

6. INGREDIENTS: 2.3.P.1
   - The listing of inactive ingredients in the DESCRIPTION section of the package insert

appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing in section 2.3.p.1

- DESCRIPTION section has been verified from Chemist's review

From Clinical Bio Review:
The test product appears to be qualitatively and quantitatively the same as the RLD except for a presence/absence of a (b) (4)

From chemistry Review:
The drug substance and the excipients are compatible with each other as has been shown from stability data. Section 3.2.P.2.1.3. All inactive ingredients of formulation are present in the RLD formulation with the exception of potassium hydroxide that is included in the RLD formulation only. Therefore the excipients are compatible with the API. There was no change in physical appearance parameters or in the assay and impurity profile of the API for Cobrek Pharmaceuticals Inc.'s formulation during stability studies.

Ingredient	**Cobrek Pharmaceuticals Inc.'s Formulation (% w/w)**	(b) (4)
Propylene Glycol, USP	(b) (4)	
Cetyl Alcohol, NF		
Stearyl Alcohol, NF		
Polysorbate 60, NF		
Dehydrated Alcohol, USP	58.00	
Purified Water, USP	QS to 100	

7. PACKAGING CONFIGURATIONS/PRODUCT LINE:
   RLD: 100 gram can and 50 gram can
   ANDA: 100 gram can and 50 gram can

8. DISPENSING/STORAGE TEMPERATURE STATEMENT COMPARISON – 2.3.P.8
   RLD: Store at controlled room temperature 68°–77°F (20°–25°C). Contents under pressure. Do not puncture or incinerate. Do not expose to heat or store at temperature above 120°F (49°C).
   ANDA: *Insert:* "Store at 20 – 25°C (68 – 77°F) [see USP Controlled Room Temperature]." Contents under pressure. Do not puncture or incinerate. Do not expose to heat or store at temperature above 120°F (49°C). Keep out of reach of children.
   Container: Store at 20 – 25ºC (68 – 77ºF) [see USP Controlled Room Temperature. Contents under pressure. Do not puncture or incinerate container. Do not expose to heat or store at temperatures above 120ºF (49ºC).

9. CONTAINER CLOSURE: 3.2.P.7
   - Container: Cobrek Pharmaceuticals, Inc. intends to package Clindamycin Phosphate Foam, 1% in 50g and 100g aluminum cans
   - Caps: Clear cover cap
   - Accelerated stability data and room temperature stability data: at 25±2^{o}C/60±5%RH

for a period of three (3) months and at 40±2^{o}C/75±5%RH for a period of Three (3) months

---

Date of Review: 4/21/09 Date of Submission: 8/26/09

Primary Reviewer: Kendra Stewart

Team Leader: Lillie Golson

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

/s/

Kendra Stewart
5/6/2009 11:54:42 AM
LABELING REVIEWER

Lillie Golson
5/6/2009 01:44:53 PM
LABELING REVIEWER

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

ANDA Number: 90-785

Date of Submission: June 15, 2009

Applicant's Name: Clindamycin Phosphate Foam, 1%

Established Name: Cobrek Pharmaceuticals, Inc.

Proprietary Name: None

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):
Do you have Final Printed Labels and Labeling – Yes

1. **CONTAINER:** (50 gram and 100 gram can)
   Satisfactory in FPL as of the June 15, 2009 submission

2. **CONTAINER CARTON:** (50 gram and 100 gram can)
   Satisfactory in FPL as of the June 15, 2009 submission

3. **PROFESSIONAL INSERT:**
   Satisfactory in FPL and SPL as of the June 15, 2009 submission

Revisions: Yes
CONTAINER: (50 gram and 100 gram can)
Please bold the statement "This package is not child resistant." and move to the primary panel.

CONTAINER CARTON: (50 gram and 100 gram can)
See CONTAINER comments.

BASIS OF APPROVAL:

Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Clindamycin Phosphate Foam 1%
NDA Number: 50-801
NDA Drug Name: Evoclin
NDA Firm: Connetics
Date of Approval of NDA Insert and supplement #: 50-851/S-006 approved July 11, 2006
Has this been verified by the MIS system for the NDA? Yes
Was this approval based upon an OGD labeling guidance? No

NOTE TO THE CHEMIST:

- I am reviewing the labeling for Clindamycin Phosphate FOM 1% and I have a question. The container states that the product is CFC free. Is the propellant used in this product CFC free? [Chemist Response: Yes]

From: Farahani, Mahnaz
Sent: Thursday, April 23, 2009 2:32 PM
To: Stewart, Kendra
Subject: RE: Labeling question for ANDA 90785

Yes,

From: Stewart, Kendra
Sent: Thursday, April 23, 2009 11:24 AM
To: Farahani, Mahnaz
Cc: Stewart, Kendra
Subject: Labeling question for ANDA 90785

Good Morning,

I am reviewing the labeling for Clindamycin Phosphate FOM 1% and I have a question. The container states that the product is CFC free. Is the propellant used in this product CFC free?

Thanks,
Kendra Stewart

NOTE TO THE FIRM REGARDING THE ACTUATOR: [Acceptable]

From: Ellen Rust [mailto (b) (6)
Sent: Wednesday, August 05, 2009 11:10 AM
To: Stewart, Kendra
Cc: 'Jim Kadow'
Subject: ANDA 90-785

Dear Kendra,

Yesterday you called to request clarification concerning the Dosage and Administration section in the Clindamycin Foam, ANDA 90-785, professional insert.
On May 6, 2009, Cobrek received a labeling deficiency letter. One of the FDA comments read as follows:

> ***In the DOSAGE AND ADMINISTRATION section – To use Clindamycin Phosphate Foam, 1%, Number 2: The instructions direct the patient to "Align the black mark with the nozzle of the actuator." Please confirm whether your container includes a black mark and whether that mark can be aligned properly with the actuator.***

Our response, sent on June 15, 2009, was to state that our container will not include a black mark, therefore the instructions concerning the black mark in the Dosage and Administration section was deleted.

My understanding of your question yesterday is that you want to confirm that no additional instructions are required in order to properly dispense the product from the can. I contacted Perrigo, the manufacturing facility, and was informed that no special instructions are required and there is no lock on the actuator.

Please let me know if I understood and answered you question completely, you can reach either Jim Kadow or me at 847-255-0303. Would you please let us know if this completes your division's review of the labeling?

Best regards,
Ellen Rust

FOR THE RECORD:

1. MODEL LABELING:
   The reference listed drug for this product is Evoclin NDA 50-801 by Connetics. The model labeling used for this review is 50-851/S-006 approved July 11, 2006.

2. MEDWATCH: (Checked on 7/30/09) - None

3. PATENT AND EXCLUSIVITY: (Checked on 7/30/09)

PATENT DATA – NDA 50-801					
Patent No	**Expiration**	**Use Code**	**Use**	**Patent Certification**	**Labeling Impact**
7141237	Jan 23, 2024			IV	None
7374747	Aug 9, 2026	U-921	TREATMENT OF ACNE VULGARIS	IV	None

EXCLUSIVITY DATA – NDA 50-801			
Code	**Reference**	**Expiration**	**Labeling Impact**
There is no unexpired exclusivity for this product.			

4. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM: 2.3.P.3
   Perrigo Israel Pharmaceuticals Ltd.
   Industrial Zone
   Yeruham, 80500
   Israel

5. USP: (Checked on 4/21/09)
   Not USP

6. INGREDIENTS: 2.3.P.1
   - The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing in section 2.3.p.1
   - DESCRIPTION section has been verified from Chemist's review

From Clinical Bio Review:
The test product appears to be qualitatively and quantitatively the same as the RLD except for a presence/absence of a (b) (4).

From chemistry Review:
The drug substance and the excipients are compatible with each other as has been shown from stability data. Section 3.2.P.2.1.3. All inactive ingredients of formulation are present in the RLD formulation with the exception of potassium hydroxide that is included in the RLD formulation only. Therefore the excipients are compatible with the API. There was no change in physical appearance parameters or in the assay and impurity profile of the API for Cobrek Pharmaceuticals Inc.'s formulation during stability studies.

Ingredient	**Cobrek Pharmaceuticals Inc.'s Formulation (% w/w)**	(b) (4)
Propylene Glycol, USP	(b) (4)	
Cetyl Alcohol, NF		
Stearyl Alcohol, NF		
Polysorbate 60, NF		
Dehydrated Alcohol, USP	58.00	

Purified Water, USP	QS to 100		(b) (4)

7. PACKAGING CONFIGURATIONS/PRODUCT LINE:
   RLD: 100 gram can and 50 gram can
   ANDA: 100 gram can and 50 gram can

8. DISPENSING/STORAGE TEMPERATURE STATEMENT COMPARISON – 2.3.P.8
   RLD: Store at controlled room temperature 68°–77°F (20°–25°C). Contents under pressure. Do not puncture or incinerate. Do not expose to heat or store at temperature above 120°F (49°C).
   ANDA: *Insert:* "Store at 20 – 25°C (68 – 77°F) [see USP Controlled Room Temperature]." Contents under pressure. Do not puncture or incinerate. Do not expose to heat or store at temperature above 120°F (49°C). Keep out of reach of children.
   Container: Store at 20 – 25ºC (68 – 77ºF) [see USP Controlled Room Temperature. Contents under pressure. Do not puncture or incinerate container. Do not expose to heat or store at temperatures above 120ºF (49ºC).

9. CONTAINER CLOSURE: 3.2.P.7
   - Container: Cobrek Pharmaceuticals, Inc. intends to package Clindamycin Phosphate Foam, 1% in 50g and 100g aluminum cans
   - Caps: Clear cover cap
   - Accelerated stability data and room temperature stability data: at 25±2^{o}C/60±5%RH for a period of three (3) months and at 40±2^{o}C/75±5%RH for a period of Three (3) months

---

Date of Review: 7/30/09 Date of Submission: 6/15/09

Primary Reviewer: Kendra Stewart

Team Leader: Lillie Golson

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-90785	ORIG-1	COBREK PHARMACEUTICALS INC	CLINDAMYCIN PHOSPHATE

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

/s/

KENDRA S STEWART
09/23/2009

LILLIE D GOLSON
09/24/2009

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-785

CHEMISTRY REVIEWS

ANDA 90-785

Clindamycin Phosphate Foam, 1%

First Generic

Cobrek Pharmaceutials, Inc.

Mahnaz Farahani, Ph.D.
Division of Chemistry I
Office of Generic Drugs

Chemistry Review # 1

Table of Contents

Chemistry Review Data Sheet

1. ANDA #90-785

2. REVIEW #: 1

3. REVIEW DATE: January 16, 2009

4. REVIEWER: Mahnaz Farahani, Ph.D.

5. PREVIOUS DOCUMENTS: None

Previous Documents	Document Date

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original application	August 26, 2008
Acceptable for filing	August 29, 2008

7. NAME & ADDRESS OF APPLICANT:

Name: Cobrek Pharmaceuticals, Inc.

Address: (a subsidiary of Pentech Pharmaceutical, Inc)
3315 Algonquin Road, Suite 310
Rolling Meadows, IL 60008

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Evoclin® (Clindamycin Phosphate) Foam, 1%
b) Non-Proprietary Name (USAN): Clindamycin Phosphate Foam, 1%

9. LEGAL BASIS FOR SUBMISSION:
Reference listed drug: Evoclin

Holder of Approved Application: Stiefel Labs Inc.
Application Number: (NDA) 050801

Strength: 1%

Patent Certification and exclusivity:
Clindamycin Phosphate, USP 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 and is the same antibiotic as is contained in the CLEOCIN PHOSPHATE Injection (NDA 050441), which was approved in 1972 (prior to November 20, 1997) and is therefore exempt from the patent listing, patent certification and exclusivity provisions in section 505(b).

10. PHARMACOL. CATEGORY: For topical application in the treatment of acne vulgaris

11. DOSAGE FORM: Foam

12. STRENGTH/POTENCY: 1%

13. ROUTE OF ADMINISTRATION: Topical

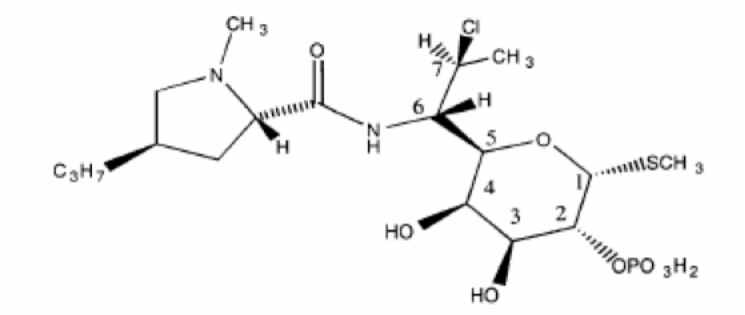
14. Rx/OTC DISPENSED: __x_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

___X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



Chemical Names:
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)

Molecular Formula: $C_{18}H_{34}C1N_2O_8PS$

Molecular Weight: 504.97 g/mole

CAS Registry Number: CAS-24729-96-2

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	(b) (4)	3	Adequate	November 2, 2007	Reviewed by S. Zuk
	III			4			

1.4 REFERENCES

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF

3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	**RECOMMENDATION**	**DATE**	**REVIEWER**
Microbiology	N/A		
EES	Pending		
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Pending		
EA	Categorical exclusion	July 8, 2008	
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. __X__ Yes ____ No If no, explain reason(s) below:

The Chemistry Review for ANDA 90-785

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability
This application is not approvable at this time.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable
N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug substance: Clindamycin Phosphate USP
The drug substance is a white or almost white crystalline powder.

Solubility: Freely soluble in water.

Solubility from USP: Freely soluble in water; slightly soluble in dehydrated alcohol; very slightly soluble in acetone; practically insoluble in chloroform, in benzene, and in ether

Polymorphism: Clindamycin phosphate is completely soluble in the formulation and therefore polymorphism is not applicable.

pKa:
1.83 ± 0.10 - Most acidic (temp: 25°C)
8.74 ± 0.60 - Most basic (temp: 25°C)

Chirality: Clindamycin phosphate contains 9 stereogenic centers and the absolute configuration is known.

Drug Product:
Clindamycin Phosphate Foam, 1% contains Clindamycin phosphate, USP, as active ingredient. The excipients are Propylene Glycol, USP, Cetyl Alcohol, NF, Stearyl Alcohol, NF, Polysorbate 60, NF, Dehydrated Alcohol, USP and Purified Water, USP. It is a topical antibiotic for topical dermatologic use. The drug product is applied to the skin as a topical solution and packaged into 50 g and 100 g aluminum cans.

B. Description of how the drug product is intended to be used

The drug product is a foam for treatment of acne vulgaris.

C. Basis for Approvability or Not-Approval Recommendation

The deficiencies are related to drug substance and drug product.
The ICH does not apply for this product because the drug substance is a semi-synthetic fermentation product.

Following this page, 27 pages withheld in full - (b)(4)

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 90-785 APPLICANT: Cobrek Pharmaceuticals Inc.

DRUG PRODUCT: Clindamycin Phosphate Foam, 1%

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Please provide [redacted] (b) (4)
2. [redacted] (b) (4)
3. [redacted] (b) (4)
4. [redacted] (b) (4) based on actual observed data. Please provide revised [redacted] (b) (4)
5. Please clarify if th [redacted] (b) (4) drug product.
6. Please explain when [redacted] (b) (4) (b) (4)
7. Please confirm that the [redacted] (b) (4)
8. Please provide [redacted] (b) (4)

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following deficiency s in your response:

1. Please provide all available drug product CRT stability data.

2. The bioequivalence and labeling information you have provided is pending review. After the review is completed, any deficiencies found will be communicated to you separately.

