

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-013

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

**PATENT INFORMATION SUBMITTED WITH THE
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**

*For Each Patent That Claims a Drug Substance
(Active Ingredient), Drug Product (Formulation and
Composition) and/or Method of Use*

NDA NUMBER

22-013

NAME OF APPLICANT / NDA HOLDER

Connetics Corporation

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

TRADE NAME (OR PROPOSED TRADE NAME)

Primolux

ACTIVE INGREDIENT(S)

Clobetasol Propionate

STRENGTH(S)

0.05%

DOSAGE FORM

Aerosol Foam

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4).

Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the *only* information relied upon by FDA for listing a patent in the Orange Book.

For hand-written or typewriter versions (only) of this report: If additional space is required for any narrative answer (i.e., one that does not require a "Yes" or "No" response), please attach an additional page referencing the question number.

FDA will not list patent information if you submit an incomplete patent declaration or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit all the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete above section and sections 5 and 6.

1. GENERAL

a. United States Patent Number

6,730,288 B1

b. Issue Date of Patent

05/04/2004

c. Expiration Date of Patent

09/08/2019

d. Name of Patent Owner

Connetics Australia Pty Ltd

Address (of Patent Owner)

8 Macro Court

City/State

Rowville, Victoria 3178

ZIP Code

Australia

FAX Number (if available)

+61 3 9763 0354

Telephone Number

+61 3 9763 0022

E-Mail Address (if available)

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States)

 Connetics Corporation

Address (of agent or representative named in 1.e.)

3160 Porter Drive

City/State

Palo Alto, California

ZIP Code

94304

FAX Number (if available)

(650) 843-2802

Telephone Number

(650) 739-2614

E-Mail Address (if available)

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above?

Yes

No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date?

Yes

No

For the patent referenced above, provide the following information on the drug substance, drug product and/or method of use that is the subject of the pending NDA, amendment, or supplement.

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? Yes No

2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? Yes No

2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). Yes No

2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.

2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) Yes No

2.6 Does the patent claim only an intermediate? Yes No

2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? Yes No

3.2 Does the patent claim only an intermediate? Yes No

3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.) Yes No

4. Method of Use

Sponsors must submit the information in section 4 separately for each patent claim claiming a method of using the pending drug product for which approval is being sought. For each method of use claim referenced, provide the following information:

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2 Claim Number (as listed in the patent) Does the patent claim referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? Yes No

4.2a If the answer to 4.2 is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product. Use: (Submit indication or method of use information as identified specifically in the proposed labeling.)

5. No Relevant Patents

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

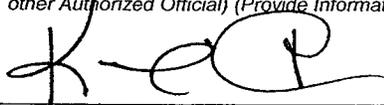
Yes

6. Declaration Certification

6.1 *The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.*

Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide Information below)



Date Signed

28 Feb 06

NOTE: Only an NDA applicant/holder may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant/holder is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).

Check applicable box and provide information below.

NDA Applicant/Holder

NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official

Patent Owner

Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name

Katrina J. Church, Executive Vice-President, Legal Affairs, Connetics Corporation

Address

3160 Porter Drive

City/State

Palo Alto, California

ZIP Code

94304

Telephone Number

(650) 739-2614

FAX Number (if available)

(650) 843-2802

E-Mail Address (if available)

The public reporting burden for this collection of information has been estimated to average 9 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:

Food and Drug Administration
CDER (HFD-007)
5600 Fishers Lane
Rockville, MD 20857

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.

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1.3.5.2 PATENT CERTIFICATION

Paragraph II Certification

Pursuant to 21 USC §355(b)(2)(A)(ii) and 21 CFR §314.50(i), Connetics Corporation certifies to the best of its knowledge that U.S. Patent Nos. 3,721,687 and 4,370,322, which claim clobetasol propionate drug substance, drug product, and method of use, owned by Glaxo Group Limited, expired on March 20, 1992 and October 5, 2001, respectively.



