CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-801

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY FOR NDA # __21-709___ SUPPL #_N/A__

Trade Name Evoclin Generic Name Clindamycin phosphate foam, 1%

Applicant Name Connetics Corporation_ HFD-540_____

Approval Date If Known _October 22, 2004_____

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?
YES /_X__/ NO /___/

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

____505(b)(2)_____

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

YES /_X_/ NO /___/

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

__N/A_____

_____

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

_____

___N/A_____

d) Did the applicant request exclusivity?

YES /_X__/ NO /___/

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

__3 years_____

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

YES /___/ NO /_X_/

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

___N/A_____

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

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

YES /___/ NO /_X__/

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

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

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

YES /_X__/ NO /___/

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

NDA# 50-782 Clindagel Topical Gel, 1%

NDA# 50-648_Clindamycin Phosphate in dextrose 5% IN

NDA# 50-636 Clindamycin Phosphate in dextrose 5% INJ

NDA# 50-635 Clindamycin Phosphate in dextrose 5%

2. Combination product.

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

YES /___/ NO /_X__/

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

NDA# _____ _____

NDA# _____ _____

NDA# _____ _____

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

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

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

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical

investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /__X_/ NO /___/

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

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

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

YES /_X__/ NO /___/

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

__N/A_____

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

YES /___/ NO /__X_/

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

YES /___/ NO /_X__/

If yes, explain:

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

YES /___/ NO /_X__/

If yes, explain:

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

Investigation #1 Study # CLN.C.001

Investigation #2 Study # CLN.C.002

Investigation #3 Study # CLN.C.003

Investigation #4 Study # CLN.C.004

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

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

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

Investigation #1	YES /___/	NO /__X_/
Investigation #2	YES /___/	NO /__X_/
Investigation #3	YES /___/	NO /__X_/

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

_____ _____

_____ _____

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

Investigation #1	YES /___/	NO /__X_/
Investigation #2	YES /___/	NO /_X__/
Investigation #3	YES /___/	NO /_X__/
Investigation #4	YES /___/	NO /_X__/

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

_____ _____

_____ _____

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

Investigation #1 Study # CLN.C.001

Investigation #2 Study # CLN.C.002

Investigation #3 Study # CLN.C.003

Investigation #4 Study # CLN.C.004

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

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

Investigation #1

IND # 64,577 YES /_X__/ NO /___/ Explain: _____

Investigation #2

IND # 64,577 YES /_X__/ NO /___/ Explain: _____

Investigation #3

IND # 64,577 YES /_X__/ NO /___/ Explain: _____

Investigation #4

IND # 64,577 YES /_X__/ NO /___/ Explain: _____

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

Investigation #1

YES /___/ Explain _____ NO /___/ Explain _____

_____ _____

_____ _____

Investigation #2

YES /___/ Explain _____ ! NO /___/ Explain _____

_____ ! _____

_____ ! _____

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

YES /___/ NO /_X__/

If yes, explain: _____

_____

_____ _____

Melinda Harris, M.S. Date

_____ _____

Jonathan Wilkin, M.D. Date

Form OGD-011347 Revised 05/10/2004

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/s/

Stanka Kukich
10/22/04 04:25:26 PM
sign off for Dr. Jonathan Wilkin, Division Director

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA # : 21-709 **Supplement Type (e.g. SE5):** N/A **Supplement Number:** N/A

Stamp Date: December 24, 2003 **Action Date:**

HFD-540 **Trade and generic names/dosage form:** [redacted] (clindamycin phosphate) Foam, 1%

Applicant: Connetics Corporation **Therapeutic Class:** 3S

Indication(s) previously approved: N/A

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: Topical administration for the treatment of acne vulgaris

Is there a full waiver for this indication (check one)?

- ☐ **Yes: Please proceed to Section A.**

X No: Please check all that apply: X **Partial Waiver** ____ **Deferred** ____ **Completed**
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Other:**_____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min ____	**kg** ____	**mo.** 0	**yr.** 0	**Tanner Stage** ____
Max ____	**kg** ____	**mo.** 11	**yr.** 11	**Tanner Stage** ____

Reason(s) for partial waiver:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- X **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**
- ☐ **Other:**_____

If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____ **kg**_____ **mo.**_____ **yr.**_____ **Tanner Stage**_____
Max_____ **kg**_____ **mo.**_____ **yr.**_____ **Tanner Stage**_____

Reason(s) for deferral:

- ❑ **Products in this class for this indication have been studied/labeled for pediatric population**
- ❑ **Disease/condition does not exist in children**
- ❑ **Too few children with disease to study**
- ❑ **There are safety concerns**
- ❑ **Adult studies ready for approval**
- ❑ **Formulation needed**

Other:_____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section D: Completed Studies

Age/weight range of completed studies:

Min _____ **kg**_____ **mo.**_____ **yr.** 12 **Tanner Stage**_____
Max_____ **kg**_____ **mo.** 11 **yr.** 17 **Tanner Stage**_____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

Melinda Harris, M.S.
Regulatory Project Manager

cc: NDA
HFD-960/ Grace Carmouze
(revised 12-22-03)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE DIVISION OF PEDIATRIC DRUG DEVELOPMENT, HFD-960, 301-594-7337.

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/s/

Melinda Harris
6/3/04 09:51:29 AM

Jill Lindstrom
6/3/04 12:16:23 PM

Markham Luke
6/3/04 02:37:24 PM
Concur with Waiver of <12 year olds for acne indication for this product.

Jonathan Wilkin
6/8/04 03:17:21 PM

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

FACSIMILE TRANSMITTAL SHEET

DATE: October 21, 2004

To: Sharon Hall	**From:** Margo Owens (for Melinda Harris) Project Manager
Company: Connetics Corporation	Division of Dermatologic & Dental Drug Products
Fax number: (650) 843-2802	**Fax number:** (301) 827-2091 or 2075
Phone number: (650) 843-2858	**Phone number:** (301) 827-2020

Subject: NDA 21-709 Submission 000

Total no. of pages including cover: 4

Comments: Attached are our minutes from the October 14, 2004, teleconference for your NDA 21-709.