3. All facilities referenced in your ANDA should be in compliance with cGMPs at the time of approval.

Sincerely yours,

<See appended electronic signature page>

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 90785 Original
ANDA 90785 DUP
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-645/MFarahani/Review Chemist /1/12/09
HFD-627/J.Fan/Team Leader/
HFD-617/R. Adigun/Project Manager/

F/T by

V:\Division I\Team 3\FIRMAM\Cobrek\90785.Rev01.doc

TYPE OF LETTER: NOT APPROVABLE – MINOR DEFICIENCIES

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

/s/

Mahnaz Farahani
3/19/2009 02:43:28 PM
CHEMIST

Rosalyn Adigun
3/20/2009 12:37:46 PM
CSO

James Fan
3/20/2009 12:56:41 PM
CHEMIST

ANDA 90-785

Clindamycin Phosphate Foam, 1%

First Generic

Cobrek Pharmaceutials, Inc.

Mahnaz Farahani, Ph.D.
Division of Chemistry I
Office of Generic Drugs

Chemistry Review # 2

Table of Contents

Chemistry Review Data Sheet

1. ANDA #90-785

2. REVIEW #: 2

3. REVIEW DATE: March 19, 2010

4. REVIEWER: Mahnaz Farahani, Ph.D.

5. PREVIOUS DOCUMENTS: None

Previous Documents	Document Date
Original application	August 26, 2008
Acceptable for filing	August 29, 2008

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Minor Amendment	April 2, 2009
Telephone amendment	February 19, 2010
Telephone amendment	March 17, 2010

7. NAME & ADDRESS OF APPLICANT:

Name: Cobrek Pharmaceuticals, Inc.

Address: (a subsidiary of Pentech Pharmaceutical, Inc)
3315 Algonquin Road, Suite 310
Rolling Meadows, IL 60008

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Evoclin® (Clindamycin Phosphate) Foam, 1%
b) Non-Proprietary Name (USAN): Clindamycin Phosphate Foam, 1%

9. LEGAL BASIS FOR SUBMISSION:
Reference listed drug: Evoclin
Holder of Approved Application: Stiefel Labs Inc.
Application Number: (NDA) 050801

Strength: 1%

Patent Certification and exclusivity:
Clindamycin Phosphate, USP 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 and is the same antibiotic as is contained in the CLEOCIN PHOSPHATE Injection (NDA 050441), which was approved in 1972 (prior to November 20, 1997) and is therefore exempt from the patent listing, patent certification and exclusivity provisions in section 505(b).

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11. DOSAGE FORM: Foam

12. STRENGTH/POTENCY: 1%

13. ROUTE OF ADMINISTRATION: Topical

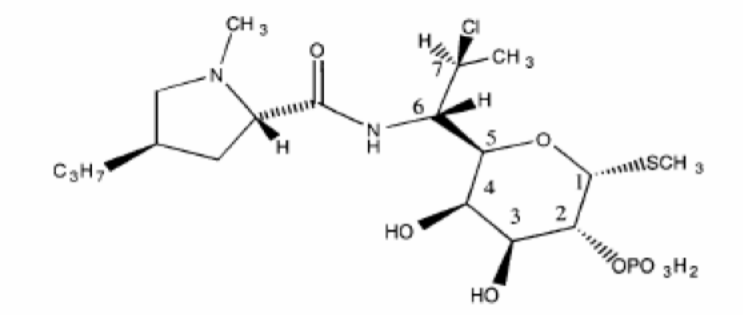
14. Rx/OTC DISPENSED: __x_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

___X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



Chemical Names:
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)

Molecular Formula: $C_{18}H_{34}C1N_2O_8PS$

Molecular Weight: 504.97 g/mole

CAS Registry Number: CAS-24729-96-2

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	(b) (4)	3	Adequate	October 7, 2009	Reviewed M. Farahani
	III			4			

1.4 REFERENCES

[1] Action codes for DMF Table:
1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	**RECOMMENDATION**	**DATE**	**REVIEWER**
Microbiology	N/A		
EES	Pending		
Methods Validation	N/A		
Labeling	Acceptable	9/23/09	KENDRA STEWART
Bioequivalence	Acceptable	8/27/09	J L Osterhout
EA	Categorical exclusion	July 8, 2008	
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ____ Yes __x__ No If no, explain reason(s) below: Minor Amendment

The Chemistry Review for ANDA 90-785

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability
ANDA is approvable

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable
N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Drug substance: Clindamycin Phosphate USP

The drug substance is a white or almost white crystalline powder.

Solubility: Freely soluble in water.

Solubility from USP: Freely soluble in water; slightly soluble in dehydrated alcohol; very slightly soluble in acetone; practically insoluble in chloroform, in benzene, and in ether

Polymorphism: Clindamycin phosphate is completely soluble in the formulation and therefore polymorphism is not applicable.

pKa:
1.83 ± 0.10 - Most acidic (temp: 25°C)
8.74 ± 0.60 - Most basic (temp: 25°C)

Chirality: Clindamycin phosphate contains 9 stereogenic centers and the absolute configuration is known.

Drug Product:
Clindamycin Phosphate Foam, 1% contains Clindamycin phosphate, USP, as active ingredient. The excipients are Propylene Glycol, USP, Cetyl Alcohol, NF, Stearyl Alcohol, NF, Polysorbate 60, NF, Dehydrated Alcohol, USP and Purified Water, USP. It is a topical antibiotic for topical dermatologic use. The drug product is applied to the skin as a topical solution and packaged into 50 g and 100 g aluminum cans.

B. Description of how the drug product is intended to be used

The drug product is a foam for treatment of acne vulgaris.

C. Basis for Approvability or Not-Approval Recommendation

This ANDA is approvable

Following this page, 20 pages withheld in full - (b)(4)

cc: ANDA 90785 Original
ANDA 90785 DUP
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-645/MFarahani/Review Chemist /3/19/2010; 3/22/10
HFD-627/J.Fan/Team Leader/3/22/10
HFD-617/T. Tran/Project Manager/

V:\Division I\Team 3\FIRMAM\Cobrek\90785.Rev02.doc

TYPE OF LETTER: ANDA is approvable

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-90785	ORIG-1	COBREK PHARMACEUTICALS INC	CLINDAMYCIN PHOSPHATE

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

/s/

MAHNAZ FARAHANI
03/31/2010

TRANG Q TRAN
03/31/2010

JAMES M FAN
03/31/2010

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-785

BIOEQUIVALENCE REVIEWS

Review of a Request for a Waiver of an In Vivo Bioequivalence Study Requirement

ANDA Number:	90-785
Drug Product:	Clindamycin Phosphate Foam, 1%
Sponsor:	Cobrek Pharmaceuticals, Inc.
Reference Listed Drug:	Evoclin®, NDA 50-801, Stiefel Laboratories Inc.,
Original Submission Date(s):	26 August 2008
Submission Date Under Review:	26 August 2008
Reviewer:	James L. Osterhout, PhD
Date of Review:	21 June 2009

1 Executive Summary

Cobrek Pharmaceuticals requests a waiver of in vivo bioequivalence study requirements for its generic Clindamycin Phosphate Foam, 1%. This product is a solution (see Appendix, page 6). The sponsor's generic formulation is qualitatively (Q1), and quantitatively (Q2), the same as the reference listed drug (RLD), Evoclin®. That is, all ingredients are within ±5% (proportionally) of the RLD amounts. In addition, the sponsor's foam dispenser and dispensing characteristics are similar to the RLD. Finally, the propellant composition is the same as the RLD using similar amounts.

1.1 Approval Recommendation

The application is acceptable. The request for a waiver of the in vivo bioequivalence study requirement is granted.

2 Current Submission

The firm has submitted the formulation of their test product in support of their request for a waiver of the in-vivo bioequivalence study requirements based on 21 CFR § 320.22 (b)(3).

The sponsor's generic formulation is qualitatively (Q1), and quantitatively (Q2), the same as the RLD. That is, all ingredients are within ±5% (proportionally) of the reference listed drug (RLD) amounts.

There are three inactive ingredients that have minute differences (see below):

Component	Test %w/w	Ref %w/w	% proportional Difference
Propylene Glycol, USP	(b) (4)	(b) (4)	(b) (4)
Stearyl Alcohol, NF			
Cetyl Alcohol, NF			

The changes in (b) (4) and (b) (4) (b) (4) are not expected to change the foam characteristics of the sponsor's proposed drug product compared to the RLD. Therefore, the performance of the test product will not be different than that of the reference product.

Stearyl and cetyl alcohol are fatty alcohols. At room temperature, they are solid waxes and are insoluble in water. They have been used as emollients, emulsifiers, and thickeners in ointments. There is reference to these compounds being penetration enhancers in numerous non-scientific publications and manufacturer information, none of which cites peer-reviewed scientific data. The book "*Percutaneous Penetration Enhancers"*, edited by Eric W. Smith and Howard I. Maibach, references a study showing that fatty alcohols may enhance penetration of melatonin, but the formulation used in that study contained 60% ethanol as a vehicle with the fatty alcohols at 5%, and there is no further reference to the actual data. Another study investigated enhanced naloxone skin penetration in cadaver skin using 10% fatty alcohol in a propylene glycol vehicle. Addition of stearyl and cetyl alcohol did not significantly enhance the penetration of naloxone.[1]

The clindamycin topical foam and lotion products contain fatty alcohols in the range of 0.5% to 2.5% w/w in the formulation. Small changes (proportionally less than 5%) in the fatty alcohol content of topical clindamycin products are not expected to affect clindamycin systemic absorption.

The RLD and the generic container and closure systems and the valves and actuators used in them are made by the same manufacturer, (b) (4). They are similar in design, delivery rate, and delivery amount (see Appendix: Pharmaceutical Development Data, page 6).

The optimal propellant in the RLD is stated to be "approximately (b) (4) ". The generic propellant has a range of (b) (4)%. This (b) (4) value for propellant corresponds with the testing the sponsor did on both the RLD and their own units, resulting in slightly higher pressure for the RLD ((b) (4)) versus their own tested batches ((b) (4)). Both the RLD and sponsor's propellants are made up of (b) (4)% propane, (b) (4)% butane, and (b) (4).

Although the amount of propellant is not considered part of the drug product, it is important for the formation of the foam as the drug product is released from the container. Both the RLD and generic products have similar amounts of propellant and form a stable foam at room temperature that breaks to a clear liquid at body temperature. The firm did not provide any data on time to break of the foam or foam breaking time. However, given the similarity between the two

[1] International Journal of Pharmaceutics, 33 (1986) 225-234

formulations and the sameness of the propellant and propellant pressure, a significant difference in the foam breaking characteristics is not expected.

2.1 Introduction

Acne vulgaris is a common skin disease that affects 85-100% of people at some time during their lives. It is characterized by noninflammatory follicular papules or comedones and by inflammatory papules, pustules, and nodules in its more severe forms. Acne vulgaris affects the areas of skin with the densest population of sebaceous follicles; these areas include the face, the upper part of the chest, and the back.

Common treatment of acne vulgaris is with topically applied antibiotics, benzoyl peroxide, and retinoids. Acne vulgaris is also treated with systemically dosed antibiotics, hormonal treatments, and isotretinoin.

The reference listed drug, Evoclin® (clindamycin phosphate) Foam, 1% is an antibiotic formulation indicated for topical application in the treatment of acne vulgaris.

Evoclin® Foam was approved based on one pivotal trial CLN.C.003. Evoclin® (clindamycin phosphate) Foam, 1% was superior to vehicle and non-inferior to Clindagel® (clindamycin phosphate gel) topical gel, 1% for the treatment of acne vulgaris in subjects 12 years of age and older. The trial was adequate and well-controlled; it was of sound design, sufficiently powered, multi-centered, randomized, vehicle-controlled against both the active and comparator drugs, and double-blinded. The trial had four arms: Evoclin® Foam, Vehicle Foam, Clindagel® and Vehicle Gel. Co-primary efficacy endpoints included success rate, based on the Investigator's Static Global Assessment dichotomized to success and failure, and percent reduction in lesion counts (total, inflammatory and non-inflammatory), of which the Sponsor needed to win on at least two of the three. The primary endpoint was at week 12, and the analysis group was pre-specified in the statistical analysis plan to be the Intent-to-Treat (ITT) Last Observation Carried Forward (LOCF) population.

The proportion of subjects who achieved success at week 12 in the Evoclin® Foam group, 31.3%, was significantly greater than the in vehicle group, 18.1%, and non-inferior to the Clindagel® group, 27.0 % (FDA analysis). Additionally, the percent reduction in all three lesion counts at week 12 for the Evoclin® Foam group was significantly greater than for the Vehicle Foam group ($p<0.004$), and non-inferior to the Clindagel® group.

3 Background

3.1 Drug Established Name, Drug Class

Drug Established Name	Clindamycin Phosphate Foam, 1%
Drug Class	Antimicrobial

3.2 Summary of Drug Information

Reference Product	Evoclin®
RLD Manufacturer	Stiefel Labs Inc.
NDA Number	N050801
RLD Approval Date	22 October 2004
Indication(s)	Clindamycin phosphate foam 1% is indicated for topical application in the treatment of acne vulgaris.
Dose Regimen(s)	Apply once daily to affected areas after the skin is washed with mild soap and allowed to fully dry. Use enough to cover the entire affected area.

3.3 Regulatory Background

Orange book entries

Active Ingredient:	CLINDAMYCIN PHOSPHATE
Dosage Form; Route:	AEROSOL, FOAM; TOPICAL
Proprietary Name:	EVOCLIN
Applicant:	STIEFEL LABS INC
Strength:	1%
Application Number:	050801
Product Number:	001
Approval Date:	Oct 22, 2004
Reference Listed Drug	Yes

A few controlled correspondences (controls) have been received by the Office of Generic Drugs regarding clindamycin phosphate foam, 1%. There is no approved ANDA for this product.

Control #08-0565 ((b) (4)) – The sponsor asked if the proposed formula was Q1 and Q2 the same as the RLD. The sponsor was contacted by phone and told that their formulation was Q1 and Q2 the same as the RLD by the Regulatory support Branch (Shimer/Kiester).

Control #09-0114 (Stiefel) – Citizen's petition requesting a stay of approval on all Clindamycin Phosphate Foam, 1% generic applications.

A citizens petition dated 23 February 2009 (FDA-2009-P-0120-0001) requested the Agency provide a 30-month stay of approval for specified ANDAs seeking approval for generic versions of old antibiotics for which Warner Chilcott, Medicis, Roche, and Stiefel, the new drug application (NDA) sponsors, have listed patents in accordance with the transition rules of the QI

Act.[2] In the FDA response (FDA-2009-P-0120-0003) dated 19 March 2009, the Agency concluded that the QI Act does not impose a 30-month stay of approval on ANDA applicants that have been sued by the NDA holder or patent owner as a result of notice of a paragraph IV certification to a patent, when the patent was submitted to an old antibiotic NDA and the ANDA was pending with the FDA at the time the patent was submitted. Therefore, the petition was denied.

3.4 Formulation

Component	ANDA 090785[3] Cobrek % w/w	NDA 050801[4] Stiefel Labs Evoclin® % w/w	% Proportional Difference
Clindamycin Phosphate	1.0	1.0	0
Dehydrated Alcohol, USP	58	(b) (4)	(b) (4)
Propylene Glycol, USP	(b) (4)		
Stearyl Alcohol, NF			
Cetyl Alcohol, NF			
Polysorbate 60, NF			
Potassium Hydroxide, NF	--		--
Purified Water, USP	Qs to 100		--

Excipient	Function
Clindamycin Phosphate	Active Ingredient
Dehydrated Alcohol, USP	(b) (4)
Propylene Glycol, USP	
Stearyl Alcohol, NF	
Cetyl Alcohol, NF	
Polysorbate 60, NF	
Potassium Hydroxide, NF	
Purified Water, USP	

Neither formulation includes the propellant. The NDA uses approximately (b) (4) propane/butane. For the NDA, the total aqueous phase concentration equals (b) (4)% (w/w) (after adding a sufficient quantity of purified water to reach 100%) and the total ethanolic phase concentration equals (b) (4)% (w/w). The generic formulation is qualitatively and quantitatively the same as the RLD, so the aqueous and ethanolic phase concentrations are the same.