28 Feb 2006

Katrina J. Church
Executive Vice-President
Legal Affairs and General Counsel

Date

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EXCLUSIVITY SUMMARY

NDA # 22-013

SUPPL # n/a

HFD # 540

Trade Name Olux-E

Generic Name clobetasol propionate

Applicant Name Connetics Corporation

Approval Date, If Known 1/12/07

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 questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES 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 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 NO

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

Three years of exclusivity

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

YES NO

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

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 NO

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

NDA#	19-322	Temovate (clobetasol propionate) Cream, 0.05%
NDA#	19-323	Temovate (clobetasol propionate) Ointment, 0.05%
NDA#	19-966	Temovate (clobetasol propionate) Solution, 0.05%
	20-337	Temovate (clobetasol propionate) Gel, 0.05%
	20-340	Temovate E (clobetasol propionate) Cream, 0.05%
	21-142	OLUX (clobetasol propionate) Aerosol Foam, 0.05%
	21-535	Clobex (clobetasol propionate) Lotion, 0.05%
	21-644	Clobex (clobetasol propionate) Shampoo, 0.05%
	21-835	Clobex (clobetasol propionate) Spray, 0.05%

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

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

NDA#

NDA#

NDA#

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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 NDAs 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 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 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

(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

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

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:

Study #CPE.C.301
Study #CPE.C.302

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

Investigation #2 YES NO

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

n/a

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

Investigation #2

YES

NO

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

n/a

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"):

Study #CPE.C.301

Study #CPE.C.302

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 # 67,818

YES

!
!
! NO
! Explain:

Investigation #2

IND # 67,818

YES

!
!
! 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:

n/a

!

!

! NO

! Explain:

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Investigation #2

YES

Explain:

n/a

!

!

! 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

If yes, explain:

Name of person completing form: Margo Owens

Title: Project Manager

Date: 1/9/2007

Name of Office/Division Director signing form: Susan Walker, M.D.

Title: Division Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

Margaret Kober
1/12/2007 03:12:22 PM
signed for Dr. Walker

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PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA #: 22-013 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: 3/17/06 Action Date: 1/17/07

HFD 540 Trade and generic names/dosage form: Primolux™ (clobetasol propionate) Foam, 0.05%

Applicant: Connetics Corporation Therapeutic Class: 3S

Indication(s) previously approved:

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

Number of indications for this application(s): 1

Indication #1: Relief of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses

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

Yes: Please proceed to Section A.

No: Please check all that apply: 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. _____ yr. < 12 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
- 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. _____ yr. <18 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}

Margo Owens
Regulatory Project Manager

cc: NDA 22-013
HFD-960/ Grace Carmouze

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

(revised 12-22-03)

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

/s/

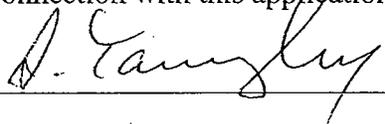
Stanka Kukich
5/11/2006 09:40:06 AM

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Debarment Certification

Clinical

Connetics Corporation 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.

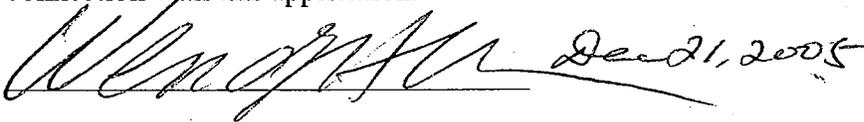


Alex Yaroshinsky, Ph.D.
Senior Director, Clinical Operations and Biostatistics

Date: Dec 22, 2005

Nonclinical

Connetics Corporation 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.



Wendy Chern, Ph.D.
Vice President, Research and Preclinical Development

Date:

Quality

Connetics Corporation 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.



Teresa Coleman
Senior Director, Corporate Compliance

Date: 09 Jan 06

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE
COVERSHEET

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: <http://www.fda.gov/cder/pdufa/default.htm>

<p>1. APPLICANT'S NAME AND ADDRESS</p> <p>CONNETICS CORP Zane Rogers Connetics Corporation 3160 Porter Drive Palo Alto CA 94304 US</p>	<p>4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER</p> <p>022013</p>
<p>2. TELEPHONE NUMBER</p> <p>650-7392908</p>	<p>5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?</p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p> <p>IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:</p> <p><input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION</p> <p><input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:</p>