Thank you.

Document to be mailed: YES ☑ NO

MEMORANDUM OF TELECON

DATE: 10/14/04, 1:00 P.M.

APPLICATION NUMBER: NDA 21-709
DRUG PRODUCT: Evoclin (clindamycin phosphate) Foam, 1%

BETWEEN:

Name:	Sharon Hall, Senior Director, Regulatory Affairs
	Katy Morton, Director, Regulatory Affairs
	Darlene O'Banion, Senior Manager, Regulatory Affairs
	David Dimmick, Vice-President, Quality
	John Statler, Senior Director, Quality
	Bill Schaber, Senior Director, Quality
	Matt Foehr, Senior Vice-President, Manufacturing
Phone:	(650) 739-2707
Representing:	Connetics Corporation

AND

Name:	Norman Schmuff, Ph.D./Acting Deputy Division Director, ONDC/DNDCIII, HFD-830
	Saleh Turujman, Ph.D./Chemistry Reviewer, DNDCIII, HFD-830
	Melinda Harris, M.S., Regulatory Project Manager, DDDDP, HFD-540

SUBJECT: NDA 21-709

The teleconference was requested by the Sponsor to discuss a request for CMC information for the submitted NDA.

1. The Agency requested that the Sponsor add to the drug product specification an acceptance criteria for the spray rate which assures the dispensation of a uniform amount of foam from the can when a standardized pressure is applied to the nozzle.

   The Sponsor responded they do not have data on this criterion.

   The Sponsor agreed to submit a proposed test and acceptance criteria when either —— have gone through or ——has passed whichever comes first.

The conversation ended amicably.

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/s/

Margo Owens
10/20/04 12:53:56 PM
CSO

Norman Schmuff
10/20/04 03:14:28 PM
CHEMIST

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/s/

Margo Owens
10/21/04 11:45:39 AM
CSO
Faxed to sponsor 10/21/04.

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

FACSIMILE TRANSMITTAL SHEET

DATE: 10/15/04

To: Darlene O'Banion	**From:** Ginny Giroux (for Melinda Harris) Project Manager
Company: Connetics Corporation	Division of Dermatologic & Dental Drug Products
Fax number: (650)843-2802	**Fax number:** (301) 827-2091 or 2075
Phone number: (650)843-2829	**Phone number:** (301) 827-2020

Subject: CMC Information Request NDA 21-709

Total no. of pages including cover:6

Comments:
Please provide your response as soon as possible by fax and also a formal submission.

Document to be mailed: YES ☑ NO

FDA Fax Memorandum

NDA Number: 21-709
Applicant: Connetics Corp.

Please include the test for ethanol content your drug product, —— (clindamycin phosphate) Foam, 1%, in your postapproval stability protocol. In common with both of the approved foam products, Luxiq Foam and Olux Foam, which are owned by Connetics Corporation, the ethanol content in —— (clindamycin phosphate) Foam, 1%, is a critical component in the foam formulation, and should be monitored through the shelf life of the drug product.

Please provide your response as soon as possible by fax and also a formal submission.

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/s/

Virginia Giroux
10/15/04 01:59:03 PM
CSO

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

FACSIMILE TRANSMITTAL SHEET

DATE: October 12, 2004

To: Darlene O'Banion	**From:** Melinda Harris, M.S. Project Manager
Company: Connetics	Division of Dermatologic & Dental Drug Products
Fax number: (650) 843-2802	**Fax number:** (301) 827-2091 or 2075
Phone number: (650) 843-2829	**Phone number:** (301) 827-2020

Subject: NDA 21-709 request for information

Total no. of pages including cover: 3

Comments: Please provide your response as soon as possible by fax and also a formal submission

Document to be mailed: YES ☑ NO

1. Please add to the drug product specification of —— Foam an acceptance criterion for the spray rate which assures the dispensation of a uniform amount of foam from the can when a standardized pressure is applied to the nozzle. In common with both of the approved foam products, Luxiq Foam and Olux Foam, which are owned by Connetics Corporation, —— Clindamycin phosphate) Foam, 1%, is subject to USP <601>, which provides methods for measuring delivery rate and delivery amounts. The absence of a standardized spray rate will only add to the variability inherent in non-metered aerosols.

2. Please provide a commitment that any production batch that has failed the drug product specification will be withdrawn from the market and reported to the Agency.

3. Please provide a commitment to place the first three production scale batches on stability as a postapproval commitment.

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/s/

Melinda Harris
10/12/04 03:05:29 PM
CSO

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Director, Division of Medication Errors and Technical Support (DMETS), HFD-420
PKLN Rm. 6-34

FROM:
Melinda Harris, M.S.
Regulatory Project Manager, HFD-540
DDDDP, CORP2, N241

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
August 17, 2004		21-709	Tradename Request	August 6, 2004

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Clindamycin Phosphate Foam, 1%		3S	October 13, 2004 if possible. PDUFA date is October 22.

NAME OF FIRM: Connetics Corporation

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*: Trade name review

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:

The Sponsor requests review of the following two names: Evoclin and ———
The previous tradename ' ——— ' was found unacceptable on July 13, 2004.
The draft Package Insert, Carton and Container Labeling is attached.
We request that the review be completed by October 13, 2004 if possible due to the October 22, 2004 due date.

PDUFA DATE: October 22, 2004
ATTACHMENTS: Draft Package Insert, Container and Carton Labels

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Melinda Harris, MS (301-827-2020)	☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

20 Page(s) Withheld

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

✓ § 552(b)(4) Draft Labeling

_____ § 552(b)(5) Deliberative Process

*Withheld Track Number: Administrative-*_____

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/s/

Melinda Harris
8/17/04 12:08:26 PM

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

FACSIMILE TRANSMITTAL SHEET

DATE: July 27, 2004

To: Sharon Hall	**From:** Melinda Harris, M.S. Project Manager
Company: Connetics Corporation	Division of Dermatologic & Dental Drug Products
Fax number: (650) 843-2802	**Fax number:** (301) 827-2091 or 2075
Phone number: (650) 843-2858	**Phone number:** (301) 827-2020

Subject: NDA 21-709 Submission 000

Total no. of pages including cover: 2

Comments: Please provide a copy of the CRF for subject 04-0453

Document to be mailed: YES ☑ NO

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/s/

Melinda Harris
7/27/04 12:07:05 PM
CSO

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications

Predecisional Agency Information

Date: July 19, 2004

From: Sonny Saini, Pharm.D. – DDMAC
Iris Masucci, Pharm.D. – DDMAC

To: Melinda Harris

Re: [redacted] (clindamycin phosphate) Foam, 1%
NDA 21-709

Description

- We recommend deleting the term [redacted] in the statement " [redacted] a non-greasy topical product, is delivered in VersaFoam, a [redacted] " because it is promotional in tone. We also recommend deleting the term [redacted] located on the proposed packaging of the product.