[2] Qualifying Individual Program Supplemental Funding Act of 2008 - Amends the Federal Food, Drug, and Cosmetic Act to make sponsors of certain antibiotic drugs eligible for a three-year or a five-year market exclusivity if a marketing application is submitted for an antibiotic drug that: (1) was approved by the Secretary of Health and Human Services before November 21, 1997; or (2) was the subject of one or more applications received by the Secretary before November 21, 1997, none of which was approved.
[3] Components and composition from CMC data on EDR
[4] Components and composition from NDA Chemistry Review No. 1

4 Conclusion and Recommendation

The proposed formulation is qualitatively and quantitatively the same as the reference listed drug, Evoclin®. Specifically, the amounts of all components are proportionally within ±5% of the RLD amounts. The valve and actuator are manufactured by the same company as those used by the RLD and are similar in shape and performance. Although the rate of flow was slightly higher for the sponsor's proposed generic product, the volume of foam produced by the sponsor's product and the RLD product are similar per actuation.

The waiver of in vivo bioequivalence testing based on 21 CFR § 320.22 (b)(3) is granted.

5 Appendix

5.1 Pharmaceutical Development Data

Table 4 - 50gr Size Containers- Pressure, Delivery Rate, and Total Delivery Amount

Sample	RLD		Perrigo's Formulation							
Batch	#D6F102	#D6D097	#10533							
Container #	1	1	1	2	3	4	5	6	7	8
Weight gas, mg	(b) (4)									
Pressure, bar										
Delivery rate, mg/sec										
Rate 1	(b) (4)									
Rate 2										
Rate 3										
Average Rate										
Delivery amount, mg										
Weight 0	(b) (4)									
Final weight										
Delivery amount										
Label Claim %										

RLD: Batch # D6F102 exp. 06/09 (50g), Batch #D6D097 exp. 04/09 (50g).

Perrigo's formulaiton batch #10553, eight samples filled in aluminum containers with 50g capacity and (b) (4).

Table 5 - 100gr Size Containers-Pressure, Delivery Rate, and Total Delivery Amount

Sample	RLD		Perrigo's Formulation						
Batch	#D6B094		#9115						
Container #	1	2	1	2	3	4	5	6	7
Weight gas, g			(b) (4)						
Pressure, bar									
Delivery rate, mg/sec									
Rate 1			(b) (4)						
Rate 2									
Rate 3									
Rate 4									
Average Rate									
Delivery amount, mg									
Weight 0			(b) (4)						
Final weight									
Delivery amount									
Label Claim %									

Sample	continued from above						
Batch	#9115						
Container #	8	9	10	11	12	13	14
Weight gas, g						(b) (4)	
Pressure, bar							
Delivery rate, mg/sec							
Rate 1						(b) (4)	
Rate 2							
Rate 3							
Rate 4							
Average Rate							
Delivery amount, mg							
Weight 0						(b) (4)	
Final weight							
Delivery amount							
Label Claim %							

RLD: Batch # D6B094 exp. 01/08 (100g).

Perrigo's formulation batch #9115, fourteen samples filled in aluminum containers with 100g capacity and (b) (4).

5.2 Excerpts from Chemistry Review #1 for the RLD, NDA 50-801

Page 11

(b) (4)

Page 12

The ingredients (b) (4)

The ratio of the aqueous and ethanolic phases (b) (4)

.

Page 22

The clindamycin phosphate used in this product is a white powder which is soluble in water. The solubility of clindamycin phosphate was determined to be (b) (4)

f the product (Module 3, Section 3.2.P.3.4).

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 90-785

APPLICANT: Cobrek Pharmaceuticals, Inc.

DRUG PRODUCT: Clindamycin Phosphate Foam, 1%

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

Please note that the bioequivalence 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 bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

Barbara M. Davit, PhD, JD
Acting Director, Division of Bioequivalence II
Office of Generic Drugs
Center for Drug Evaluation and Research

Linked Applications	Submission Type/Number	Sponsor Name	Drug Name / Subject
ANDA 90785	ORIG 1	COBREK PHARMACEUTICALS INC	CLINDAMYCIN PHOSPHATE

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/s/

JAMES L OSTERHOUT
08/27/2009

DENA R HIXON
08/27/2009
I concur.

BARBARA M DAVIT
08/28/2009

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 90-785

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

C O B R E K
PHARMACEUTICALS, INC.
CORPORATE AND ADMINISTRATIVE OFFICES

3315 Algonquin Road
Suite 310
Rolling Meadows, IL 60008
Phone 847.255.0303
Fax 847.255.2112

August 26, 2008

Gary Buehler, R.Ph.
Director
OGD, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: Pre-Assigned ANDA Application
Original Abbreviated New Drug Application 90-785
Clindamycin Phosphate Foam, 1%

Dear Mr. Buehler:

Cobrek Pharmaceuticals, Inc. a subsidiary of Pentech Pharmaceuticals, Inc. is hereby submitting electronically an original Abbreviated New Drug Application for Clindamycin Phosphate Foam, 1% (pre-assigned ANDA #90-785). Please note that this electronic application has been organized according to the ICH electronic Common Technical Document (eCTD) format.

The reference listed drug is Evoclin® (Clindamycin Phosphate) Foam, 1%; the application holder is Stiefel Laboratories (formerly Connetics Corporation). Cobrek has submitted comparative information demonstrating that Cobrek's product has the same active ingredient, dosage form, route of administration, conditions of use and labeling, except for changes due to different manufacturer and manufacturing, as the reference listed drug. This information is presented in Module 1 **Section 1.12.12**, comparing: the active ingredient; conditions of use; route of administration; dosage form; strength; and labeling for the products supplied by Cobrek Pharmaceuticals, Inc. and by Stiefel Laboratories (formerly Connectics Corporation).

This submission is an electronic submission (eCTD) contained on one (1) CD ROM.

Cobrek Pharmaceuticals, Inc. is filing an Archival Form FDA 2626 (Blue Folder) that includes one (1) CD-ROM, which contains all the information required in the ANDA. The CD-ROM is approximately 65 MB and has been checked for viruses using Symantec Anti Virus Corporate Edition 10.0.0.359. Also included in the Blue Folder are all the original signed forms, statements and certifications that require original signatures. Copies of these documents are also included in the CD-ROM in PDF format.

Cobrek Pharmaceuticals, Inc. commits to resolve any issues identified in the method validation process after approval.

Please refer to the attached **Executive Summary** for more detailed information on the organization of this ANDA.

We trust the information submitted is sufficient for this Abbreviated New Drug Application to be evaluated. Please contact me by phone at (847) 255-0303 or by fax at (847) 255-2112 if you have any questions or if I can assist you with the review of this application.

Sincerely,

James L. Kadow
V.P., Regulatory Affairs

C O B R E K
PHARMACEUTICALS, INC.
CORPORATE AND ADMINISTRATIVE OFFICES

3315 Algonquin Road
Suite 310
Rolling Meadows, IL 60008
Phone 847.255.0303
Fax 847.255.2112

August 26, 2008

Peter Rickman, Director
Division of Labeling and Program Support
OGD, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: Pre-Assigned ANDA Application
Original Abbreviated New Drug Application 90-785
Clindamycin Phosphate Foam, 1%
FIELD NOTIFICATION

Dear Mr. Rickman:

As a courtesy, this letter is to inform you that on August 25, 2008, Cobrek Pharmaceuticals, Inc. (Cobrek) submitted to the Office of Generic Drugs (OGD) an electronic, original Abbreviated New Drug Application (ANDA) for Clindamycin Phosphate Foam, 1% (pre-assigned ANDA #90-785).

Cobrek is providing this information as notice that the electronic version of the ANDA will be available to the International Group at FDA from OGD through the Agency's normal processes for electronic review.

Please contact me by phone at (847) 255-0303 or by fax at (847) 255-2112 if you have any questions or if you need any additional information.

Sincerely,

James L. Kadow
V.P., Regulatory Affairs

M E M O R A N D U M

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

DATE : September 8, 2008

TO : Director
Division of Bioequivalence (HFD-650)

FROM : Chief, Regulatory Support Branch
Office of Generic Drugs (HFD-615)

SUBJECT: Examination of the bioequivalence study submitted with an ANDA 90-785 for Clindamycin Phosphate Foam, 1% to determine if the application is substantially complete for filing.

Cobrek Pharmaceuticals Inc. has submitted ANDA 90-785 for Clindamycin Phosphate Foam, 1%. It is a first generic. In order to accept an ANDA that contains a first generic, the Agency must formally review and make a determination that the application is substantially complete. Included in this review is a determination that the bioequivalence study is complete, and could establish that the product is bioequivalent.

Please evaluate whether the request for study submitted by Cobrek Pharmaceuticals Inc. on August 26, 2008 for its Clindamycin Phosphate product satisfies the statutory requirements of "completeness" so that the ANDA may be filed.

A "complete" bioavailability or bioequivalence study is defined as one that conforms with an appropriate FDA guidance or is reasonable in design and purports to demonstrate that the proposed drug is bioequivalent to the "listed drug".

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

/s/

Eda Howard
9/10/2008 07:46:43 AM
APPLICATIONS EXA

BIOEQUIVALENCE CHECKLIST for First Generic ANDA
FOR APPLICATION COMPLETENESS

ANDA # 90-785 **FIRM NAME:** **Cobrek Pharmaceuticals, Inc.**
(a subsidiary of Pentech Pharmaceuticals)

DRUG NAME Clindamycin Phosphate Foam, 1%

DOSAGE FORM Foam Aerosol (a quick-breaking foam solution formulation)

SUBJ: Request for examination of: request for waiver completeness for a solution formulation.

Requested by: _____ Date: _____
Chief, Regulatory Support Team, (HFD-615)

	Summary of Findings by Division of Bioequivalence
☐	**Study meets statutory requirements**
☐	**Study does NOT meet statutory requirements**
	Reason:
☒	**Waiver meets statutory requirements**
☐	**Waiver does NOT meet statutory requirements**
	Reason:

RECOMMENDATION: ☒ **COMPLETE** ☐ **INCOMPLETE**

Reviewed by:

_____Om Anand, Ph.D._____ Date: _____09/12/2008_____
Reviewer

_____ Paul Seo, Ph.D. _____ Date: ____ 09/12/2008 _____
Team Leader

Item Verified:	YES	NO	Required Amount	Amount Sent	Comments
Protocol	☐	☒			Not applicable because of Waiver Request
Assay Methodology	☐	☒			Not applicable because of Waiver Request
Procedure SOP	☐	☒			Not applicable because of Waiver Request
Methods Validation	☐	☒			Not applicable because of Waiver Request
Study Results Ln/Lin	☐	☒			Not applicable because of Waiver Request
Adverse Events	☐	☐			Not applicable
IRB Approval	☐	☒			Not applicable because of Waiver Request
Dissolution Data	☐	☒			Not applicable because the product is a solution for topical use.
Pre-screening of Patients	☐	☒			Not applicable because of Waiver Request
Chromatograms	☐	☒			Not applicable because of Waiver Request
Consent Forms	☐	☒			Not applicable because of Waiver Request
Composition	☒	☐	1	1	Composition is available in Module 2, Quality Overall Summary pg # 15.
Summary of Study	☒	☐	1	1	Module 2, Quality Overall Summary pg # 15.
Individual Data & Graphs, Linear & Ln	☐	☒			Not applicable because of Waiver Request
PK/PD Data Disk Submitted)	☐	☒			Not applicable because of Waiver Request

Randomization Schedule	☐	☒			Not applicable because of Waiver Request
Protocol Deviations	☐	☒			Not applicable because of Waiver Request
Clinical Site	☐	☒			Not applicable because of Waiver Request
Analytical Site	☐	☒			Not applicable because of Waiver Request
Study Investigators	☐	☒			Not applicable because of Waiver Request
Medical Records	☐	☒			Not applicable because of Waiver Request
Clinical Raw Data	☐	☒			Not applicable because of Waiver Request
Test Article Inventory	☐	☒			Not applicable
BIO Batch Size	☐	☒			Not applicable because of Waiver Request
Assay of Active Content Drug	☒	☐	1	1	COA available in Module 3, section 3.2.P.5.4 Batch analysis.
Content Uniformity	☒	☐	1	1	COA available in Module 3, section 3.2.P.5.4 Batch analysis.
Date of Manufacture	☒	☐	1	1	Feb 27, 2008. (lot # 011277: Module 3, section 3.2.P.5.4.)
Exp. Date of RLD	☐	☒			Not applicable
BioStudy Lot Numbers	☐	☒			Not applicable because of Waiver Request.
Statistics	☐	☒			Not applicable because of Waiver Request
Summary results provided by the firm indicate studies pass BE criteria	☐	☒			Not applicable because of Waiver Request

Waiver requests for other strengths / supporting data	☐	☒			Not applicable because of Waiver Request
Waiver requests	☒	☐	1	1	Waiver request is available in module 1 of electronic submission.

Additional Comments regarding the ANDA:

Given the similarity in formulation between the product proposed in ANDA 090785* from Cobrek (a subsidiary of Pentech) and that proposed in ANDAs [redacted] and [redacted] from [redacted] (accepted for filing and contains a waiver request for *in vivo* BE studies under 320.22(b)(3)), it is possible that BE can be demonstrated for the test product with respect to Evoclin®, (NDA # 050801) using *in vitro* assays alone. As a result, the DBE finds ANDA 090785 acceptable for filing. However, if future chemistry reviews of this application find that the test and reference formulations are not true solutions, or if the DBE finds the *in vitro* assays submitted to be inconclusive in demonstrating BE, then the DBE may request additional studies as appropriate (*in vivo* and/or *in vitro*) to assess BE.

* Formulation of the Foam Aerosol (a quick-breaking foam solution formulation) is as follows:

Component	Composition of Cobrek's Formulation % (w/w)	Composition of RLD Formulation % (w/w) ①
Clindamycin Phosphate, USP	1.0*	1.0*
Ethyl Alcohol [redacted] (Dehydrated Alcohol, USP)	58	58
Propylene Glycol USP	[redacted]	[redacted]
[redacted] (Stearyl Alcohol ,NF)		
[redacted] (Cetyl Alcohol , NF)		
[redacted] (Polysorbate 60 ,NF)		
Potassium Hydroxide	Not used	
Purified Water, USP	Qs to 100	Qs to 100

* Equivalent to 10 mg Clindamycin per gram product.

** For [redacted]

① Amounts of ingredients contained in Evoclin® were determined using product labeling, patent information and reverse engineering.