<p>3. PRODUCT NAME</p> <p>Primolux (Emulsion Formulation Clobetasol Propionate Foam, 0.05%)</p>	<p>6. USER FEE I.D. NUMBER</p> <p>PD3006451</p>
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7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

<input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)	<input type="checkbox"/> A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE
<input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act	<input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? YES NO

Public reporting burden for this collection of information is estimated to average 30 minutes 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 CBER, HFM-99 1401 Rockville Pike Rockville, MD 20852-1448	Food and Drug Administration CDER, HFD-94 12420 Parklawn Drive, Room 3046 Rockville, MD 20852	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.
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<p>SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE</p> 	<p>TITLE</p> <p>VP Reg. Affairs</p>	<p>DATE</p> <p>27 Feb. 2006</p>
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9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION

\$767,400.00

(BE PRMT CLOSE G) (Print Cover sheet)

NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 22-013

Supplement #

Efficacy Supplement Type SE-

Trade Name: Primolux Foam

Established Name: Emulsion Formulation Clobetasol Propionate Foam

Strengths: 0.05%

Applicant: Connetics Corporation

Agent for Applicant: n/a

Date of Application: March 14, 2006

Date of Receipt: March 16, 2006

Date clock started after UN: n/s

Date of Filing Meeting: May 3, 2006

Filing Date: May 15, 2006

Action Goal Date (optional): January 17, 2007

User Fee Goal Date: January 17, 2007

Indication(s) requested:

Type of Original NDA: (b)(1) (b)(2)
OR
Type of Supplement: (b)(1) (b)(2)

NOTE:

- (1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. 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), complete Appendix B.
- (2) If the application is a supplement to an NDA, please indicate whether the NDA is a (b)(1) or a (b)(2) application:

NDA is a (b)(1) application OR NDA is a (b)(2) application

Therapeutic Classification: S P
Resubmission after withdrawal? Resubmission after refuse to file?
Chemical Classification: (1,2,3 etc.) 3
Other (orphan, OTC, etc.)

Form 3397 (User Fee Cover Sheet) submitted: YES NO

User Fee Status: Paid Exempt (orphan, government)
Waived (e.g., small business, public health)

NOTE: If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling.

Version: 12/15/2004

This is a locked document. If you need to add a comment where there is no field to do so, unlock the document using the following procedure. Click the 'View' tab; drag the cursor down to 'Toolbars'; click on 'Forms.' On the forms toolbar, click the lock/unlock icon (looks like a padlock). This will allow you to insert text outside the provided fields. The form must then be relocked to permit tabbing through the fields.

If you need assistance in determining if the applicant is claiming a new indication for a use, please contact the user fee staff.

- Is there any 5-year or 3-year exclusivity on this active moiety in an approved (b)(1) or (b)(2) application? YES NO
If yes, explain: There is existing 3-year exclusivity on two applications containing the active moiety clobetasol propionate. They are: NDA 21-644 for Clobex Shampoo (expires Feb. 05, 2007) and NDA 21-835 Clobex Spray (expires Oct. 27, 2008).

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

- 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)]? YES NO

If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

- Is the application affected by the Application Integrity Policy (AIP)? YES NO
If yes, explain:

- If yes, has OC/DMPQ been notified of the submission? YES NO

- Does the submission contain an accurate comprehensive index? YES NO

- Was form 356h included with an authorized signature? YES NO
If foreign applicant, both the applicant and the U.S. agent must sign.

- Submission complete as required under 21 CFR 314.50? YES NO
If no, explain: This is an eCTD. No TOC provided in the hard copy archival volume. However, a TOC is provided electronically in Module 1.

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

Additional comments:

- If an electronic NDA in Common Technical Document format, does it follow the CTD guidance? N/A YES NO

- Is it an electronic CTD (eCTD)? N/A YES NO
If an electronic CTD, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments: The entire application is submitted in electronic format. All forms and certifications requiring a signature were provided in paper.