- [redacted]

Clinical Studies

- The study presented in this section was conducted in patients with mild to moderate severity acne vulgaris. Is [redacted] specifically indicated for patients with **mild to moderate** acne vulgaris?

Indications and Usage

- We recommend including in the first sentence of this section the severity of acne vulgaris that [redacted]

Warnings

- [redacted]

Adverse Reactions

- The adverse reactions table includes events that occurred more commonly with vehicle foam than with [redacted] As recommended in the draft guidance on the Adverse Reactions section of labeling, we suggest deletion of all events occurring more commonly in the vehicle group.

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/s/

Sonny Saini
7/21/04 10:19:53 AM
DDMAC REVIEWER

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

FACSIMILE TRANSMITTAL SHEET

DATE: April 1, 2004

To: Sharon Hall	**From:** Melinda Harris, M.S. Project Manager
Company: Connetics Corporation	Division of Dermatologic & Dental Drug Products
Fax number: (650) 843-2802	**Fax number:** (301) 827-2091 or 2075
Phone number: (650) 843-2858	**Phone number:** (301) 827-2020

Subject: NDA 21-709 Submission 000

Total no. of pages including cover: 2

Comments: Please provide a copy of Form 3542a regarding patent information for the above NDA. Also please provide several tradenames for consideration.

Document to be mailed: YES ☑ NO

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/s/

Melinda Harris
4/1/04 12:25:02 PM
CSO

Office of Drug Safety

MEMO

To: Jonathan Wilkin, M.D.
Director, Division of Dermatologic and Dental Products, HFD-540

From: Kim Culley, R.Ph.
Safety Evaluator, Division of Medication Errors and Technical Support
Office of Drug Safety, HFD-420

Through: Alina Mahmud, R.Ph.
Team Leader, Division of Medication Errors and Technical Support
Office of Drug Safety, HFD-420

Carol Holquist, R.Ph.
Deputy Director, Division of Medication Errors and Technical Support
Office of Drug Safety, HFD-420

CC: Melinda Harris, M.S.
Project Manager, Division of Dermatologic and Dental Products, HFD-540

Date: March 18, 2004

Re: ODS Consult 04-0079; ——— (Clindamycin Phosphate) Foam, 1%; NDA 21-709

NOTE: This review contains proprietary and confidential information that should not be released to the public.

This memorandum is in response to a February 24, 2004 request from your Division for a review of the container label, carton and package insert labeling for ——— A proprietary name review (ODS consult number 03-0288) for — was performed by DMETS on October 23, 2003 and found unacceptable due to potential confusion with ———

In the review of the . — container label, carton and insert labeling, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

A. CONTAINER LABEL

1. The green color stripe design is distracting and interferes with the readability of the proprietary and established name. DMETS is also concerned with confusion between other Connetics manufactured/marketed products. In a side-by-side comparison of three topical foams marketed by Connetics, [redacted] and Olux®, DMETS found the labels too similar in appearance thus potentially creating problems in differentiating between the products.

2. Please disclose where the expiration date is noted. If not on the container label or dispensing can, please add the expiration date to the label, preferably near the control number.

B. CARTON LABELING

See comments A1 and A2.

C. PACKAGE INSERT (DOSAGE AND ADMINISTRATION, HOW SUPPLIED)

1.

2.

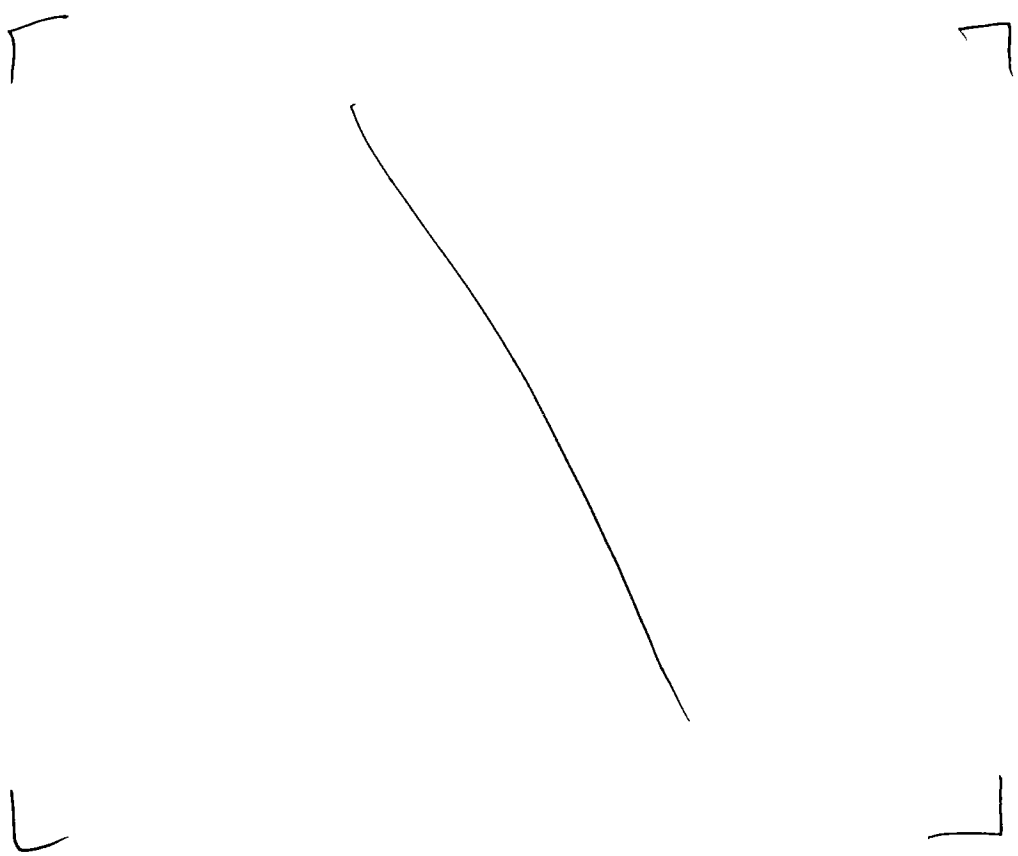
3.