Productivity :

ANDA : 90785

Reviewer: Anand, Om **Date Completed:**

Verifier: **Date Verified:**

Division: Division of Bioequivalence

Description: Clindamycin Phosphate Foam, CHK list

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*		
6432	8/26/2008	Paragraph 4	Paragraph 4 Checklist	1	1	Edit	Delete
				Bean Total:	1		

DIVISION OF BIOEQUIVALENCE 2 REVIEW COMPLEXITY SUMMARY

First Generic Checklist	1
Grand Total	**1**

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

/s/

Paul Seo

9/15/2008 10:57:14 AM

CLINICAL REVIEW TEAM CHECKLIST FOR GENERIC ANDA
FOR APPLICATION COMPLETENESS

ANDA# _90-785_____ **FIRM NAME Cobrek Pharmaceuticals Inc.**_____

DRUG NAME _Clindamycin Phosphate Foam, 1%_____

DOSAGE FORM __Topical Foam_____

Requested by: ____Eda Howard_____ Date: _9/8/08_____
Chief, Regulatory Support Team, (HFD-615)

	Summary of Findings by Clinical Review Team
	Study meets statutory requirements
	Study does NOT meet statutory requirements
	Reason:
X	**Waiver meets statutory requirements**
	Waiver does NOT meet statutory requirements
	Reason:

RECOMMENDATION: **_X__COMPLETE** **___INCOMPLETE**

Reviewed by:

_____ Date: _____
Reviewer
Carol Y. Kim, Pharm.D.
Clinical Reviewer

_____ Date: _____
Dena R. Hixon, M.D.
Associate Director for Medical Affairs

Item Verified:	YES	NO	Required Amount	Amount Sent	Comments
Composition	X				The test product appears to be qualitatively and quantitatively the same as the RLD except for a presence/absence of a (b) (4).
Waiver requests/supporting data	X				The sponsor states that their product is a solution and requests a waiver of the BE study requirement per 21 CFR 320.22(b)(3).

Comments to be conveyed to the sponsor

Your application is acceptable for filing.

Comments not to be conveyed to the sponsor

The sponsor states that their product, Clindamycin Phosphate Foam 1%, is a hydroalcoholic, quick-breaking foam, solution eligible for a waiver of the BE study requirement.

The OGD has determined that a topical solution may be eligible for a waiver of *in vivo* BE study requirement provided that the generic product meets all the conditions of 21 CFR 320.22 (b) (3).

The sponsor submitted the following data for justification of a waiver of the bioequivalence study requirement:

1. Analysis of the manufacturing process demonstrating that their product is a solution.
   a. Microscopic Birefringence Analysis and solubility study show that their product and the RLD foams are single phase clear solutions.
   b. "Time to break Study" (CM08-003) shows that both test and reference products change from a foam to a liquid within seconds when exposed to skin temperatures.
   c. "Breaking Time Study" (CM08-004) shows that "breaking times" are the same between the products at 33^{o}C, 35^{o}C and 40^{o}C and are temperature-dependent.
2. Pharmaceutical development of the test product.
3. Physical characteristics of inactive ingredients for the RLD and the test product.
4. The sponsor's comparative formulation analysis shows less than +/-5% difference in the amount of inactive ingredients between the test and the reference products except for (b) (4). The test formulation does not contain potassium

hydroxide but the RLD contains potassium hydroxide [redacted] that there are no potential concerns with respect to bioequivalence.

Component	Composition of Cobrek's Formulation % (w/w)	Composition of RLD Formulation % (w/w) [1]
Clindamycin Phosphate, USP	1.0*	1.0*
Ethyl Alcohol [redacted] (Dehydrated Alcohol, USP)	58	58
Propylene Glycol USP	[redacted]	[redacted]
[redacted] (Stearyl Alcohol ,NF)		
[redacted] (Cetyl Alcohol , NF)		
[redacted] (Polysorbate 60 ,NF)		
Potassium Hydroxide	Not used	
Purified Water, USP	Qs to 100	Qs to 100

* Equivalent to 10 mg Clindamycin per gram product.

** For [redacted].

[1]Amounts of ingredients contained in Evoclin® were determined using product labeling, patent information and reverse engineering.

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

/s/

Dena Hixon

9/26/2008 01:37:27 PM

COBRxEK

Pharmaceuticals, Inc.
A Subsidiary of Pentech Pharmaceuticals, Inc.
Corporate and Administrative Offices

3315 Algonquin Road
Suite 310
Rolling Meadows, IL 60008
Phone 847-225-0303
Fax 847-255-2112

October 28, 2008

Gary Buehler, R.Ph.
Director
OGD, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

New Correspondence

RE: ANDA 90-785, Abbreviated New Drug Application
Clindamycin Phosphate Foam, 1%

Dear Mr. Buehler:

In response to the request for corrected documentation by Regulatory Reviewer, Peter Chen, on October 27, 2008, Cobrek Pharmaceuticals, Inc. herein submits a new correspondence for Clindamycin Phosphate Foam, 1%.

Enclose you will find the following

1. A copy of the fax request from Peter Chen.
2. A completed form FDA 3674.
3. A revised Debarment Certification Statement.
4. An Environmental Impact Statement from Cobrek.
5. Revised Side-By-Side Comparisons for the proposed package insert, carton and container.

We trust the information submitted completely responds to Mr. Chen's requests. Please contact me by phone at (847) 255-0303 or by fax at (847) 255-2112 if you have any questions or if I can assist you with the review of this amendment.

Sincerely,

James L. Kadow

James L. Kadow

VP, Regulatory Affairs

FDA FAX

ANDA 90-785

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

TO: Cobrek Pharmaceuticals TEL: 847-255-0303

ATTN: James L. Kadow FAX: 847-255-2112

FROM: Peter Chen TEL: (240) 276-8436

Dear Sir:

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Clindamycin Phosphate Foam, 1%.

Total Pages (1)

SPECIAL INSTRUCTIONS: Please respond to the items identified below as a new correspondence to the ANDA within 10 business days. You can fax (240) 276-8440 or email (peter.chen@fda.hhs.gov) the intial response followed by a hardcopy to the ANDA.

1. Please submit a filled form FDA 3674.
2. Please revise your Conviotions statement to remove the qualifier"to the best of our knowledge..." and resubmit.
3. Please submit an Environmental Impact Analysiss Statement from the sponsor of the ANDA as listed on the 356h form.
4. Please provide direct notation and highlight the areas on the proposed package insert, carton and container side-by-side labels where there are differences compared to the RLD.

COBREK™

Pharmaceuticals, Inc.
A Subsidiary of Pentech Pharmaceuticals, Inc.
Corporate and Administrative Offices

3315 Algonquin Road
Suite 310
Rolling Meadows, IL 60008
Phone 847-225-0303
Fax 847-255-2112

October 31, 2008

Gary Buehler, R.Ph.
Director
OGD, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

New Correspondence

Re: ANDA 90-785, Abbreviated New Drug Application Clindamycin Phosphate Foam, 1%

Dear Mr. Buehler:

In response to the request for correct documentation by Regulatory Reviewer, Peter Chen, on October 27, 2008, Cobrek Pharmaceuticals, Inc. hereby submits an electronic new correspondence for Clindamycin Phosphate Foam, 1% subsequent to our e-mail response on October 28, 2008 (**Attachment 1**).

The following documents are included:

1. A completed form **FDA 3674**
2. A revised **Debarment Certification Statement**
3. An **Environmental Impact Statement** from Cobrek
4. Revised side-by-side comparisons for the proposed package insert, carton and container:

   1-14-1-2-annotated-draft-labeling-text

   1-14-3-1-annotated-comparison-listed-drug

Cobrek Pharmaceuticals, Inc. is filing an Archival Form FDA 2626 (Blue Folder) that includes one (1) CD-ROM, which contains all the information required. The CD-ROM is approximately 2 MB and has been checked for viruses using Symantec Anti Virus Corporate Edition 10.0.0.359. Also included in the Blue Folder are all the original signed forms, statements and certifications that require original signatures. Copies of these documents are also included in the CD-ROM in PDF format.

Please contact me by phone at (847) 255-0303 or by fax at (847) 255-2112 if you have any questions.

Sincerely,

Mary Valencia for

James L. Kadow

VP, Regulatory Affairs

ANDA CHECKLIST FOR CTD or eCTD FORMAT
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION FOR FILING

For More Information on Submission of an ANDA in Electronic Common Technical Document (eCTD) Format please go to: http://www fda.gov/cder/regulatory/ersr/ectd.htm
***For a Comprehensive Table of Contents Headings and Hierarchy please go to:**
http://www fda.gov/cder/regulatory/ersr/5640CTOC-v1.2.pdf
**** For more** CTD and eCTD informational links **see the final page of the ANDA Checklist**
*** **A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage** http://www.fda.gov/cder/ogd/ ***

ANDA #: 90-785 **FIRM NAME**: COBREK PHARMACEUTICALS INC.

PIV: NO **Electronic or Paper Submission:** ECTD FORMAT (ELECTRONIC DATA)

RELATED APPLICATION(S):

First Generic Product Received? YES PER MARTY 9/08/08

Bio Assignments:		**Micro Review (No)**
☒ **BPH**	☐ **BCE**	
☐ **BST**	☐ **BDI**	

DRUG NAME: CLINDAMYCIN PHOSPHATE
DOSAGE FORM: FOAM, 1%
Random Queue: 6
Chem Team Leader: Susan Zuk Chem PM: Roberta Szydlo Labeling Reviewer: Jacqueline Council
Bio PM: Aaron Sigler

Letter Date: AUGUST 26, 2008 **Received Date**: AUGUST 29, 2008

Comments: **EC- 1 YES** **On Cards:** YES
Therapeutic Code: 4010905 ANTIBIOTIC ACNE INDICATION ONLY

Archival copy: ECTD FORMAT **Sections** I
Review copy: NA E-Media Disposition: YES SENT TO EDR
Not applicable to electronic sections

PART 3 Combination Product Category N Not a Part3 Combo Product
(Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm

Reviewing CSO/CST Peter Chen	**Recommendation:**
Date 10/31/2008	☒ **FILE** ☐ **REFUSE to RECEIVE**
Supervisory Concurrence/Date: _____	**Date:** _____

ADDITIONAL COMMENTS REGARDING THE ANDA:

10/27/2008 Tcon with James Kadow

The following comments faxed 10/27/08:

1. Please submit a filled form FDA 3674.

Adequate for filing per 10/28/2008 correspondence; checked 9.a

2. Please revise your Convictions statement to remove the qualifier"to the best of our knowledge..." and resubmit.

Adequate for filing per 10/28/2008 correspondence

3. Please submit an Environmental Impact Analysiss Statement from the sponsor of the ANDA as listed on the 356h form.

Adequate for filing per 10/28/2008 correspondence

4. Please provide direct notation and highlight the areas on the proposed package insert, carton and container side-by-side labels where there are differences compared to the RLD.

Adequate for filing per 10/28/2008 correspondence

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, Parts 314 & 601)

Form Approved: OMB No. 0910-0430
Expiration Date: April 30, 2009
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Cobrek Pharmacueticals, Inc (a subsidiary of Pentech Pharmacueticals, Inc.)	08/26/2008
TELEPHONE NO. *(Include Area Code)*	FACSIMILE *(FAX)* Number *(Include Area Code)*
(847) 255-0303	(847) 255-2112
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: 3315 Algonquin Road, Suite 310 Rolling Meadows, IL 60008	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE N/A

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(if previously issued)* 90785

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Clindamycin Foam, 1%	N/A

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*		CODE NAME *(If any)*
See Attachment		N/A
DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Foam	1%	Topical

(PROPOSED) INDICATION(S) FOR USE:
indicated for topical application in the treatment of acne vulgaris

APPLICATION DESCRIPTION

APPLICATION TYPE *(check one)* ☐ NEW DRUG APPLICATION (CDA, 21 CFR 314.50) ☒ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (BLA, 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 Evoclin® Holder of Approved Application Connetics

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

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: N/A

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

REASON FOR SUBMISSION
For Market Approval

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

NUMBER OF VOLUMES SUBMITTED N/A 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.

See Attachment

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

See Attachment

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

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE:
James L. Kadow	James L. Kadow, V.P, Regulatory Affairs	08/26/2008
ADDRESS *(Street, City, State, and ZIP Code)*		Telephone Number
3315 Algonquin Road, Suite 310 Rolling Meadows, IL 60008		(847) 255-0303

Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (HFM-99)
1401 Rockville Pike
Rockville, MD 20852-1448

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

MODULE 1
ADMINISTRATIVE

ACCEPTABLE

1.1	**1.1.2 Signed and Completed Application Form (356h) (original signature)** (Check Rx/OTC Status) RX YES	☒
1.2	**Cover Letter** Dated: AUGUST 26, 2008	☒

1.2.1	**Form FDA 3674 (PDF) CAN'T LOCATE** *1. Please submit a filled form FDA 3674* *Adequate for filing per 10/28/2008 correspondence; 9.a*	☒
*	**Table of Contents (paper submission only)** YES	☒
1.3.2	**Field Copy Certification (original signature)** NA **(N/A for E-Submissions)**	☒
1.3.3	**Debarment Certification-GDEA (Generic Drug Enforcement Act)/Other:** 1. Debarment Certification (original signature) YES 2. List of Convictions statement (original signature) *2. Please revise your Convictions statement to remove the qualifier"to the best of our knowledge..."* *Adequate for filing per 10/28/2008 correspondence*	☒
1.3.4	**Financial Certifications** Bioavailability/Bioequivalence Financial Certification (Form FDA 3454) Disclosure Statement (Form FDA 3455, submit copy to Regulatory Branch Chief)	☒
1.3.5	**1.3.5.1 Patent Information** Patents listed for the RLD in the Electronic Orange Book Approved Drug Products with Therapeutic Equivalence Evaluations **1.3.5.2 Patent Certification** 1. Patent number(s) antibiotic 2. Paragraph: (Check all certifications that apply) MOU ☐ PI ☐ PII ☐ PIII ☐ PIV ☐ (Statement of Notification) ☐ 3. Expiration of Patent(s): NA a. Pediatric exclusivity submitted? b. Expiration of Pediatric Exclusivity? 4. Exclusivity Statement: YES	☒
1.4.1	**References** Letters of Authorization 1. DMF letters of authorization a. Type II DMF authorization letter(s) or synthesis for Active Pharmaceutical Ingredient submitted (b) (4) b. Type III DMF authorization letter(s) for container closure submitted 2. US Agent Letter of Authorization (U.S. Agent [if needed, countersignature on 356h])	☒
1.12.11	**Basis for Submission** NDA# : 50-801 Ref Listed Drug: EVOCLIN Firm: CONNETICS ANDA suitability petition required? NA If Yes, then is change subject to PREA (change in dosage form, route or active ingredient) see section 1.9.1	☒

MODULE 1 (Continued)
ADMINISTRATIVE

ACCEPTABLE

1.12.12	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use Same as RLD 2. Active ingredients Same as RLD 3. Inactive ingredients Same as RLD except Potassium Hydroxide (b) (4) 4. Route of administration Same as RLD 5. Dosage Form Same as RLD 6. Strength Same as RLD	☒
1.12.14	**Environmental Impact Analysis Statement** YES *3. Please submit an Environmental Impact Statement from the sponsor of the ANDA. as listed on the 356h form.* *Adequate for filing per 10/28/2008 correspondence*	☒
1.12.15	**Request for Waiver** Request for Waiver of In-Vivo BA/BE Study(ies): YES DBE review for completeness found Bio Waiver meets regulations	☒
1.14.1	**Draft Labeling (Mult Copies N/A for E-Submissions)** **1.14.1.1** 4 copies of draft (each strength and container) submitted **1.14.1.2** 1 side by side labeling comparison of containers and carton with all differences annotated and explained *4. Please provide direct notation and highlight the areas on the proposed package insert, carton and container side-by-side labels where there are differences compared to the RLD.* *Adequate for filing per 10/28/2008 correspondence* **1.14.1.3** 1 package insert (content of labeling) submitted electronically submitted ***Was a proprietary name request submitted? no (If yes, send email to Labeling Reviewer indicating such.)	☒
1.14.3	**Listed Drug Labeling** **1.14.3.1** 1 side by side labeling (package and patient insert) comparison with all differences annotated and explained *4. Please provide direct notation and highlight the areas on the proposed package insert, carton and container side-by-side labels where there are differences compared to the RLD.* *Adequate for filing per 10/28/2008 correspondence* **1.14.3.3** 1 RLD label and 1 RLD container label submitted	☒