- Patent information submitted on form FDA 3542a? YES 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 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 NO
(Forms 3454 and 3455 must be included and must be signed by the APPLICANT, not an agent.)
NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.
- Field Copy Certification (that it is a true copy of the CMC technical section)? Y NO
- PDUFA and Action Goal dates correct in COMIS? YES NO
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.
- List referenced IND numbers: 67,818
- End-of-Phase 2 Meeting(s)? Date(s) 11/29/04 NO
If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) 12/14/05 NO
If yes, distribute minutes before filing meeting.

Project Management

- Was electronic "Content of Labeling" submitted? YES NO
If no, request in 74-day letter.
- All labeling (PI, PPI, MedGuide, carton and immediate container labels) consulted to DDMAC? YES NO
- Risk Management Plan consulted to ODS/IO? N/A YES NO
- Trade name (plus PI and all labels and labeling) consulted to ODS/DMETS? Y NO
- MedGuide and/or PPI (plus PI) consulted to ODS/DSRCS? N/A YES NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling, submitted? N/A 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 YES NO
- Has DOTCDP been notified of the OTC switch application? YES NO

Clinical

- If a controlled substance, has a consult been sent to the Controlled Substance Staff? YES NO

Chemistry

- Did applicant request categorical exclusion for environmental assessment? YES NO
If no, did applicant submit a complete environmental assessment? YES NO
If EA submitted, consulted to Florian Zielinski (HFD-357)? YES NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES NO
- If a parenteral product, consulted to Microbiology Team (HFD-805)? YES NO

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Appendix A to NDA Regulatory Filing Review

An application is likely to be a 505(b)(2) application if:

- (1) it relies on literature to meet any of the approval requirements (unless the applicant has a written right of reference to the underlying data)
- (2) it relies on the Agency's previous approval of another sponsor's drug product (which may be evidenced by reference to publicly available FDA reviews, or labeling of another drug sponsor's drug product) to meet any of the approval requirements (unless the application includes a written right of reference to data in the other sponsor's NDA)
- (3) it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)
- (4) it seeks approval for a change from a product described in an OTC monograph and relies on the monograph to establish the safety or effectiveness of one or more aspects of the drug product for which approval is sought (see 21 CFR 330.11).

Products that may be likely to be described in a 505(b)(2) application include combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations), OTC monograph deviations, new dosage forms, new indications, and new salts.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, please consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007).

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**Appendix B to NDA Regulatory Filing Review
Questions for 505(b)(2) Applications**

1. Does the application reference a listed drug (approved drug)? YES NO

If "No," skip to question 3.

2. Name of listed drug(s) referenced by the applicant (if any) and NDA/ANDA #(s): Temovate Ointment, 0.05%, NDA 19-323

3. The purpose of this and the questions below (questions 3 to 5) is to determine if there is an approved drug product that is equivalent or very similar to the product proposed for approval and that should be referenced as a listed drug in the pending application.

- (a) Is there a pharmaceutical equivalent(s) to the product proposed in the 505(b)(2) application that is already approved?

YES NO

(Pharmaceutical equivalents are drug products in identical dosage forms that: (1) contain identical amounts of the identical active drug ingredient, i.e., the same salt or ester of the same therapeutic moiety, or, in the case of modified release dosage forms that require a reservoir or overage or such forms as prefilled syringes where residual volume may vary, that deliver identical amounts of the active drug ingredient over the identical dosing period; (2) do not necessarily contain the same inactive ingredients; and (3) meet the identical compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times, and/or dissolution rates. (21 CFR 320.1(c))

If "No," skip to question 4. Otherwise, answer part (b).

- (b) Is the approved pharmaceutical equivalent(s) cited as the listed drug(s)? YES NO
(The approved pharmaceutical equivalent(s) should be cited as the listed drug(s).)

If "Yes," skip to question 6. Otherwise, answer part (c).

- (c) Have you conferred with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007)? YES NO

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

4. (a) Is there a pharmaceutical alternative(s) already approved? YES NO

(Pharmaceutical alternatives are drug products that contain the identical therapeutic moiety, or its precursor, but not necessarily in the same amount or dosage form or as the same salt or ester. Each such drug product individually meets either the identical or its own respective compendial or other applicable standard of identity, strength, quality, and purity, including potency and, where applicable, content uniformity, disintegration times and/or dissolution rates. (21 CFR 320.1(d)) Different dosage forms and strengths within a product line by a single manufacturer are thus pharmaceutical alternatives, as are extended-release products when compared with immediate- or standard-release formulations of the same active ingredient.)