4.

5.

6.

7.



In summary, DMETS recommends implementation of the label and labeling revisions outlined in this memo that may lead to safer use of the product. If you have any questions or need clarification, please contact Sammie Beam, Project Manager, at 301-827-3242.

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/s/

Kimberly Culley
3/26/04 09:18:47 AM
DRUG SAFETY OFFICE REVIEWER

Alina Mahmud
3/26/04 10:14:24 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
3/26/04 02:50:09 PM
DRUG SAFETY OFFICE REVIEWER

Jerry Phillips
3/29/04 08:04:09 AM
DRUG SAFETY OFFICE REVIEWER

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 21-709 Supplement # N/A SE1 SE2 SE3 SE4 SE5 SE6 SE7 SE8

Trade Name: [redacted]
Generic Name: clindamycin phosphate foam
Strengths: 1%

Applicant: Connetics Corporation

Date of Application: December 22, 2003
Date of Receipt: December 24, 2003
Date clock started after UN: N/A
Date of Filing Meeting: February 19, 2004
Filing Date: March 7, 2004
Action Goal Date (optional): User Fee Goal Date: October 24, 2004

Indication(s) requested: Topical Administration for the treatment of acne vulgaris

Type of Original NDA: (b)(1) _____ (b)(2) _X_____
OR
Type of Supplement: **N/A** (b)(1) _____ (b)(2) _____
NOTE: A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application is a (b)(2) application, complete the (b)(2) section at the end of this review.

Therapeutic Classification: S ____**X**_____ P _____
Resubmission after withdrawal? ___**N/A**_____ Resubmission after refuse to file? ___**N/A**_____
Chemical Classification: (1,2,3 etc.) ____**3**_____
Other (orphan, OTC, etc.) ___**N/A**_____

User Fee Status: Paid ___ Exempt (orphan, government) __**X**__**505(b)2 that does not require a fee**___
Waived (e.g., small business, public health) _____

Form 3397 (User Fee Cover Sheet) submitted: YES **X** NO
User Fee ID # ___**N/A**_____
Clinical data? YES __**X**_ **and referenced NDA # 50-782**

Is there any 5-year or 3-year exclusivity on this active moiety in either a (b)(1) or a (b)(2) application?

YES NO **X**

If yes, explain:

Does another drug have orphan drug exclusivity for the same indication? YES NO **X**

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

N/A **X** YES NO

Is the application affected by the Application Integrity Policy (AIP)? YES NO **X**
If yes, explain.

If yes, has OC/DMPQ been notified of the submission? N/A **X** YES NO

- Does the submission contain an accurate comprehensive index? YES **X** NO
- Was form 356h included with an authorized signature? YES **X** NO
  If foreign applicant, both the applicant and the U.S. agent must sign.
- Submission complete as required under 21 CFR 314.50? YES **X** NO

  If no, explain:

- If an electronic NDA, does it follow the Guidance? N/A **X** YES NO
  If an electronic NDA, all certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  N/A

  Additional comments:

- If in Common Technical Document format, does it follow the guidance? N/A YES **X** NO

- Is it an electronic CTD? N/A YES **X** NO
  If an electronic CTD, all certifications must be in paper and require a signature.
  Which parts of the application were submitted in electronic format?

  Table of contents for electronic components, Nonclinical literature references, Clinical literature references, labeling, and Case Report Tabulations

  Additional comments:

- Patent information included with authorized signature? YES **X** NO

- Exclusivity requested? YES, ____**3**___years NO
  Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.

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

NOTE: Debarment Certification should use wording in FD&C Act section 306(k)(1) i.e., *"[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application."* Applicant may not use wording such as "To the best of my knowledge . . . ."

- Financial Disclosure forms included with authorized signature? YES **X** NO
  (Forms 3454 and 3455 must be used and must be signed by the APPLICANT.)

- Field Copy Certification (that it is a true copy of the CMC technical section)? YES **X** NO

Refer to 21 CFR 314.101(d) for Filing Requirements

- PDUFA and Action Goal dates correct in COMIS? YES **X** NO
  If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.

- Drug name/Applicant name correct in COMIS? If not, have the Document Room make the corrections.
  yes
- List referenced IND numbers: **64,577**

- End-of-Phase 2 Meeting(s)? Date(s) **April 10, 2002** NO
  If yes, distribute minutes before filing meeting.

- Pre-NDA Meeting(s)? Date(s) **November 19, 2003**

  If yes, distribute minutes before filing meeting.

Project Management

- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC?
  YES NO **X** **will be sent after filing**
- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? YES **X**
  tradename has been sent NO X to ODS, will be sent after filing

- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A **X** YES NO

- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted?
  N/A **X** YES NO

If Rx-to-OTC Switch application:

- OTC label comprehension studies, all OTC labeling, and current approved PI consulted to ODS/DSRCS?
  N/A **X** YES NO

- Has DOTCDP been notified of the OTC switch application? N/A **X** YES NO

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff?
  N/A **X** YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES **X** NO
  If no, did applicant submit a complete environmental assessment? YES NO
  If EA submitted, consulted to Nancy Sager (HFD-357)? YES **X** NO

- Establishment Evaluation Request (EER) submitted to DMPQ? YES **X** NO

- If a parenteral product, consulted to Microbiology Team (HFD-805)? YES NO N/A **X**

If 505(b)(2) application, complete the following section:

- Name of listed drug(s) and NDA/ANDA #: **NDA 50-872 Clindagel® (clindamycin phosphate) Topical Gel 1%**

- Describe the change from the listed drug(s) provided for in this (b)(2) application (for example, "This application provides for a new indication, otitis media" or "This application provides for a change in dosage form, from capsules to solution").