HOW SUPPLIED
Clindamycin Phosphate Foam, 1%, containing clindamycin phosphate equivalent to 10 mg clindamycin per gram, is available as follows:
100 gram can (NDC 45802-**660**-33)
50 gram can (NDC 45802-**660**-32)

MODULE 2
SUMMARIES ACCEPTABLE

2.3	**Quality Overall Summary (QOS)** **E-Submission: PDF** submitted **Word Processed e.g., MS Word** submitted A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage http://www fda.gov/cder/ogd/ **Question based Review (QbR)** **2.3.S** **Drug Substance (Active Pharmaceutical Ingredient)** **2.3.S.1 General Information** **2.3.S.2 Manufacture** **2.3.S.3 Characterization** **2.3.S.4 Control of Drug Substance** **2.3.S.5 Reference Standards or Materials** **2.3.S.6 Container Closure System** **2.3.S.7 Stability** **2.3.P** **Drug Product** **2.3.P.1 Description and Composition of the Drug Product** **2.3.P.2 Pharmaceutical Development** **2.3.P.2.1 Components of the Drug Product** **2.3.P.2.1.1 Drug Substance** **2.3.P.2.1.2 Excipients** **2.3.P.2.2 Drug Product** **2.3.P.2.3 Manufacturing Process Development** **2.3.P.2.4 Container Closure System** **2.3.P.3 Manufacture** **2.3.P.4 Control of Excipients** **2.3.P.5 Control of Drug Product** **2.3.P.6 Reference Standards or Materials** **2.3.P.7 Container Closure System** **2.3.P.8 Stability**	☒
2.7	**Clinical Summary (Bioequivalence)** **Model Bioequivalence Data Summary Tables** **E-Submission: PDF** **Word Processed e.g., MS Word** **2.7.1 Summary of Biopharmaceutic Studies and Associated Analytical Methods** **2.7.1.1 Background and Overview** Table 1. Submission Summary Table 4. Bioanalytical Method Validation Table 6. Formulation Data **2.7.1.2 Summary of Results of Individual Studies** Table 5. Summary of In Vitro Dissolution **2.7.1.3 Comparison and Analyses of Results Across Studies** Table 2. Summary of Bioavailability (BA) Studies Table 3. Statistical Summary of the Comparative BA Data **2.7.1.4 Appendix** **2.7.4.1.3 Demographic and Other Characteristics of Study Population** Table 7. Demographic Profile of Subjects Completing the Bioequivalence Study **2.7.4.2.1.1 Common Adverse Events** Table 8. Incidence of Adverse Events in Individual Studies	☐

MODULE 3

3.2.S DRUG SUBSTANCE ACCEPTABLE

3.2.S.1	**General Information** **3.2.S.1.1 Nomenclature** **3.2.S.1.2 Structure** **3.2.S.1.3 General Properties**	☒
3.2.S.2	**Manufacturer** **3.2.S.2.1** **Manufacturer(s) (This section includes contract manufacturers and testing labs)** **Drug Substance (Active Pharmaceutical Ingredient)** 1. Name and Full Address(es)of the Facility(ies) submitted 2. Function or Responsibility submitted 3. Type II DMF number for API submitted 4. CFN or FEI numbers submitted	☒
3.2.S.3	**Characterization submitted**	☒
3.2.S.4	**Control of Drug Substance (Active Pharmaceutical Ingredient)** **3.2.S.4.1 Specification** Testing specifications and data from drug substance manufacturer(s) submitted **3.2.S.4.2 Analytical Procedures** submitted **3.2.S.4.3 Validation of Analytical Procedures** 1. Spectra and chromatograms for reference standards and test samples submitted IR 2. Samples-Statement of Availability and Identification of: a. Drug Substance submitted b. Same lot number(s) Lot 010092 **3.2.S.4.4 Batch Analysis** 1. COA(s) specifications and test results from drug substance mfgr(s) Lot 49010KJ00 2. Applicant certificate of analysis submitted Lot 010092 **3.2.S.4.5 Justification of Specification submitted**	☒
3.2.S.5	**Reference Standards or Materials submitted**	☒
3.2.S.6	**Container Closure Systems submitted**	☒
3.2.S.7	**Stability submitted**	☒

MODULE 3

3.2.P DRUG PRODUCT ACCEPTABLE

3.2.P.1	**Description and Composition of the Drug Product** 1. Unit composition submitted 2. Inactive ingredients and amounts are appropriate per IIG YES. Proposed product is Q1/Q2 the same versus the RLD except for Potassium Hydroxide (b) (4). This is an allowable change per 314.94.	☒
3.2.P.2	**Pharmaceutical Development** Pharmaceutical Development Report submitted	☒
3.2.P.3	**Manufacture** **3.2.P.3.1 Manufacture(s)** (Finished Dosage Manufacturer and Outside Contract Testing Laboratories) 1. Name and Full Address(es)of the Facility(ies) submitted 2. CGMP Certification: YES 3. Function or Responsibility submitted 4. CFN or FEI numbers submitted **3.2.P.3.2 Batch Formula** submitted **3.2.P.3.3 Description of Manufacturing Process and Process Controls** 1. Description of the Manufacturing Process submitted 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified submitted MBR (b) (4) 3. If sterile product: Aseptic fill / Terminal sterilization NA 4. Reprocessing Statement submitted **3.2.P.3.4 Controls of Critical Steps and Intermediates submitted** **3.2.P.3.5 Process Validation and/or Evaluation** 1. Microbiological sterilization validation NA 2. Filter validation (if aseptic fill) NA	☒
3.2.P.4	**Controls of Excipients (Inactive Ingredients)** Source of inactive ingredients identified submitted **3.2.P.4.1 Specifications** 1. Testing specifications (including identification and characterization) submitted 2. Suppliers' COA (specifications and test results) submitted **3.2.P.4.2 Analytical Procedures** **3.2.P.4.3 Validation of Analytical Procedures** **3.2.P.4.4 Justification of Specifications** Applicant COA submitted	☒

MODULE 3

3.2.P DRUG PRODUCT

ACCEPTABLE

3.2.P.5	**Controls of Drug Product** **3.2.P.5.1 Specification(s)** submitted **3.2.P.5.2 Analytical Procedures** submitted **3.2.P.5.3 Validation of Analytical Procedures** Samples - Statement of Availability and Identification of: 1. Finished Dosage Form submitted 2. Same lot numbers Lot 011277 and 011278 **3.2.P.5.4 Batch Analysis** Certificate of Analysis for Finished Dosage Form submitted 50 g Cans: Lot 011278 100 G Cans: Lot 011277 **3.2.P.5.5 Characterization of Impurities submitted** **3.2.P.5.6 Justification of Specifications submitted**	☒
3.2.P.7	**Container Closure System** 1. Summary of Container/Closure System (if new resin, provide data) submitted 2. Components Specification and Test Data submitted 3. Packaging Configuration and Sizes submitted 4. Container/Closure Testing submitted 5. Source of supply and suppliers address submitted	☒
3.2.P.8	**3.2.P.8.1 Stability (Finished Dosage Form)** 1. Stability Protocol submitted 2. Expiration Dating Period (b)(4) months **3.2.P.8.2 Post-approval Stability and Conclusion** Post Approval Stability Protocol and Commitments submitted **3.2.P.8.3 Stability Data** 1. 3 month accelerated stability data submitted 2. Batch numbers on stability records the same as the test batch **yes**	☒

MODULE 3

3.2.R Regional Information

ACCEPTABLE

3.2.R (Drug Substance)	**3.2.R.1.S Executed Batch Records for drug substance (if available)** **3.2.R.2.S Comparability Protocols** **3.2.R.3.S Methods Validation Package NA** Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☐

3.2.R (Drug Product)	**3.2.R.1.P.1** **Executed Batch Records** Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures) Batch Reconciliation and Label Reconciliation Theoretical Yield (b) (4) Actual Yield (b) (4) Packaged Yield 100 g Cans: (b) (4); 50 g Cans: (b) (4) **3.2.R.1.P.2 Information on Components** **3.2.R.2.P Comparability Protocols** **3.2.R.3.P Methods Validation Package** NA Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☒

MODULE 5

CLINICAL STUDY REPORTS

ACCEPTABLE

5.2	**Tabular Listing of Clinical Studies**	☐
5.3.1 (complete study data)	**Bioavailability/Bioequivalence** **1. Formulation data same?** a. Comparison of all Strengths (check proportionality of multiple strengths) b. Parenterals, Ophthalmics, Otics and Topicals per 21 CFR 314.94 (a)(9)(iii)-(v) **2. Lot Numbers of Products used in BE Study(ies):** **3. Study Type:** (Continue with the appropriate study type box below)	☐

	5.3.1.2 Comparative BA/BE Study Reports 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. Summary Bioequivalence tables: Table 10. Study Information Table 12. Dropout Information Table 13. Protocol Deviations **5.3.1.3** **In Vitro-In-Vivo Correlation Study Reports** 1. Summary Bioequivalence tables: Table 11. Product Information Table 16. Composition of Meal Used in Fed Bioequivalence Study **5.3.1.4** **Reports of Bioanalytical and Analytical Methods for Human Studies** 1. Summary Bioequivalence table: Table 9. Reanalysis of Study Samples Table 14. Summary of Standard Curve and QC Data for Bioequivalence Sample Analyses Table 15. SOPs Dealing with Bioanalytical Repeats of Study Samples **5.3.7** **Case Report Forms and Individual Patient Listing**	☐
5.4	**Literature References**	☐
	Possible Study Types:	
Study Type	**IN-VIVO BE STUDY(IES) with PK ENDPOINTS** (i.e., fasting/fed/sprinkle) NA 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted: YES SENT TO EDR 3. In-Vitro Dissolution: NA	☐
Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** NO 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria: 90% CI of the proportional difference in success rate between test and reference must be within (-0.20, +0.20) for a binary/dichotomous endpoint. For a continuous endpoint, the test/reference ratio of the mean result must be within (0.80, 1.25). 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted	☐
Study Type	**IN-VITRO BE STUDY(IES)** (i.e., in vitro binding assays) NO 1. Study(ies) meets BE criteria (90% CI of 80-125) 2. EDR Email: Data Files Submitted: 3. In-Vitro Dissolution:	☐

Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** 1. Solutions (Q1/Q2 sameness): a. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming) 2. Suspensions (Q1/Q2 sameness): a. In-Vivo PK Study 1. Study(ies) meets BE Criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted b. In-Vivo BE Study with Clinical End Points 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria (90% CI within +/- 20% of 80-125) 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted c. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming)	☐
Study Type	**IN-VIVO BE STUDY(IES) with PD ENDPOINTS** (e.g., topical corticosteroid vasoconstrictor studies) 1. Pilot Study (determination of ED50) 2. Pivotal Study (study meets BE criteria 90%CI of 80-125)	☐
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** 1. In-Vivo PK Study 1. Study(ies) meet BE Criteria (90% CI of 80-125, C max, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted 2. Adhesion Study 3. Skin Irritation/Sensitization Study	☐

Updated 8/11/2008

Search results from the "OB_Rx" table for query on "050801."

Active Ingredient:	CLINDAMYCIN PHOSPHATE
Dosage Form;Route:	AEROSOL, FOAM; TOPICAL
Proprietary Name:	EVOCLIN
Applicant:	STIEFEL LABS INC
Strength:	1%
Application Number:	050801
Product Number:	001
Approval Date:	Oct 22, 2004
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: View

Return to Electronic Orange Book Home Page

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through September, 2008
Patent and Generic Drug Product Data Last Updated: October 24, 2008

Patent and Exclusivity Search Results from query on Appl No 050801 Product 001 in the OB_Rx list.

Patent Data

There are no unexpired patents for this product in the Orange Book Database.

[Note: Title I of the 1984 Amendments does not apply to drug products submitted or approved under the former Section 507 of the Federal Food, Drug and Cosmetic Act (antibiotic products). Drug products of this category will not have patents listed.]

Exclusivity Data

There is no unexpired exclusivity for this product.

View a list of all patent use codes
View a list of all exclusivity codes

Return to Electronic Orange Book Home Page

CLINICAL REVIEW TEAM CHECKLIST FOR GENERIC ANDA
FOR APPLICATION COMPLETENESS

ANDA# _90-785_____ **FIRM NAME Cobrek Pharmaceuticals Inc.**_____

DRUG NAME _Clindamycin Phosphate Foam, 1%_____

DOSAGE FORM __Topical Foam_____

Requested by: ____Eda Howard_____ Date: _9/8/08_____
Chief, Regulatory Support Team, (HFD-615)

	Summary of Findings by Clinical Review Team
	Study meets statutory requirements
	Study does NOT meet statutory requirements
	Reason:
X	**Waiver meets statutory requirements**
	Waiver does NOT meet statutory requirements
	Reason:

RECOMMENDATION: **_X__COMPLETE** **___INCOMPLETE**

Reviewed by:

_____ Date: _____
Reviewer
Carol Y. Kim, Pharm.D.
Clinical Reviewer

_____ Date: _____
Dena R. Hixon, M.D.
Associate Director for Medical Affairs

BIOEQUIVALENCE CHECKLIST for First Generic ANDA
FOR APPLICATION COMPLETENESS

ANDA # 90-785 **FIRM NAME:** **Cobrek Pharmaceuticals, Inc.**
(a subsidiary of Pentech Pharmaceuticals)

DRUG NAME Clindamycin Phosphate Foam, 1%

DOSAGE FORM Foam Aerosol (a quick-breaking foam solution formulation)

SUBJ: Request for examination of: request for waiver completeness for a solution formulatio

Requested by: _____ Date: _____
Chief, Regulatory Support Team, (HFD-615)

	Summary of Findings by Division of Bioequivalence
☐	**Study meets statutory requirements**
☐	**Study does NOT meet statutory requirements**
	Reason:
☒	**Waiver meets statutory requirements**
☐	**Waiver does NOT meet statutory requirements**
	Reason:

RECOMMENDATION: ☒ **COMPLETE** ☐ **INCOMPLETE**

Reviewed by:

_____Om Anand, Ph.D._____ Date: _____09/12/2008_____
Reviewer

_____ Paul Seo, Ph.D. _____ Date: ____ 09/12/2008 _____
Team Leader

MODULE 3 QUALITY

3.2.P Drug Product

3.2.P.1 Description and Composition of the Drug Product

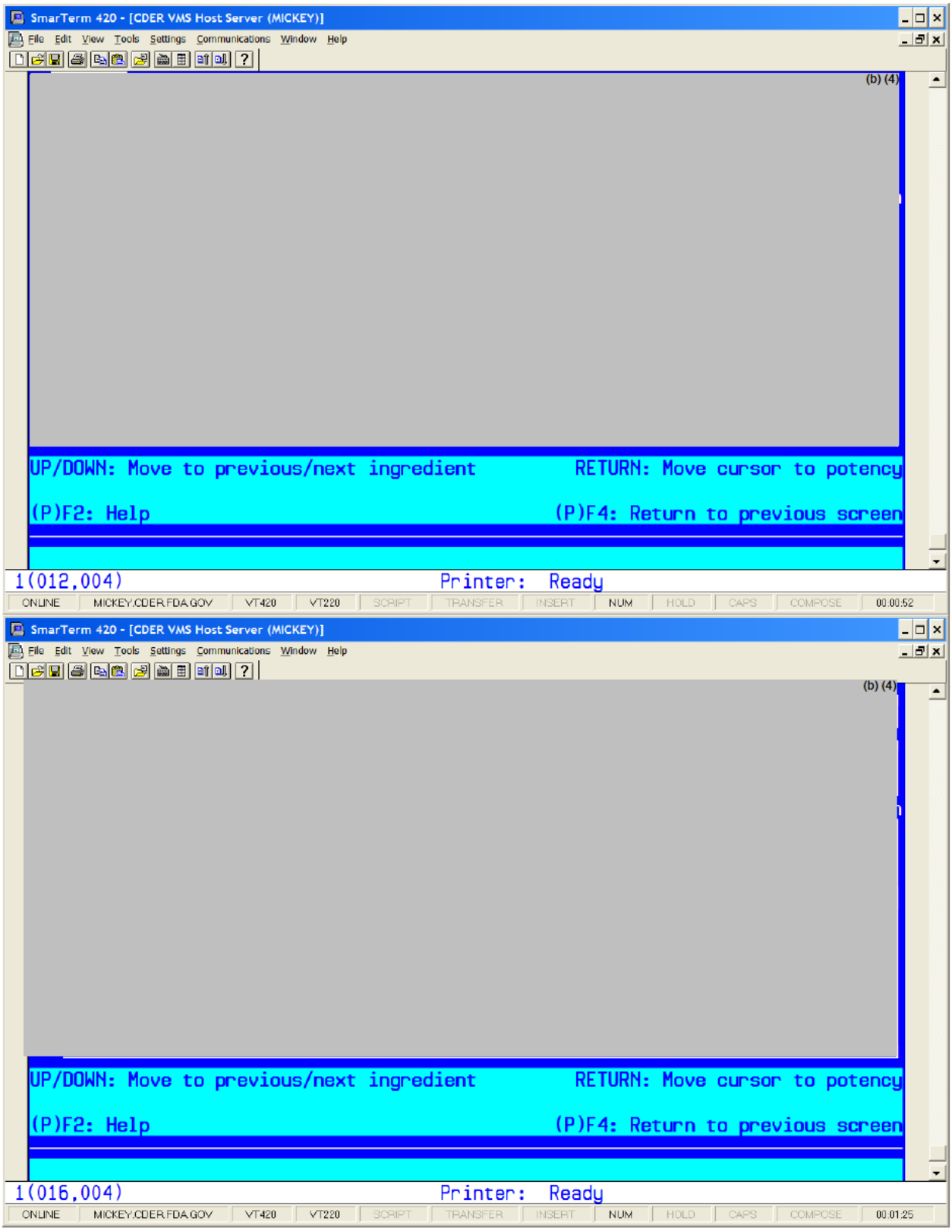
Qualitative and Quantitative Composition of Proposed Drug Product

The following table presents the qualitative and quantitative composition for Cobrek Pharmaceuticals, Inc.'s proposed Clindamycin Phosphate Foam, 1%.

INGREDIENTS	GRADE	FUNCTION	QUANTITY		
			mg/g	% w/w	ANDA Batch** (b) (4) kg
ACTIVE					
Clindamycin Phosphate		Active Ingredient	10.0*	1.0*	(b) (4)
INACTIVE:					
Propylene Glycol, USP	USP	(b) (4)		(b) (4)	(b) (4)
Cetyl Alcohol, NF	NF				
Stearyl Alcohol, NF	NF				
Polysorbate 60, NF	NF				
Dehydrated Alcohol, USP	USP		580.0	58.0	
Purified Water, USP	USP		QS to 1000	(QS to 100)	
TOTAL			1000.0	100.00	

*The amount of Clindamycin Phosphate is calculated according to its potency hence the quantity of Clindamycin Phosphate to be used is based on 100.00% assay value.

** The proposed commercial batch size is identical to the ANDA batch - (b) (4)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RETURN: Move cursor to potency
(P)F2: Help
(P)F4: Return to previous screen
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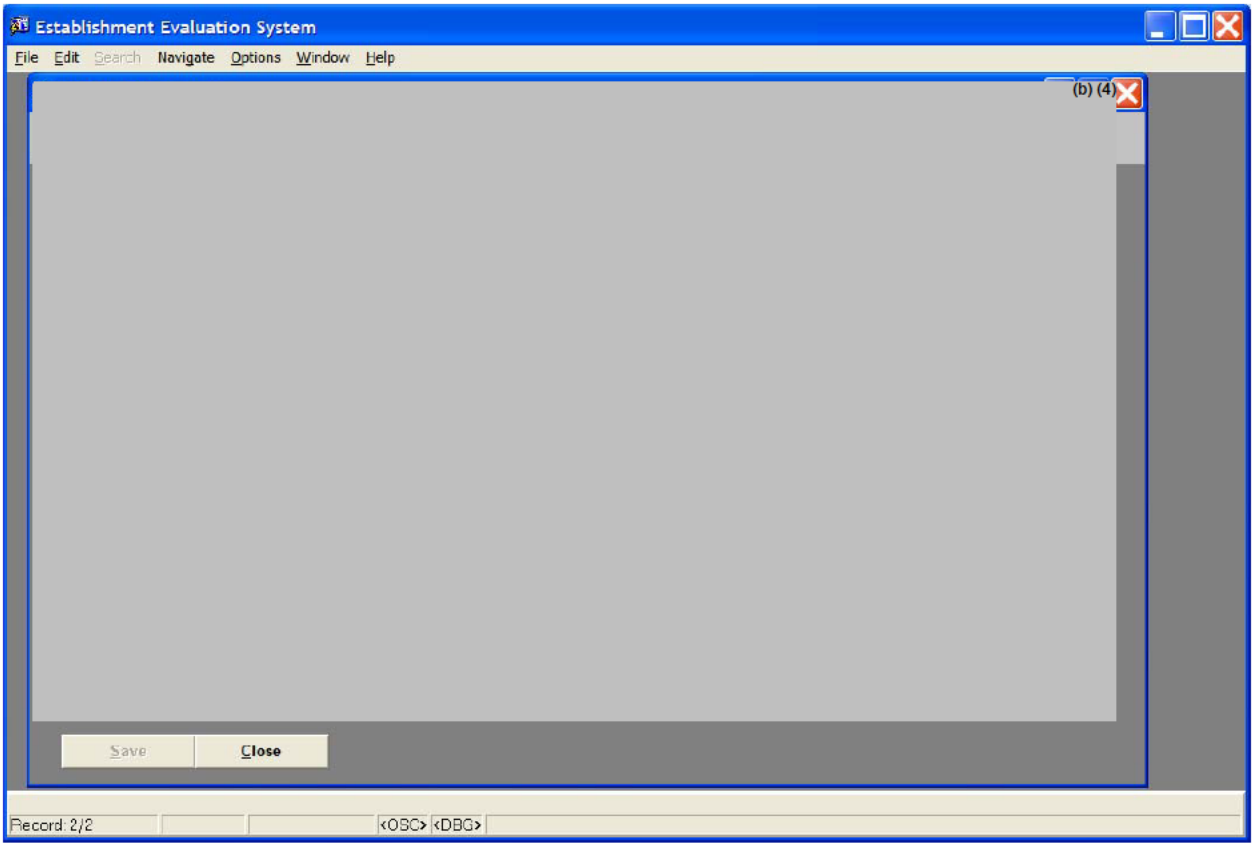
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********** -COMM. JOURNAL- ********** DATE OCT-27-2008 ***** TIME 13:18 *********

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FILE NO.=211

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-FDA CDER OGD LPS -

********** - ***** - **********

FDA FAX

ANDA 90-785

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

TO: Cobrek Pharmaceuticals TEL: 847-255-0303

ATTN: James L. Kadow FAX: 847-255-2112

FROM: Peter Chen TEL: (240) 276-8436

Dear Sir:

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Clindamycin Phosphate Foam, 1%.

Total Pages (1)

SPECIAL INSTRUCTIONS: Please respond to the items identified below as a new correspondence to the ANDA within 10 business days. You can fax (240) 276-8440 or email (peter.chen@fda.hhs.gov) the intial response followed by a hardcopy to the ANDA.

1. Please submit a filled form FDA 3674.
2. Please revise your Convictions statement to remove the qualifier"to the best of our knowledge..." and resubmit.
3. Please submit an Environmental Impact Analysiss Statement from the sponsor of the ANDA as listed on the 356h form.
4. Please provide direct notation and highlight the areas on the proposed package insert, carton and container side-by-side labels where there are differences compared to the RLD.

ANDA 90-785 Clindamycin Phosphate Foam New Correspondence - Message (HT...

Reply | Reply to All | Forward

File Edit View Insert Format Tools Actions Help

From: Marcella Valencia [mvalencia@cobrek.com]
Sent: Tue 10/28/2008 4:41 PM
To: Chen, Peter
Cc: jkadow@cobrek.com
Subject: ANDA 90-785 Clindamycin Phosphate Foam New Correspondence

Attachments: 90-785 new correspondence.pdf (3 MB)

Mr. Chen,

Attached is our response to your request for corrected documentation. A hard copy with pdf labeling files will be submitted as well.

Contact Jim Kadow or myself at (847) 255-0303 if you require any additional information.

Best Regards.

Marcy Valencia

R & D / QA Coordinator
Cobrek Pharmaceuticals, Inc.

Tel: (847) 255-0303
Fax: (847) 255-2112

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

/s/

Saundra Middleton
11/12/2008 01:46:28 PM
Signing for Martin Shimer

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 90-785

Cobrek Pharmaceuticals, Inc.
(a subsidiary of Pentech Pharmaceuticals, Inc.)
Attention: James L. Kadow
3315 Algonquin Road, Suite 310
Rolling Meadows, IL 60008

Dear Sir:

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 our facsimile dated October 27, 2008 and your correspondence dated October 28, 2008.

NAME OF DRUG: Clindamycin Phosphate Foam, 1%

DATE OF APPLICATION: August 26, 2008

DATE (RECEIVED) ACCEPTABLE FOR FILING: August 29, 2008

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:

Roberta Szydlo
Project Manager
240-276-8476

Sincerely yours,

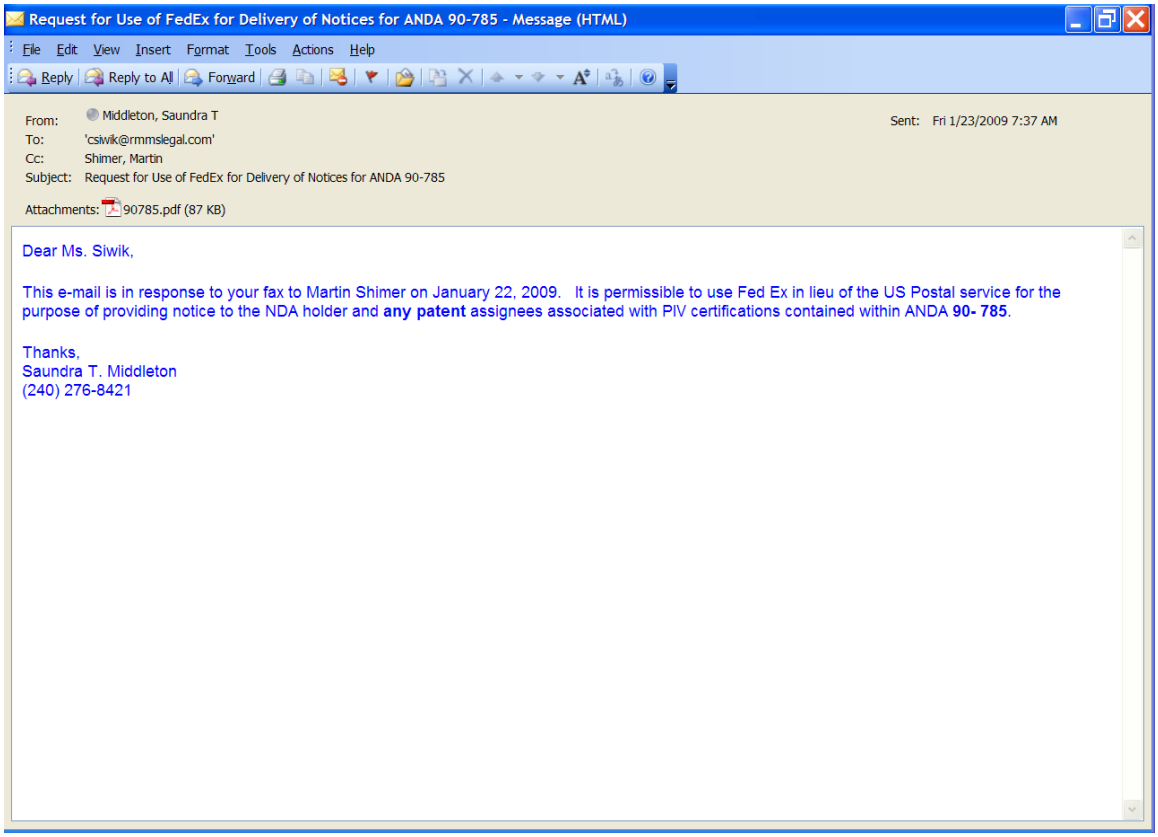
{See appended electronic signature page}

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

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

/s/

Saundra Middleton
11/12/2008 01:47:32 PM
Signing for Wm Peter Rickman


Request for Use of FedEx for Delivery of Notices for ANDA 90-785 - Message (HTML)
File Edit View Insert Format Tools Actions Help
Reply Reply to All Forward
From: Middleton, Saundra T
Sent: Fri 1/23/2009 7:37 AM
To: 'csiwik@rmmslegal.com'
Cc: Shimer, Martin
Subject: Request for Use of FedEx for Delivery of Notices for ANDA 90-785
Attachments: 90785.pdf (87 KB)
Dear Ms. Siwik,
This e-mail is in response to your fax to Martin Shimer on January 22, 2009. It is permissible to use Fed Ex in lieu of the US Postal service for the purpose of providing notice to the NDA holder and any patent assignees associated with PIV certifications contained within ANDA 90- 785.
Thanks,
Saundra T. Middleton
(240) 276-8421

RAKOCZY MOLINO MAZZOCHI SIWIK LLP

6 WEST HUBBARD STREET
SUITE 500
CHICAGO, IL 60610
www.rmmslegal.com

312-527-2157 main phone
312-527-4205 main fax

FAX COVER SHEET

Client/Matter Number:
0124-0031

FROM: Christine J. Siwik

DIRECT LINE: (312) 222-6304

DATE: January 22, 2009

NUMBER OF PAGES (INCLUDING COVER): 2

TO:	FAX NUMBER:	PHONE NUMBER:
MARTIN SHIMER CHIEF, REGULATORY SUPPORT BRANCH; OGD; CDER	(240) 276-8428	(240) 276-8420

PRIVILEGED & CONFIDENTIAL

RAKOCZY MOLINO MAZZOCHI SIWIK LLP

6 WEST HUBBARD STREET
SUITE 500
CHICAGO, IL 60610
www.rmmslegal.com

312-527-2157 main phone
312-527-4205 main fax

Christine J. Siwik
312.222.6304 Direct Phone
312.222.6324 Direct Fax
csiwik@rmmslegal.com

PRIVILEGED AND CONFIDENTIAL ANDA COMMUNICATION, ANDA No. 90-785

January 22, 2009

VIA FACSIMILE AND E-MAIL
Mr. Martin Shimer
Chief, Regulatory Support Branch
Office of Generic Drugs, HFD-615
Center For Drug Evaluation and Research
5630 Fishers Lane
Rockville, MD 20857

Re: ANDA No. 90-785
Clindamycin Phosphate Foam, 1%

Dear Mr. Shimer:

On behalf of Cobrek Pharmaceuticals, Inc. (a subsidiary of Pentech Pharmaceuticals, Inc.), holder of ANDA No. 90-785 for Clindamycin Phosphate Foam, 1%, we hereby request permission to send Cobrek's notice of paragraph IV certification to the holder of NDA No. 50-801 for Evoclin® (Clindamycin Phosphate) foam 1%, and the owner of the associated Orange Book listed patents via Fed Ex®, in lieu of the U.S. Postal System.