If "No," skip to question 5. Otherwise, answer part (b).

- (b) Is the approved pharmaceutical alternative(s) cited as the listed drug(s)? YES NO
(The approved pharmaceutical alternative(s) should be cited as the listed drug(s).) SEE

ATTACHMENT #1 for list of other pharmaceutical alternatives.

NOTE: If there is more than one pharmaceutical alternative approved, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (ORP) (HFD-007) to determine if the appropriate pharmaceutical alternatives are referenced.

If "Yes," skip to question 6. Otherwise, answer part (c).

- (c) Have you conferred with the Director, Division of Regulatory Policy II, ORP? YES NO

If "No," please contact the Director, Division of Regulatory Policy II, ORP. Proceed to question 6.

5. (a) Is there an approved drug product that does not meet the definition of "pharmaceutical equivalent" or "pharmaceutical alternative," as provided in questions 3(a) and 4(a), above, but that is otherwise very similar to the proposed product? YES NO

If "No," skip to question 6.

If "Yes," please describe how the approved drug product is similar to the proposed one and answer part (b) of this question. Please also contact the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007), to further discuss.

- (b) Is the approved drug product cited as the listed drug? YES NO
6. 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"). **This application provides for a change in dosage form of the reference listed drug, Temovate ointment, 0.05%, NDA 19-323.**
7. 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 (see 21 CFR 314.101(d)(9)).) YES NO
8. 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 21 CFR 314.101(d)(9)). YES NO
9. 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 21 CFR 314.54(b)(2))? If yes, the application should be refused for filing under 21 CFR 314.101(d)(9). YES NO
10. Are there certifications for each of the patents listed for the listed drug(s)? YES NO
11. Which of the following patent certifications does the application contain? (Check all that apply and identify the patents to which each type of certification was made, as appropriate.)

- 21 CFR 314.50(i)(1)(i)(A)(1): The patent information has not been submitted to FDA. (Paragraph I certification)
Patent number(s):

21 CFR 314.50(i)(1)(i)(A)(2): The patent has expired. (Paragraph II certification)
Patent number(s): 3,721,687 and 4,370,322 (SEE ATTACHMENT #2 for paragraph certification statement)

21 CFR 314.50(i)(1)(i)(A)(3): The date on which the patent will expire. (Paragraph III certification)
Patent number(s):

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. (Paragraph IV certification)
Patent number(s):

NOTE: IF FILED, and if the applicant made a "Paragraph IV" certification [21 CFR 314.50(i)(1)(i)(A)(4)], the applicant must **subsequently** submit a signed certification stating that the NDA holder and patent owner(s) were notified the NDA was filed [21 CFR 314.52(b)]. The applicant must also submit documentation showing that the NDA holder and patent owner(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 as described in the corresponding use code in the Orange Book. Applicant must provide a statement that the method of use patent does not claim any of the proposed indications. (Section viii statement)
Patent number(s):

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).
Patent number(s):

Written statement from patent owner that it consents to an immediate effective date upon approval of the application.
Patent number(s):

12. Did the applicant:

- Identify which parts of the application rely on information (e.g. literature, prior approval of another sponsor's application) that the applicant does not own or to which the applicant does not have a right of reference?
YES NO
- Submit a statement as to whether the listed drug(s) identified has received a period of marketing exclusivity?
YES NO
- Submit a bioavailability/bioequivalence (BA/BE) study comparing the proposed product to the listed drug?
N/A YES 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 YES NO

13. If the (b)(2) applicant is requesting 3-year exclusivity, did the applicant submit the following information required by 21 CFR 314.50(j)(4):

- Certification that at least one of the investigations included meets the definition of "new clinical investigation" as set forth at 314.108(a).
YES 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 NO

- EITHER

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

IND# 67,818 NO

OR

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

YES NO

14. Has the Associate Director for Regulatory Affairs, OND, been notified of the existence of the (b)(2) application?

YES NO

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NDA Regulatory Filing Review
NDA 22-013 Primolux (clobetasol propionate) Foam, 0.05%