  Change in dosage form

- Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? (Normally, FDA will refuse-to-file such NDAs.)
  YES NO **X**

- Is the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (See 314.54(b)(1)). If yes, the application should be refused for filing under 314.101(d)(9).
  YES NO **X**

- Is the rate at which the product's active ingredient(s) is absorbed or otherwise made available to the site of action unintentionally less than that of the RLD? (See 314.54(b)(2)). If yes, the application should be refused for filing under 314.101(d)(9).
  YES NO **X**

- Which of the following patent certifications does the application contain? Note that a patent certification must contain an authorized signature.

  ____ 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA.

  __**X**_ 21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired.

  ____ 21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire.

____ 21 CFR 314.50(i)(1)(i)(A)(4): The patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted.

IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must submit a signed certification that the patent holder was notified the NDA was filed [21 CFR 314.52(b)]. Subsequently, the applicant must submit documentation that the patent holder(s) received the notification ([21 CFR 314.52(e)].

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

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

____ 21 CFR 314.50(i)(3): Statement that applicant has a licensing agreement with the patent owner (must also submit certification under 21 CFR 314.50(i)(1)(i)(A)(4) above.)
____ Written statement from patent owner that it consents to an immediate effective date upon approval of the application.

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

    YES **X** NO
  - Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?

    YES NO **X**
  - Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?

    N/A YES **X** NO
  - Certify that it is seeking approval only for a new indication and not for the indications approved for the listed drug if the listed drug has patent protection for the approved indications and the applicant is requesting only the new indication (21 CFR 314.54(a)(1)(iv).?

    N/A **X** YES NO
- If the (b)(2) applicant is requesting exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):
  - Certification that each of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).

    YES **X** NO
  - A list of all published studies or publicly available reports that are relevant to the conditions for which the applicant is seeking approval.

    YES **X** NO

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

  IND # **64,577**__ NO

  OR

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

  N/A **X** YES NO

- Has the Director, Div. of Regulatory Policy II, HFD-007, been notified of the existence of the (b)(2) application?

  YES **X** NO

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/s/

Melinda Harris
3/4/04 11:10:55 AM
CSO

Mary Jean Kozma Fornaro
3/4/04 03:28:26 PM
CSO

ATTACHMENT

MEMO OF FILING MEETING

DATE: February 19, 2004

BACKGROUND:
— is a 505(b)2 NDA application for the topical application in the treatment of Acne Vulgaris. The NDA reference drug is Clindagel (NDA 50-782).

ATTENDEES: Jonathan Wilkin, M.D., Stanka Kukich, M.D., Barbara Hill, Ph.D., Terri Rumble, R.N., B.S.N., Wilson DeCamp, Ph.D., and Albert Sheldon, Ph.D. in addition to the reviewers listed below.

ASSIGNED REVIEWERS:

Discipline	**Reviewer**	**Review Date**
Medical:	Jill Lindstrom, M.D.	July 15, 2004
Secondary Medical:	Markham Luke, M.D., Ph.D.	
Statistical:	Steve Thomson, M.S.	July 15, 2004
Pharmacology:	Jill Merrill, Ph.D. (not present)	September 15, 2004
Statistical Pharmacology:	N/A	
Chemistry:	Saleh Turujman, Ph.D. (not present)	September 1, 2004
Environmental Assessment (if needed):	N/A	
Biopharmaceutical:	Dennis Bashaw, Pharm.D.	June 15, 2004
Microbiology, sterility:	N/A	
Microbiology, clinical (for antimicrobial products only):	Fred Marsik, Ph.D.	
DSI:	Roy Blay, Ph.D. (not present)	
Regulatory Project Management:	Melinda Harris, M.S.	
Other Consults:	N/A	

Per reviewers, are all parts in English or English translation? YES X NO
If no, explain:

CLINICAL FILE ___X___ REFUSE TO FILE _____

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

CLINICAL MICROBIOLOGY NA _____ FILE __X____ REFUSE TO FILE _____

STATISTICS FILE ___X___ REFUSE TO FILE _____

BIOPHARMACEUTICS		FILE ___X___	REFUSE TO FILE _____
• Biopharm. inspection needed:			YES NO X
PHARMACOLOGY	NA _____	FILE ___X___	REFUSE TO FILE _____
• GLP inspection needed:			YES NO X
CHEMISTRY		FILE __X____	REFUSE TO FILE _____
• Establishment(s) ready for inspection?			YES X NO
• Microbiology			YES NO X

ELECTRONIC SUBMISSION:
Any comments:
None.

REGULATORY CONCLUSIONS/DEFICIENCIES:

_____ The application is unsuitable for filing. Explain why:

___X____ The application, on its face, appears to be well organized and indexed. The application appears to be suitable for filing.

___X____ No filing issues have been identified.

_____ Filing issues to be communicated by Day 74. List (optional):

ACTION ITEMS:

1. If RTF, notify everybody who already received a consult request of the RTF action. Cancel the EER.

2. If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.

3. Document filing issues/no filing issues conveyed to applicant by Day 74.

_____
Melinda Harris, M.S.
Regulatory Project Manager, HFD-540

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/s/

Melinda Harris
3/2/04 09:41:17 AM
CSO

Jonathan Wilkin
3/2/04 03:16:53 PM
MEDICAL OFFICER

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:			FROM:	
Division of Drug Marketing, Advertising and Communications, HFD-42 PKLN Rm. 17B04			Melinda Harris, M.S. Project Manager Division of Dermatologic and Dental Drug Products	
DATE February 25, 2004	IND NO.	NDA NO. 21-709	TYPE OF DOCUMENT New NDA	DATE OF DOCUMENT December 22, 2003
NAME OF DRUG ——— (clindamycin phosphate) Foam, 1%	PRIORITY CONSIDERATION		CLASSIFICATION OF DRUG 3S	DESIRED COMPLETION DATE End of review labeling meeting is scheduled for 8/18/04

NAME OF FIRM: Connetics Corporation

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- X☐ OTHER *(SPECIFY BELOW)*:

New NDA

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Labels for the Carton/Container and the Physician Insert are attached for your review.