We look forward to hearing from you soon, as this is a time-sensitive request. If you have any questions, please do not hesitate to call me at (312) 222-6304. Thank you.

Very truly yours,

RAKOCZY MOLINO MAZZOCHI SIWIK LLP

/ERF

Christine J. Siwik

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

/s/

Saundra Middleton
4/22/2009 08:53:00 AM
CSO

COBRxEK™

Pharmaceuticals, Inc.
Corporate and Administrative Offices

3315 Algonquin Road
Suite 310
Rolling Meadows, IL 60008
Phone 847-225-0303
Fax 847-255-2112

January 28, 2009

Gary Buehler, R.Ph.
Director
OGD, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Amendment
Patent Certification and Statement Concerning
Notice to Patent Owner and NDA Holder

RE: ANDA 90-785
Clindamycin Phosphate Foam, 1%

Dear Mr. Buehler:

Cobrek Pharmaceuticals, Inc. a subsidiary of Pentech Pharmaceuticals, Inc. is hereby submitting electronically an amendment to the original Abbreviated New Drug Application for Clindamycin Phosphate Foam, 1% (ANDA #90-785), to revise our patent certifications to include a Paragraph IV certification to patents 7,141,237 and 7,374,747. The FDA's electronic Orange Book was updated to include U.S. Patents No. 7,141,237 and No. 7,374,747 for Evoclin® (Clindamycin Phosphate) Foam 1%, NDA No. 050801. A copy of the current orange book information is provided in **Module 1 Section 1351-patent-information.**

Cobrek Pharmaceuticals, Inc. is providing a Paragraph IV Patent Certification and Statement Concerning Notice to Patent Owner and NDA Holder, included in **Module 1 Section 1352-patent-certification,** as well as an Exclusivity Statement, included in **Module 1 Section 1353-patent-exclusivity-certification.**

This submission is an electronic submission (eCTD) contained on one (1) CD ROM.

Cobrek Pharmaceuticals, Inc. is filing an Archival Form FDA 2626 (Blue Folder) that includes one (1) CD-ROM. The CD-ROM is approximately 1MB and has been checked for viruses using McAfee(r) VirusScan(r) Enterprise 8.0.0. Also included in the Blue Folder are all the original signed forms, statements and certifications that require original signatures. Copies of these documents are also included in the CD-ROM in PDF format.

Please contact me by phone at (847) 255-0303 or by fax at (847) 255-2112 if you have any questions or if I can assist you with the review of this application.

Sincerely,

James L. Kadow
VP, Regulatory Affairs

COBREK™

Pharmaceuticals, Inc.
Corporate and Administrative Offices

3315 Algonquin Road
Suite 310
Rolling Meadows, IL 60008
Phone 847-225-0303
Fax 847-255-2112

February 9, 2009

Gary Buehler, Director
OGD, CDER, FDA
Metro Park North II
7500 Standish Place
Room 150
Rockville, MD 20855-2764

PATENT AMENDMENT

RE: ANDA 90-785
Clindamycin Phosphate Foam, 1%

Dear Mr. Buehler:

In accordance with 21 C.F.R.§314.95(e), Cobrek is hereby submitting electronically a patent amendment to the original Abbreviated New Drug Application for Clindamycin Phosphate Foam, 1% (ANDA 90-785) to include documentation of receipt of the notice required under 21 C.F.R.§314.95(a).

On August 26, 2008, Cobrek Pharmaceuticals, Inc. a subsidiary of Pentech Pharmaceuticals, Inc. submitted an eCTD abbreviated new drug application (ANDA) to the U.S. Food and Drug Administration for Clindamycin Phosphate Foam, 1% (ANDA 90-785). On January 28, 2009 the application was amended to include a Paragraph IV patent certification due to an update in the FDA's electronic Orange Book which added U.S. Patents No. 7,141,237 and No. 7,374,747 for Evoclin® (Clindamycin Phosphate) Foam, 1% NDA No. 050801 and at the same time notice letters were sent to the patent holders as required by 21 C.F.R.§314.95(d).

Cobrek certifies that on January 28, 2009 Notice of Certification letters were sent out to Stiefel Laboratories, Inc. (Stiefel) in accordance with 21 C.F.R.§314.95(a). Stiefel is the owner of United States Patent number 7,141,237 and Patent number 7,374,747. Stiefel is the holder of the approved application under 505(b) of the Federal Food, Drug, and Cosmetic Act for the listed drug, Evoclin® (Clindamycin Phosphate) Foam, 1% NDA No. 050801 for which Cobrek is seeking approval. United States Patent numbers 7,141,237 and 7,374,747 are the subject of Cobrek's Paragraph IV certification. The content of the notice letter complied with the requirements set forth in 21 C.F.R.§314.95(c).

The notice letters were sent to the patent holders on behalf of Cobrek by the law firm Rakoczy Molino Mazzochi Siwik LLP via Federal Express with advance agreement by Saundra T. Middleton on behalf of Martin Shimer, Branch Chief, Regulatory Support (**attachment 1.12.4-1 fda correspondence**).

Cobrek certifies that the documentation of receipt of notice requirements stated in 21 C.F.R.§314.95(e) have been satisfied, and in accordance with 21 C.F.R.§314.95(e), Cobrek has enclosed Federal Express (FedEx) Delivery Tracking Documents, as proof of receipt of notification **(attachment 1.3.5-1)**. The FedEx Tracking Documents indicate that all of the notice letters sent to Stiefel were received by February 2, 2009.

Cobrek Pharmaceuticals, Inc. is filing an Archival Form FDA 2626 (Blue Folder) that includes one (1) CD-ROM. The CD-ROM is approximately 1MB and has been checked for viruses using Symantec Anti Virus Corporate Edition 10.0.0.359. Also included in the Blue Folder are the original signed 356h form and cover letter. Copies of these documents are also included in the CD-ROM in PDF format.

Please contact me by phone at (847) 255-0303 or by fax at (847) 255-2112 if you have any questions or if I can assist you with the review of this application.

Sincerely,

James L. Kadow
VP, Regulatory Affairs

attachments

COMPLETE RESPONSE -- MINOR

ANDA 90-785

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Cobrek Pharmaceuticals, Inc. TEL: 847-255-0303

ATTN: James L. Kadow FAX: 847-255-2112

FROM: Rosalyn Adigun FDA CONTACT PHONE: (240) 276-8518

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated August 26, 2008, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Clindamycin Phosphate Foam.

SPECIAL INSTRUCTIONS: See CMC comments provided

Please submit your response in electronic format. This will improve document availability to review staff.

We have completed the review of your ANDA and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, our recommendations to address these issues in the following attachments (1 page). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

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

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 90-785 APPLICANT: Cobrek Pharmaceuticals Inc.

DRUG PRODUCT: Clindamycin Phosphate Foam, 1%

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Please provide [redacted] (b) (4)

2. [redacted] (b) (4).

3. [redacted] (b) (4)

4. [redacted] (b) (4) based on actual observed data. Please provide revised [redacted] (b) (4)

5. Please clarify if the [redacted] (b) (4) drug product.

6. Please explain when [redacted] (b) (4).

7. Please confirm that the [redacted] (b) (4).

8. Please provide [redacted] (b) (4)

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following deficiency s in your response:

1. Please provide all available drug product CRT stability data.

2. The bioequivalence and labeling information you have provided is pending review. After the review is completed, any deficiencies found will be communicated to you separately.

3. All facilities referenced in your ANDA should be in compliance with cGMPs at the time of approval.

Sincerely yours,

{See appended electronic signature page}

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

James Fan
3/20/2009 12:58:46 PM
James Fan for Rashmikant Patel

COBRxEK™
Pharmaceuticals, Inc.
Corporate and Administrative Offices

3315 Algonquin Road
Suite 310
Rolling Meadows, IL 60008
Phone 847-225-0303
Fax 847-255-2112

April 2, 2009

Dr. Rashmikant Patel
Division of Chemistry I
Food and Drug Administration
Office of Generic Drugs, CDER
Document Control Room
Metro Park North II, HFD-600
7500 Standish Place, Room # 150
Rockville, MD 20855-2773

Minor Amendment

RE: **ANDA 90-785, Abbreviated New Drug Application**
Clindamycin Phosphate Foam, 1%

Dear Dr. Patel:

In response to the deficiency letter received on March 20, 2009 **(Attachment 1)**, Cobrek Pharmaceuticals, Inc. submits herein a minor amendment for Clindamycin Phosphate Foam, 1% ANDA 90-785.

Clindamycin Phosphate Foam, 1% Minor Amendment was created in eCTD format in accordance with the following FDA Guidance: "Providing Regulatory Submissions in Electronic Format - Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications", dated April 2006.

Whenever the text of a section or subpart is referenced either as text or as an attachment, there is a blue hyperlink to the file where the referenced text or attachment can be found within the ANDA.

The FDA observations appear in bold italic font below, with our response immediately following each comment.

A. Deficiencies:

1. Please provide (b) (4) .

Module 3 section 3.2.S.4, **Attachment 3.2.S.4-1** includes the (b) (4)

Following this page, 5 pages withheld in full - (b)(4)

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in you response:

1. Please provide all available drug product CRT stability data.

Nine (9) months controlled room temperature stability data, accrued to date, for Clindamycin Phosphate Foam, 1%, packaged into 100g, aluminum cans (**Attachment 3.2.P.8.3-2**) and 50g aluminum cans (**Attachment 3.2.P.8.3-13**), results of six (6) months and nine (9) months are added to Module 3 section 3.2.P.8.3, stability data. The controlled room temperature evaluation is ongoing. As more controlled room temperature becomes available, this additional data will be submitted to the Agency.

2. The bioequivalence and labeling information you have provided is pending review. After the review is completed, any deficiencies found will be communicated to you separately.

Cobrek Pharmaceuticals Inc. acknowledges that the bioequivalence and labeling of our application is pending review and that the deficiencies, if any, will be communicated to us separately.

3. All facilities referenced in your ANDA should be in compliance with CGMP at the time of approval.

Cobrek Pharmaceuticals Inc. acknowledges that all facilities referenced in ANDA #90-785 relative to the manufacturing and testing of Clindamycin Phosphate Foam, 1%, must be in compliance with cGMP at the time of approval.

Cobrek Pharmaceuticals Inc. is filing an Archival Form FDA 2626 (Blue Folder) that includes one (1) CD-ROM, which contains all the information required in the Minor Amendment. The CD-ROM is approximately 11 MB and has been checked for viruses using Symantex AntiVirus Corporate Edition 10.0.0.359. Also included in the Blue Folder are the original signed Form FDA 356h and Field Copy Certifications. Copies of these documents are also included in the CD-ROM in PDF format.

Cobrek Pharmaceuticals Inc. also certifies that a letter has been sent to Peter Rickman, Director, Division of Labeling and Program Support, OGD, CDER, FDA, informing that an electronic Minor Amendment for ANDA 090-785 Clindamycin Phosphate Foam, 1% has been submitted to the FDA's Office of Generic Drug (OGD), CDER, and that this Minor Amendment can be accessed from the FDA's headquarters main server.

We trust the information submitted completely responds to the March 20, 2009 deficiency letter. Please contact me by phone at (847) 255-0303 or by fax at (847) 255-2112 if you have any questions or if I can assist you with the review of this application.

Sincerely,

James L. Kadow
VP, Regulatory Affairs

Telephone Fax

ANDA 90-785

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773

TO: Cobrek Pharmaceuticals, Inc.

TEL: 847-255-0303

ATTN: James Kadow

FAX: 847-255-2112

FROM: Kendra Stewart
Kendra.Stewart@fda.hhs.gov
240-276-8998

Dear Sir:

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Clindamycin Phosphate Foam 1%.

Pages (including cover): 3

SPECIAL INSTRUCTIONS:

Labeling comments

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

ANDA Number:	90-785
Date of Submission:	August 26, 2008
Applicant's Name:	Clindamycin Phosphate Foam 1%
Established Name:	Cobrek Pharmaceuticals, Inc.
Proprietary Name:	None

LABELING DEFICIENCIES:

1. **CONTAINER:** (50 gram and 100 gram can)
   a. Please revise "Dosage…" to "Usual Dosage…"
   b. Add the statement "This package is not child resistant."
   c. Please enhance the prominence of the net quantity statement

2. **CONTAINER CARTON:** (50 gram and 100 gram can)
   See container comments 1.a. and 1.b.

3. **PROFESSIONAL INSERT:**
   In the DOSAGE AND ADMINISTRATION section – To Use Clindamycin Phosphate Foam, 1%, Number 2: The instructions direct the patient to "Align the black mark with the nozzle of the actuator." Please confirm whether your container includes a black mark and whether that mark can be aligned properly with the actuator.

Revise your labeling, as instructed above, and submit final printed labeling electronically. In addition, please review the guidance for industry titled "Providing Regulatory Submissions in Electronic Format-Content of Labeling". Please provide the labeling in the Structured Product Labeling (SPL) format.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -
http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

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.

{See appended electronic signature page}

_____

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

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

/s/

Lillie Golson
5/6/2009 01:43:56 PM
Lillie Golson for Wm. Peter Rickman

COBREK™

June 15, 2009

William Peter Rickman, Director
Division of Labeling and Program Support
Office of Generic Drugs, CDER
Document Control room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Labeling Amendment and Submission of SPL

Re: ANDA 90-785
Clindamycin Phosphate Foam, 1%
Submission of Final Printed Labeling

Dear Mr. Rickman:

In reference to the labeling deficiency letter, dated May 6, 2009, **Attachment 1** on our ANDA # 90-785 for Clindamycin Phosphate Foam, 1%, Cobrek Pharmaceuticals, Inc. (a subsidiary of Pentech Pharmaceuticals, Inc.) hereby submits the following response.

The labeling for the 50g and 100g container labels, 50g and 100g outer folding carton labels and the package insert has been revised in accordance with FDA comments.

The final printed labeling is included in Module 1 Section 1.14.2 which is replacing the originally submitted 1.14.1 Draft Labeling.

Response to Labeling Deficiencies:

1. **CONTAINER (50 gram and 100 gram)**

Comment a: Please revise "Dosage…" to "Usual Dosage..."

Response a: "Dosage" has been revised to read as "Usual Dosage".

Comment b: Add the statement "This package is not child resistant."

Response b: The statement "This package is not child resistant." has been added.

Comment c: Please enhance the prominence of the net quantity statement.

Response c: The prominence of the net quantity statement has been enhanced.

2. CONTAINER CARTON (50 g and 100 g can)

Comment: See container comments 1.a. and 1.b.

Response: Comments 1.a and 1.b. have been revised to meet FDA requests.

3. PROFESSIONAL INSERT

Comment: In the DOSAGE AND ADMINISTRATION section – To use Clindamycin Phosphate Foam, 1%, Number 2: The instructions direct the patient to "Align the black mark with the nozzle of the actuator." Please confirm whether your container includes a black mark and whether that mark can be aligned properly with the actuator.

Response: Our container will not include a black mark; hence we have deleted the sentence in the DOSAGE AND ADMINISTRATION section – To use Clindamycin Phosphate Foam, 1%, Number 2, which refers to it.

In accordance with FDA request and in order to facilitate the review of the submission, Section **11422-annotated final-printed-labeling-text** includes a side-by-side comparison of the final printed labeling (FPL) with the draft labeling submitted August 26, 2008, with all differences annotated and explained. The side-by-side comparison is provided as follows:

- Container labels **Tables 1.14.2.2-1, 1.14.2.2-2**
- Outer folding carton labels **Tables 1.14.2.2-3, 1.14.2.2-4**
- Package insert labeling test **Table 1.14.2.2-5**

The reference listed drug, Evoclin (clindamycin phosphate) Foam, 1% labeling in Structured Product Labeling (SPL) format has been posted on the NLM DailyMed website, therefore, our final printed package insert is provided in Structured Product Labeling, along with PDF and MS Word format to assist in the Agency's review. The electronic container labels and carton are provided in PDF format only.