ATTACHMENT 1

List of other pharmaceutical alternatives for Primolux (clobetasol propionate) Foam, 0.05% (not including the reference listed drug, Temovate Ointment, 0.05%, NDA 19-323)

Olux (clobetasol propionate) Foam, 0.05%	NDA 21-142
Temovate E (clobetasol propionate) Cream, 0.05%	NDA 20-340
Temovate (clobetasol propionate) Gel, 0.05%	NDA 20-337
Clobex (clobetasol propionate) Lotion, 0.05%	NDA 21-535
Temovate (clobetasol propionate) Cream, 0.05%	NDA 19-322
Clobex (clobetasol propionate) Shampoo, 0.05%	NDA 21-644
Temovate (clobetasol propionate) Solution, 0.05%	NDA 19-966
Clobex (clobetasol propionate) Spray, 0.05%	NDA 21-835

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ATTACHMENT 2

(Applicant's Patent Certification Statement – Paragraph II)

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13.5.2 PATENT CERTIFICATION

Paragraph 3 Certification

Pursuant to 21 USC §355(b)(2)(A)(ii) and 21 CFR §314.50(f), Connetics Corporation certifies to the best of its knowledge that U.S. Patent Nos. 3,721,687 and 4,370,322, which claim clobetasol propionate drug substance, drug product, and method of use, owned by Glaxo Group Limited, expired on March 20, 1992 and October 5, 2001, respectively.



Katrina J. Church
Executive Vice-President
Legal Affairs and General Counsel

20 Feb 2006

Date

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

/s/

Margo Owens
1/9/2007 04:59:10 PM
CSO

Revised RPM filing review

Margaret Kober
1/11/2007 10:54:17 AM
CSO

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REQUEST FOR CONSULTATION

TO (Division/Office):
**Director, Division of Medication Errors and
Technical Support (DMETS), HFD-420
WhiteOak**

FROM:
**Margo Owens
Project Manager
Division of Dermatologic and Dental Products,
HFD-540**

DATE
12/22/06

IND NO.

NDA NO.
22-013

TYPE OF DOCUMENT
New NDA

DATE OF DOCUMENT
Dec. , 2006

NAME OF DRUG
TRADENAME (Emulsion
clobetasol propionate) Foam,
0.05%

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG
3S

DESIRED COMPLETION DA
Action target – Jan. 12, 2007
PDUFA – 1/16/2007

NAME OF FIRM: Connetics Corporation

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE--NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> SAFETY/EFFICACY | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> PAPER NDA | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | | Trade name review #4 |

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- | | |
|--|---|
| <input type="checkbox"/> TYPE A OR B NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END OF PHASE II MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|---|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE IV STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG EXPERIENCE

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

V. SCIENTIFIC INVESTIGATIONS

CLINICAL

PRECLINICAL

COMMENTS, CONCERNS, and/or SPECIAL INSTRUCTIONS:

Please note, the applicant has submitted a new proposed tradename for your review. Please review the new proposed tradenames Olux-E. The Sponsor has not submitted a Patient Package Insert.

PDUFA DATE: January 16, 2007

ATTACHMENTS:

Archival NDA 22-013
HFD-540/RPM, Margo Owens
HFD-540/Patricia Brown, M.D., Medical Officer
Jill Lindstrom, M.D., Lead Medical Officer

SIGNATURE OF REQUESTER
Margo Owens

METHOD OF DELIVERY (Check one)
 MAIL HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

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18 December 2006

Susan J. Walker, MD, Director
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatologic & Dental Drug Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

**RE: NDA 22-013/Amendment 019
EF Clobetasol Foam, 0.05%
Request for Change in Proposed Trade Name to Olux-ETM**

Attention: Margo Owens, Regulatory Project Manager (HFD-540)

Dear Dr. Walker:

Connetics Corporation (Connetics) is requesting a change to the proposed trade name EF Clobetasol Foam, 0.05%, NDA 22-013. As agreed with the Agency during the 18 December 2006 teleconference, Olux-ETM is the newly proposed tradename that replaces all previously submitted names. Connetics will submit can and carton labels as soon as they are available which is anticipated to be during the week of 18 December 2006.