An end of review labeling meeting has been scheduled for August 18, 2004. Please provide comments in a sufficient amount of time prior to the meeting.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Melinda Harris, M.S. (7-2049)	X☐ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

11 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

✓ § 552(b)(5) Draft Labeling

Withheld Track Number: Administrative- 1

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/s/

Melinda Harris
2/25/04 10:47:42 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-709

Connetics
Attention: Sharon L. Hall
Senior Director, Regulatory Affairs
3290 West Bayshore Road
Palo Alto, CA 94303

Dear Ms. Hall:

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

Name of Drug Product: ——— (clindamycin phosphate) Foam, 1%

Review Priority Classification: Standard (S)

Date of Application: December 22, 2003

Date of Receipt: December 24, 2003

Our Reference Number: NDA 21-709

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on February 22, 2004, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be October 24, 2004.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirements. We acknowledge receipt of your request for a waiver of pediatric studies for this application. Once the application has been filed we will notify you whether we have waived the pediatric study requirement for this application.

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

U.S. Postal Service:
Center for Drug Evaluation and Research
Division of Dermatologic & Dental Drug Products

HFD-540
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatologic & Dental Drug Products
HFD-540
9201 Corporate Boulevard
Rockville, Maryland 20850

If you have any questions, call Melinda Harris, M.S., Regulatory Project Manager, at (301) 827-2020.

Sincerely,

[See appended electronic signature page]

Mary Jean Kozma-Fornaro
Supervisor, Project Management Staff
Division of Dermatologic & Dental Drugs
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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/s/

Mary Jean Kozma Fornaro
2/13/04 11:45:16 AM

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

FACSIMILE TRANSMITTAL SHEET

DATE: 9 February 2004

To: Sharon Hall	**From:** Melinda Harris, M.S. Project Manager
Company: Connetics Corporation	Division of Dermatologic & Dental Drug Products
Fax number: (650) 843-2802	**Fax number:** (301) 827-2091 or 2075
Phone number: (650) 843-2858	**Phone number:** (301) 827-2020

Subject: NDA 21-709

Total no. of pages including cover: 3

Comments: Comments regarding the tradename and carton/container are provided

Document to be mailed: YES ☑ NO

1 Page(s) Withheld

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

_____ § 552(b)(5) Deliberative Process

✓ § 552(b)(5) Draft Labeling

Withheld Track Number: Administrative- 1

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/s/

Melinda Harris
2/9/04 11:08:17 AM
CSO

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Frances LeSane
Supervisory Project Manager
DAIDP, HFD-520

FROM:
Melinda Harris, M.S.
Project Manager, HFD-540
Division of Dermatologic and Dental Drug Products

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
February 5, 2004		21-709	New NDA	December 22, 2003

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
—— (Clindamycin Phosphate Foam) 1%		3S	February 19, 2004 is the filing date, PDUFA due date is October 24, 2004

NAME OF FIRM: Connetics Corporation

REASON FOR REQUEST

I. GENERAL

E--NDA MEETING
☐ END OF PHASE II MEETING
☐ RESUBMISSION
☐ SAFETY/EFFICACY
☐ PAPER NDA
☐ CONTROL SUPPLEMENT

III. BIOPHARMACEUTICS

☐ DIUTION
☐ BIOAVAILABILTY STUDIES
☐ PHASE IV STUDIES
☐ DEFICIENCY LETTER RESPOE
☐ PROTOCOL-BIOPHARMACEUTICS
☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
☐ SUMMARY OF ADVERSE EXPERIENCE
☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL
☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

Please assess the Microbiology section of the NDA and the proposed draft labeling with regard to the proposed Microbiology and Clinical Pharmacology sections. If possible please forward comments to me before the filing meeting date of February 19, 2004. I apologize for the short notice. If you have any questions or need additional information, please contact me at x7-2049. I will bring up the volumes for review.

Thank you,
Melinda Harris

SIGNATURE OF REQUESTER
Melinda Harris, M.S.
Project Manager
7-2049

METHOD OF DELIVERY (Check one)
☐ MAIL ☐ XHAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

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/s/

Melinda Harris
2/9/04 09:00:46 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 21-709

Connetics Corporations
Attention: Sharon Hall
Senior Director, Regulatory Affairs
3290 West Bayshore Road
Palo Alto, CA 94303

Dear Ms. Hall:

Please refer to your December 22, 2003, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for ——— (clindamycin phosphate) Foam, 1%.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on February 19, 2004, in accordance with 21 CFR 314.101(a).

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

If you have any questions, call Melinda Harris, M.S., Regulatory Project Manager, at (301) 827-2020.

Sincerely,

{See appended electronic signature page}

Jonathan Wilkin, M.D.
Director
Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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/s/

Jonathan Wilkin
3/2/04 03:20:04 PM

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED:	**DESIRED COMPLETION DATE:**	**ODS CONSULT #:** 04-0230
August 18, 2004	October 13, 2004 **PDUFA DATE:** October 22, 2004	

TO: Jonathan Wilkin, MD
Director, Division of Dermatologic and Dental Drug Products
HFD-540

THROUGH: Melinda Harris
Project Manager
HFD-540

PRODUCT NAME:	**NDA SPONSOR:** Connetics Corporation
Evoclin (Clindamycin Phosphate Foam) 1% **NDA#: 21-709**	

SAFETY EVALUATOR: Kristina C. Arnwine, PharmD

RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Evoclin. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections based upon approval of other proprietary or established names from the signature date of this document.

2. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review to minimize potential errors with the use of this product.