Cobrek Pharmaceuticals, Inc. (a subsidiary of Pentech Pharmaceuticals, Inc.) is filing an Archival Form FDA 2626 (Blue Folder) that includes one (1) CD-ROM, which contains all the information required in the "Labeling Amendment". The CD-ROM is approximately 3 MB and has been checked for viruses using Symantex AntiVirus Corporate Edition 10.0.0.359. Also included in the Blue Folder is the original signed Form FDA 356h. A copy of this document is also included in the CD-ROM in PDF format.

Cobrek Pharmaceuticals, Inc. (a subsidiary of Pentech Pharmaceuticals, Inc.)will submit any necessary revisions to match the RLD labeling for FDA review according to the appropriate filing mechanism.

Should you have any questions, please contact me by phone at (847) 255-0303 or by fax at (847) 255-2112.

Sincerely,

James L. Kadow
V.P., Regulatory Affairs

cc: Kendra Stewart – FDA Project Manager

BIOEQUIVALENCY COMMENTS

ANDA 90-785

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

APPLICANT: Cobrek Pharmaceuticals, Inc. TEL: 847-255-0303, ext. 128

ATTN: James L. Kadow FAX: 847-255-2112

FROM: Debra M. Catterson PROJECT MANAGER: (240) 276-8963
(240) 276-8966 (fax)

Dear Sir:

This facsimile is in reference to the bioequivalency data submitted on August 26, 2008, pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Clindamycin Phosphate Foam, 1%.

The Division of Bioequivalence has completed its review of the submission(s) referenced above and has provided comments which are presented on the attached __1__ page. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

Please direct any questions concerning this communication to the project manager identified above.

SPECIAL INSTRUCTIONS:

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 90-785 APPLICANT: Cobrek Pharmaceuticals, Inc.

DRUG PRODUCT: Clindamycin Phosphate Foam, 1%

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

Please note that the bioequivalence 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 bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

Barbara M. Davit, Ph.D., J.D.
Acting Director, Division of Bioequivalence II
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

DEBRA M CATTERSON
08/29/2009

BARBARA M DAVIT
08/31/2009

February 19, 2010

Mahnaz Farahani
Chemist
OGD, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Telephone Amendment

RE: ANDA 90-785, Abbreviated New Drug Application
Clindamycin Phosphate Foam, 1%

Dear Dr. Farahani:

In response to the telephone call from you and James Fan on February 18, 2010, Cobrek Pharmaceuticals, Inc. submits herein a telephone amendment for Clindamycin Phosphate Foam, 1% ANDA 90-785.

We are sending the Amendment via Fax, but will also submit the amendment electronically since the Clindamycin Phosphate Foam, 1% application was created in eCTD format in accordance with the following FDA Guidance: "Providing Regulatory Submissions in Electronic Format - Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications", dated April 2006.

Whenever the text of a section or subpart is referenced either as text or as an attachment, there is a blue hyperlink to the file where the referenced text or attachment can be found within the Amendment.

The FDA observations appear in bold italic font below, with our response immediately following each comment.

1. ***Please provide current stability data.***

   Updated stability data through 18 months for the submission lots 011277 (100g can) and 011278 (50g can) has been provided. (m3-2-3-8-3-stability-data-18months)

2. (b) (4) For the ease of review copies of the specifications and test data have been included in this telephone amendment.

We trust the information submitted completely responds to your questions communicated in you February 18, 2010 telephone call. Please contact me by phone at (847) 255-0303 or by fax at (847) 255-2112 if you have any questions or if I can assist you with the review of this application.

Sincerely,

James L. Kadow
Vice President of Regulatory Affairs

March 17, 2010

James Fan
OGD, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Telephone Amendment

RE: ANDA 90-785, Abbreviated New Drug Application
Clindamycin Phosphate Foam, 1%

Dear Dr. Fan:

In response to our telephone discussions concerning the (b) (4) specifications for the finished drug product that we had with you and Mahnaz Farahani concluding on March 16, 2010, Cobrek Pharmaceuticals, Inc. submits herein a telephone amendment for Clindamycin Phosphate Foam, 1% ANDA 90-785. In our discussion on March 16, 2010 we expressed concern about our product manufactured in anticipation of launch being able to meet the revised (b) (4) specifications a(b) (4) months. You told us that we could also shorten our expiration period to 18 months. We agree that this is a reasonable approach and are requesting an 18 months expiry for the drug product.

We are sending the Amendment via Fax, but will also submit the amendment electronically since the Clindamycin Phosphate Foam, 1% application was created in eCTD format in accordance with the following FDA Guidance: "Providing Regulatory Submissions in Electronic Format - Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications", dated April 2006.

Whenever the text of a section or subpart is referenced either as text or as an attachment, there is a blue hyperlink to the file where the referenced text or attachment can be found within the Amendment.

As per our agreement we have (b) (4) specifications as follows:

(b) (4)	Former Specifications Submitted April 2, 2009	Current (Revised) Specifications Submitted March 17, 2010
	(b) (4)	

The following documents are provided:

- The revised stability monograph (**QC.W.ST.30700917.05**)
- Updated stability reports through (b) (4) months for the pivotal batches
    - 50 gram can (**Stability report #011278**)
    - 100 gram can (**Stability report #011277**)
- Revision to Proposed Expiration Period (**3.2.P.8.1 - Proposed Expiration Dating Period**)

We trust the information submitted accurately reflects the agreed upon specifications. Please contact me by phone at (847) 255-0303 or by fax at (847) 255-2112 if you have any questions or if I can assist you with the review of this application.

Sincerely,

James L. Kadow

James L. Kadow
Vice President of Regulatory Affairs

OGD APPROVAL ROUTING SUMMARY

ANDA # 90-785 Applicant Cobrek Pharmaceuticals, Inc.
Drug Clindamycin Phosphate Foam Strength(s) 1%

APPROVAL ☒ **TENTATIVE APPROVAL** ☐ **SUPPLEMENTAL APPROVAL (NEW STRENGTH)** ☐ **OTHER** ☐

REVIEWER: | **DRAFT Package** | **FINAL Package**

1. **Martin Shimer**
Chief, Reg. Support Branch
Date 21 Oct 2009 | Date 3/31/10
Initials MHS | Initials rlw

Contains GDEA certification: Yes ☒ No ☐ (required if sub after 6/1/92)
Determ. of Involvement? Yes ☐ No ☒
Pediatric Exclusivity System
RLD = Evoclin NDA# 50-801
Date Checked N/A
Nothing Submitted ☐
Written request issued ☐
Study Submitted ☐

Patent/Exclusivity Certification: Yes ☒ No ☐
If Para. IV Certification- did applicant
Notify patent holder/NDA holder Yes ☒ No ☐
Was applicant sued w/in 45 days: Yes ☐ No ☐
Has case been settled: Yes ☐ No ☐ Date settled:
Is applicant eligible for 180 day
Generic Drugs Exclusivity for each strength: Yes ☒ No ☐
Date of latest Labeling Review/Approval Summary _____
Any filing status changes requiring addition Labeling Review Yes ☐ No ☒
Type of Letter: Full Approval.

Comments: ANDA submitted on 8/29/2008, BOS=Evoclin NDA 50-801, 125(d)(2) FDAMA exemption submitted in lieu of certification. ANDA ack for filing on 8/29/2008(LO dated 11/12/2008). On 1/29/2009 the sponsor submitted PIV certifications to both the '237 and '747 patents. On 2/10/2009 the sponsor submitted a FedEx RR from Connetics Corp in Palo Alto CA signed and dated 1/29/2009, FedEx RR from Stiefel in Coral Gables FL signed and dated 1/29/2009, FedEx RR from Nath and Assoc in Alexandria VA signed and dated 1/29/2009, FedEx RR from Stiefel Research in Rowville Victoria AU signed and dated 2/2/2009.

Firm provided PIV certs to patents that were listed after the ANDA was submitted. Under post-MMA statute, there can be no opportunity for a 30 month stay if the ANDA sponsor is sued within 45 days. As the applicant submitted their PIV certifications in an amendment and provided notice prior to 2/5/2009 they are considered a first-filer under the QI act(passed October of 2008).

This ANDA is eligible for Full Approval with an award of 180 day exclusivity.

2. Project Manager, Nitin Patel Team 3
Review Support Branch
Date 10/13/2009 | Date 3/31/10
Initials NP | Initials TTforNP

Original Rec'd date 8/26/2008
Date Acceptable for Filing 8/29/2009
Patent Certification (type) old antibiotic
Date Patent/Exclus.expires N/A
Citizens' Petition/Legal Case Yes ☒ No ☐
(If YES, attach email from PM to CP coord)
First Generic Yes ☒ No ☐
Priority Approval Yes ☐ No ☒
(If yes, prepare Draft Press Release, Email it to Cecelia Parise)
Acceptable Bio reviews tabbed Yes ☐ No ☒
Bio Review Filed Electronically: Yes ☒ No ☐
Suitability Petition/Pediatric Waiver Yes ☐
Pediatric Waiver Request Accepted ☐ Rejected ☐ Pending ☐
Previously reviewed and tentatively approved ☐ Date _____
Previously reviewed and CGMP def. /NA Minor issued ☐ Date _____

EER Status Pending ☐ Acceptable ☒ OAI ☐
Date of EER Status 3/17/10
Date of Office Bio Review 8/28/2009
Date of Labeling Approv. Sum 9/24/2009
Labeling Acceptable Email Rec'd Yes ☒ No ☐
Labeling Acceptable Email filed Yes ☒ No ☐
Date of Sterility Assur. App. N/A
Methods Val. Samples Pending Yes ☐ No ☒
MV Commitment Rcd. from Firm Yes ☐ No ☐
Modified-release dosage form: Yes ☐ No ☒
Interim Dissol. Specs in AP Ltr: Yes ☐

Comments: EES pending for Perrigo Israel DP manufacturing site. OC email of 10/6/2009 informs that no dates have been set for the inspection of this facility. See email below for CP status:

From: Parise, Cecelia M
Sent: Monday, October 19, 2009 11:10 AM
To: Patel, Nitin K. (CDER/OGD)
Subject: RE: ANDA 90-785; Clindamycin Topical Aerosol Foam

If the RLD is Evoclin the petition response has already been answered

Cec

3. Labeling Endorsement

Reviewer: Labeling Team Leader:
Date10/19/2009; 3/23/10 Date10/19/2009; 3/31/10
Name/InitialsKS Name/InitialsLG

Comments:

_____

From: Golson, Lillie D
Sent: Wednesday, March 31, 2010 11:17 AM
To: Tran, Trang; Golson, Lillie D
Subject: FW: Request for labeling endorsement for ANDA-090785 Product Name: CLINDAMYCIN PHOSPHATE Dosage Form: EMULSION, AEROSOL FOAM Applicant: COBREK PHARMACEUTICALS INC

Hi Trang,

Please endorse the AP routing form on behalf of Kendra and me.

Thanks

Lillie

_From: Stewart, Kendra
Sent: Tuesday, March 23, 2010 2:38 PM
To: Tran, Trang; Golson, Lillie D
Subject: RE: Request for labeling endorsement for ANDA-090785 Product Name: CLINDAMYCIN PHOSPHATE Dosage Form: EMULSION, AEROSOL FOAM Applicant: COBREK PHARMACEUTICALS INC

No problem.

Lillie,

I checked Drugs@FDA,Medwatch, OB and USP
The labeling AP summary signed by Lillie Golson on 9/24/09 remains acceptable.

Kendra Stewart
Kendra S. Stewart, R.Ph., Pharm.D.
Food and Drug Administration
Center for Drug Evaluation and Research
Labeling Reviewer

_____

From: Golson, Lillie D
Sent: Monday, October 19, 2009 5:00 PM
To: Patel, Nitin K. (CDER/OGD); Golson, Lillie D
Subject: FW: Request for labeling endorsement; ANDA 90-785; Clindamycin Phosphate Foam, 1%; Cobrek Pharmaceuticals

Hi Nitin,

Please endorse on behalf of Kendra and me.

Thanks

_____

4. David Read **(PP IVs Only)** Pre-MMA Language included ☐ Date 23Oct09
OGD Regulatory Counsel, Post-MMA Language Included ☐ InitialsDTR
Comments:Changes to AP ltr saved to V drive.

5. Div. Dir./Deputy Dir. Date10/23/09
Chemistry Div. I InitialsPS

Comments:CMC OK ees pending. Note: EES is acceptable 3/17/10/RLWest/3/31/10.

6. Frank Holcombe **First Generics Only** Date3/23/10
Assoc. Dir. For Chemistry Initials RMP
Comments: (First generic drug review)
EES pending.Otherwise,the FGAA is satisfactory.

Note: EES is acceptable 3/17/10/RLWest/3/31/10.

7. Vacant Date_____
Deputy Dir., DLPS Initials_____
RLD = Evoclin Topical Aerosol 1%
Stiefel Laboratories, Inc. NDA 50-801

8. Peter Rickman Date 3/31/10
Director, DLPS Initials rlw/for
Para.IV Patent Cert: Yes☐ No☐;Pending Legal Action: Yes ☐No ☐;Petition: Yes☐ No☐
Comments:Bioequivalence waiver granted under 21 CFR 320.22(b)(3). Drug product formulation is "Q&Q" to that of the RLD. In addition, container closure system and propellant were assessed and found acceptable. Office-level bio endorsed 8/27/09, 8/28/09.

Final-printed labeling (FPL) found acceptable for approval 9/24/09; as endorsed 10/19/09.

CMC found acceptable for approval (Chemistry Review #2).

OR

8. Robert L. West Date 3/31/10
Deputy Director, OGD Initials RLWest
Para.IV Patent Cert: Yes☒ No☐; Pending Legal Action: Yes☐ No☒; Petition: Yes☐ No☒
Press Release Acceptable ☐
Comments: Acceptable EES dated 3/17/10 (Verified 3/31/10). No "OAI" Alerts noted.

Refer to the discussion provided above by M.Shimer as to why the '237 and '747 listed patents do not block approval of this ANDA. There are no additional patents or exclusivity listed in the current "Orange Book" for this drug product.

This ANDA is recommended for approval.

9. Gary Buehler Date 3/31/10
Director, OGD Initials rlw/for
Comments:
First Generic Approval ☐ PD or Clinical for BE ☐ Special Scientific or Reg.Issue ☐
Press Release Acceptable ☐

10. Project Manager, Nitin Patel Team 3 Date3/31/10

Review Support Branch Initials _____
_____Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:
3/31/10Date notified of approval by phone
3/31/10Date approval letter faxed

FDA Notification:
3/31/10Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-90785	ORIG-1	COBREK PHARMACEUTICALS INC	CLINDAMYCIN PHOSPHATE

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

/s/

TRANG Q TRAN
03/31/2010

March 31, 2010

Gary Buehler, R.Ph.
Director
OGD, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

180 Day Exclusivity Start Date

RE: ANDA 90-785, Abbreviated New Drug Application
Clindamycin Phosphate Foam, 1%
eCTD Sequence: 0008

Dear Mr. Buehler:

As requested in the approval letter for Clindamycin Phosphate Foam, 1% ANDA 90-785 dated March 31, 2010 we are informing the agency of the date the exclusivity begins to run.

The date of commercial marketing as identified in section 505(j)(5)(B)(iv) of the Act began on March 31, 2010, therefore the date the exclusivity begins to run is also March 31, 2010

Please contact me by phone at (847) 255-0303 or by fax at (847) 255-2112 if you have any questions or if I can assist you with this supplement.

Sincerely,

James L. Kadow
Vice President of Regulatory Affairs
Cobrek Pharmaceuticals, Inc.