The amendment is being submitted in electronic format with an approximate size of 1 MB. Connetics certifies that this electronic submission is virus-free. This submission was scanned by Symantec AntiVirus Corporate Edition version 10.1 prior to submission.

If you have questions concerning this submission, you may contact me at (650) 843-2829 or Edward F. Smith III, Senior Director, Regulatory Affairs at (650) 739-2688. The Regulatory Affairs facsimile number is (650) 843-2802.

Sincerely,

Darlene O'Banion
Senior Manager, Regulatory Affairs

DEPARTMENT OF HEALTH AND HUMAN SERVICES FOOD AND DRUG ADMINISTRATION APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE <i>(Title 21, Code of Federal Regulations, Parts 314 & 601)</i>		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 Connetics Corporation		DATE OF SUBMISSION 12/18/2006
TELEPHONE NO. (Include Area Code) 650-843-2829		FACSIMILE (FAX) Number (Include Area Code) 650-843-2802
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 3160 Porter Drive Palo Alto, CA 94304		AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE
PRODUCT DESCRIPTION		
NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) <u>22-013</u>		
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) EF Clobetasol Propionate Foam, 0.05%		PROPRIETARY NAME (trade name) IF ANY
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any) 21-Chloro-9-fluoro-11β,17-dihydroxy-16β-methylpregna-1,4-diene-3, 20-dione 17-propionate		CODE NAME (if any)
DOSAGE FORM: Foam, Aerosol	STRENGTHS: 0.05%	ROUTE OF ADMINISTRATION: Topical
(PROPOSED) INDICATION(S) FOR USE: Relief of inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses		
APPLICATION DESCRIPTION		
APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)		
IF AN NOA, IDENTIFY THE APPROPRIATE TYPE <input type="checkbox"/> 505 (b)(1) <input checked="" type="checkbox"/> 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 <u>Temovate Ointment, 0.05%</u> Holder of Approved Application <u>Glaxo Smith Kline</u>		
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER		
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____		
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)		
REASON FOR SUBMISSION Request for Change in Proposed Trade Name to Olux-E		
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)		
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input checked="" type="checkbox"/> 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. Not applicable to this submission		
Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application) Not applicable to this submission		

This application contains the following items: *(Check all that apply)*

<input type="checkbox"/>	1. Index
<input type="checkbox"/>	2. Labeling <i>(check one)</i> <input type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input checked="" type="checkbox"/>	20. OTHER <i>(Specify)</i> Request for Change in Proposed Trade Name to Olux-E

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, 810, 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 <i>Darlene O'Banion</i>		TYPED NAME AND TITLE Darlene O'Banion	DATE: 12/18/2006
ADDRESS (Street, City, State, and ZIP Code) 3160 Porter Drive, Palo Alto, CA 94304		Telephone Number (650) 843-2829	

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:

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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

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Margo Owens
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Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

Date: November 15, 2006

To: Darlene O'Banion/Ed Smith
Connetics Corporation

Phone: (650) 739-2688
Fax: (650) 843-2802

From: Margo Owens, Project Manager
Phone: (301) 796-2110
Fax: (301) 796-9894 or 9895

This transmission includes 3 pages (including this page)

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FDA Facsimile Memorandum

Date: November 15, 2006
To: Darlene O'Banion/Edward Smith
Regulatory Affairs
Connetics Corporation
From: Margo Owens, Project Manager
Subject: NDA 22-013 Primolux (clobetasol propionate) Foam, 0.05%

The Clinical Reviewer has the following informational request for your NDA 22-013 Primolux (clobetasol propionate) Foam, 0.05%.

Clinical Informational Request:

Please submit samples of the product, both active (EF Clobetasol .05%) foam and vehicle foam to the following address:

Margo Owens
Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food and Drug Administration
Building 22/Room 5165
10903 New Hampshire Ave.
Silver Spring, MD 20903

Please call if you have questions.