3. DDMAC finds the proprietary name Evoclin acceptable from a promotional perspective.

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PROPRIETARY NAME REVIEW

DATE OF REVIEW: September 23, 2004

NDA#: 21-709

NAME OF DRUG: Evoclin (Clindamycin Phosphate Foam) 1%

NDA HOLDER: Connetics Corporations

I. INTRODUCTION:

This consult was written in response to a request from the Division of Dermatologic and Dental Drug Products (HFD-540), for assessment of the proprietary name, Evoclin, regarding potential name confusion with other proprietary or established drug names. Container labels, carton and insert labeling were provided for review and comment.

PRODUCT INFORMATION

Evoclin is a topical antibiotic, containing clindamycin phosphate, USP, delivered in VersaFoam. Evoclin is indicated for topical application in the treatment of acne vulgaris. The usual dose of Evoclin is to apply Evoclin once daily to the skin where acne lesions appear. Evoclin is supplied in a 50 gram can containing clindamycin phosphate equivalent to 10 mg clindamycin per gram.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2] as well as several FDA databases[3] for existing drug names which sound-alike or look-alike to Evoclin to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted[4]. The Saegis[5] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

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[1] MICROMEDEX Integrated Index, 2004, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[3] AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-04, and the electronic online version of the FDA Orange Book.
[4] WWW location http://www.uspto.gov/tmdb/index.html.
[5] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

A. EXPERT PANEL DISCUSSION (EPD)

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

1. DDMAC finds the proprietary name Evoclin acceptable from a promotional perspective.

2. The Expert Panel identified eight proprietary names that were thought to have the potential for confusion with Evoclin. These products are listed in table 1 (see below), along with the dosage forms available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	**Dosage form(s), Established name**	**Usual adult dose***	**Other****
Evoclin	Clindamycin Phosphate Foam 1 %	Apply once daily to skin where lesions appear. Use enough to cover the entire affected area.	
Esclim	Estradiol Transdermal Patch 0.0375 mg/24 hr, 0.05 mg/24 hr, 0.075 mg/24 hr, 0.1 mg/24 hr	Place patch on clean, dry area of the skin twice weekly.	LA
Levaquin	Levofloxacin Tablets: 250 mg, 500 mg, 750 mg Injection: 500 mg and 750 mg Concentrate Injection: 250 mg, 500 mg, and 750 mg premix bags	250 mg to 750 mg every 24 hours for 3 days to 28 days depending on indication	SA
Focalin	Dexmethylphenidate HCl Tablets 2.5 mg, 5 mg, 10 mg	Take one tablet by mouth twice daily	SA
Focalin XR***	Dexmethylphenidate HCl Tablets 5 mg, 10 mg, 20 mg, 30 mg, 40 mg	Take one tablet by mouth once daily.	
Edecrin	Ethacrynic Acid Tablets: 25 mg, 50 mg Powder for Injection: 50 mg	Initial Oral Dose: 50 to 200 mg once daily; Maintenance: 50 mg to 200 mg every other day, Parenteral: 50 mg once	SA
Elocon	Mometasone Furoate Ointment, Cream, and Lotion 0.1%	Apply to affected area 2 to 4 times daily	LA
EpiQuin Micro	Hydroquinone Cream 4%	Apply to affected skin twice daily.	SA
Epogen	Epoetin Alfa 2000 units/mL, 3000 units/mL, 4000 units/mL, 10,000 units/mL, 20,000 units/mL, and 40,000 units/mL	CRF pts: 50 to 100 units/kg 3 times/week IV or SC Surgery pts: 300 units/kg/day SC for 10 days before surgery Chemotherapy pts: 150 units/kg SC 3 times weekly	SA

*Frequently used, not all-inclusive.
**L/A (look-alike), S/A (sound-alike)

B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search module returns a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered to have significant phonetic or orthographic similarities to Evoclin were discussed by the Expert Panel (EPD).

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Evoclin with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 123 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Evoclin (see below). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: Evoclin apply qd as dir #1	"Prescription number two is Evoclin. Apply once a day as directed. Dispense #1."
Inpatient RX: Evoclin QD as dir	

2. Results:

Three respondents interpreted the proposed name as Eviquin and one respondent interpreted the name as Eviquen. Eviquin and Eviquen sound similar to the currently marketed product EpiQuin Micro.

E. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Evoclin, the primary concerns related to look-alike and sound-alike confusion with Esclim, Levaquin, Focalin, Focalin XR***, Edecrin, Elocon, EpiQuin Micro, and Epogen. Upon further review of the names gathered from EPD and POCA, the names Edecrin, Epogen, Focalin, and Focalin XR were not reviewed further due to a lack of convincing look-alike/sound-alike similarities with Evoclin in addition to numerous differentiating product characteristics such as product strength, indication for use, route of administration and dosage form. Additionally, DMETS conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, three respondents interpreted the proposed name as Eviquin and one respondent interpreted the name as Eviquen. Eviquin and Eviquen sound similar to the currently marketed product EpiQuin Micro. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Evoclin.

1. Evoclin can look similar to Esclim when scripted. Esclim is an estradiol transdermal system indicated for the treatment of moderate to severe vasomotor symptoms associated with menopause; treatment of hypoestrogenism caused by hypogonadism, castration, or primary ovarian failure; and vulvar and vaginal atrophy. Evoclin and Esclim both begin with the letter 'E,' which along with the similar endings ('clin' vs. 'clim') are the principal contributions to the look-alike characteristics of each name. However, the letters immediately following the 'E' in both names are different ('vo' vs. 's'). Evoclin and Esclim also differ in product characteristics such as dosage form (foam vs. transdermal patch), dosing frequency (once daily vs. twice weekly), usual dose (sufficient amount vs. one patch), product strength (1% vs. 0.0375 mg/24 hr, 0.05 mg/24 hr, 0.075 mg/24 hr, 0.1 mg/24 hr), and indication (acne vs. menopause, hypoestrogenism, castration, ovarian failure, vulvar and vaginal atrophy). Overall, the differences between the middle of each name and the product characteristics decrease the potential for medication errors.

2. Evoclin can sound similar to Levaquin when pronounced. Levaquin is a fluoroquinolone antibiotic indicated for the treatment of bronchitis, sinusitis, pyelonephritis, prostatitis, pneumonia, skin and skin structure infections, and urinary tract infections. Evoclin and Levaquin both have three syllables. The beginnings ('Evo' vs. 'Leva') and endings ('clin' vs. 'quin') of each name can rhyme depending on how they are pronounced which is the primary contribution to the sound-alike characteristics of each name. In addition, both names have three syllables. However, Evoclin and Levaquin do not overlap in product characteristics such as dosage form (foam vs. tablet and injection), route of administration (topical vs. oral and intravenous), usual dosage (sufficient amount vs. 250 mg to 750 mg), and product strength (1% vs. 250 mg, 500 mg, and 750 mg). Evoclin and Levaquin can overlap in dosing frequency (once daily). Overall, the differing product characteristics decrease the potential for medication errors due to name confusion between Evoclin and Levaquin.

3. Evoclin can look similar to Elocon when scripted. Elocon is a topical corticosteroid indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid responsive dermatoses. Elocon and Evoclin both begin with the letter 'E' and end with the letter 'n' which are the principal contributions to the look-alike characteristics. In addition, the letter 'o' is presented in a similar position (3rd) in each name. Both names contain the letter 'l,' however, it is presented in different positions in each name (2nd vs. 5th), which helps to differentiate the two names. Evoclin and Elocon overlap in route of administration (topical) and have overlapping numerals in their product strength (0.1% vs. 1%). Evoclin and Elocon differ in dosage form (foam vs. ointment, cream, or lotion) and dosage frequency (once daily vs. two to four times daily). Overall, the differences between the middle of each

name along with the differing product characteristics decrease the potential for medication errors.

4. Evoclin and EpiQuin Micro can sound similar when pronounced. EpiQuin Micro is a pigment agent indicated for the gradual bleaching of hyperpigmented skin conditions (e.g. freckles, senile lentigines, age spots, cholasma, and melasma) and other forms of melanin hyperpigmentation. EpiQuin Micro is also indicated for the gradual treatment of ultraviolet-induced dyschromia and discoloration resulting from the use of oral contraceptives, pregnancy, hormone replacement therapy, or skin trauma. EpiQuin Micro is the only available dosage form for this product. Thus the modifier may be omitted by prescribers increasing the potential for look-alike confusion between Evoclin and EpiQuin. This is because the modifier 'Micro' does not provide any differentiating product characteristics. Evoclin and EpiQuin both begin with the letter 'E.' In addition, although the last syllable of each are different, they do rhyme ('clin' vs. 'quin'). Furthermore, both products contain three syllables, which also contributes to the sound-alike similarities. However, the second syllable of each name is different ('vo' vs. 'pi'). Evoclin and EpiQuin overlap in route of administration (topical). Evoclin and EpiQuin do not overlap in dosage form (foam vs. cream) or product strength (1% vs. 4%). However, since these two products are each only available in one dosage form with one product strength, this information does not need to be specified in order to dispense a product. Furthermore, even though the approved dosing frequency of EpiQuin is twice daily, EpiQuin could possibly be prescribed for use at bedtime, in order to prevent photosensitivity, in which case Evoclin and EpiQuin could have overlapping dosing frequencies of once daily. In the prescription studies performed by DMETS, three respondents interpreted a verbal prescription for Evoclin as Eviquin and one respondent interpreted the name as Eviquen. Both of these responses sound similar to EpiQuin. DMETS feels that although the responses from the prescription study sound similar to EpiQuin, according to the results of the prescription studies, there were no positive findings that Evoclin was actually confused with EpiQuin. The difference between the beginnings of the names decreases the potential for medication errors due to name confusion between Evoclin and Epiquin.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, carton and insert labeling of Evoclin, DMETS has attempted to focus on safety issues relating to possible medication errors. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS

1. Revise the established name to read (Clindamycin Phosphate Foam).

2. DMETS notes the sponsor is proposing the same product layout for another pending topical foam product, [redacted]. Thus, it appears that the sponsor is potentially planning to use the same product layout for other products as well. Postmarketing surveillance has shown that similar labeling across manufacturers' product lines may result in medication errors. DMETS recommends that the sponsor differentiate each product label and labeling so that it is readily distinguishable from other topical foam products.

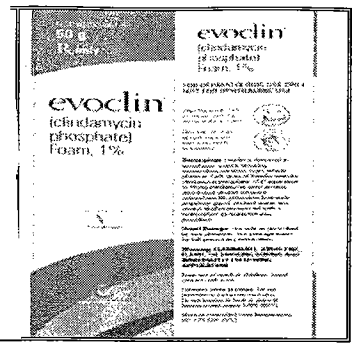

Figure 1.

Proposed carton labeling for

Evoclin.

3.

4.

B. PACKAGE INSERT LABELING (Instruction for applying Evoclin)

1.

2.

3.

4.

V. RECOMMENDATIONS:

A. DMETS has no objections to the use of the proprietary name Evoclin. This is considered a final decision. However, if the approval of this application is delayed beyond 90 days from the signature date of this document, the name must be re-evaluated. A re-review of the name will rule out any objections based upon approval of other proprietary or established names from the signature date of this document..

B. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review that might lead to safer use of the product. We would be willing to revisit these issues if the Division receives another draft of the labeling from the manufacturer.

C. DDMAC finds the proprietary name Evoclin acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, project manager, at 301-827-2102.

Kristina C. Arnwine, PharmD
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Attachment A

Verbal	Inpatient Written	Outpatient Written
Epiclens	Evaclen	Evoclin
Evaclin	Evoclen	Evoclin
Evaquin	Evoclen	Evoclin
Eviclin	Evoclen	Evoclin
Eviclin	Evoclen	Evoclin
Eviquen	Evoclin	Evoclin
Eviquin	Evoclin	Evoclin
Eviquin	Evodem	Evoclin
Eviquin	Evoden	Evoclin
Evoquin	Evoden	Evoclin
	Evoden	Evoclin
	Evoden	Evoclin
	Evoden	Evodin
	Evoden	Evodin
	Evodin	Evodin
	Evodin	Evodin
	Evodur	Evoilin
		Evolclin
		Ivoclin

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