Margo Owens
Project Manager

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

FACSIMILE TRANSMITTAL SHEET

Date: November 13, 2006

To: Darlene O'Banion/Ed Smith
Connetics Corporation

Phone: (650) 843-2829
Fax: (650) 843-2802

From: Margo Owens, Project Manager
Phone: (301) 796-2110
Fax: (301) 796-9894 or 9895

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FDA Facsimile Memorandum

Date: November 13, 2006
To: Darlene O'Banion/Edward Smith
Regulatory Affairs
Connetics Corporation
From: Margo Owens, Project Manager
Subject: NDA 22-013 Primolux (clobetasol propionate) Foam, 0.05%

Ms. O'Banion and Mr. Smith,

The Division of Dermatology and Dental Products, Division of Medication Errors and Technical Support (DMETS), and the Division of Drug Marketing, Advertising, and Communications (DDMAC) have concluded their review of the proposed tradename, Primolux Foam, 0.05% and have requested that the following comments be conveyed to you regarding your NDA 22-013 Primolux (clobetasol propionate) Foam, 0.05%.

DDMAC Comments:

DDMAC objects to the proposed name Primolux (clobetasol foam, 0.05%) because it overstates the efficacy of the drug product by misleadingly implying it is superior to other treatment options. Primolux can be broken down into two parts, "primo" and "lux." Primo has various definitions consistent with "the first or leading part." Similarly, primo is recognized as a slang term meaning "of the finest quality, excellent" or "exceptionally good of its kind, first class; highly or most valuable." (www.m-w.com/cgi-bin/dictionary/primo, <http://www.bartleby.com/61/98/P0559800.html>; accessed 11/08/06). Therefore the proposed trade name misleadingly implies that this clobetasol formulation is better than competitor products, in particular **Olux** (clobetasol foam, 0.05%) and **Luxiq** (betamethasone foam, 0.12%) when this has not been demonstrated by substantial evidence or substantial clinical experience. In absence of substantial evidence to support that this particular clobetasol foam formulation is superior to other corticosteroid foam formulations, the proposed trade name is misleading.

Division of Dermatology and Dental Products Comments:

The Division concurs with DDMAC's objection to the proposed name Primolux (clobetasol propionate) Foam, 0.05%.

DMETS Comments:

DMETS has no objections to the use of the proprietary name, Primolux™.

Please submit additional proposed trade names as soon as possible. You may send your additional trade names to my attention via email or other expedited means to expedite the process (followed by an official submission).

Please call if you have questions.

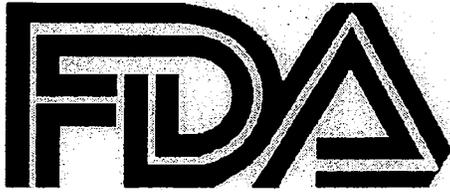
Margo Owens
Project Manager

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FACSIMILE TRANSMITTAL SHEET

Date: October 26, 2006

To: Darlene O'Banion/Ed Smith
Connetics Corporation

Phone: (650) 843-2829
Fax: (650) 843-2802

From: Margo Owens, Project Manager
Phone: (301) 796-2110
Fax: (301) 796-9894 or 9895

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FACSIMILE TRANSMITTAL SHEET

Date: October 19, 2006

To: Darlene O'Banion/Ed Smith
Connetics Corporation

Phone: (650) 843-2829
Fax: (650) 843-2802

From: Margo Owens, Project Manager
Phone: (301) 796-2110
Fax: (301) 796-9894 or 9895

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FDA Facsimile Memorandum

Date: October 19, 2006
To: Darlene O'Banion/Edward Smith
Regulatory Affairs
Connetics Corporation
From: Margo Owens, Project Manager
Subject: NDA 22-013 Primolux (clobetasol propionate) Foam, 0.05%

Ms. Obanion,

The Chemistry Reviewer has the following information request for your NDA 22-013 Primolux (clobetasol propionate) Foam, 0.05%.

CMC Information Request:

1. Tighten the acceptance criterion for "Pressure" in the drug product specification to reflect the actual batch data. To be consistent with the similar approved products, an acceptance criterion of NLT \leftarrow is recommended.
2. All the hand-written corrections in the executed batch record should be incorporated in the master batch record.
3. Include detailed instructions in the master batch record for the visual inspection for oil phase, water phase, and active phase to check for completion of dissolution.
4. The submitted executed batch record contained the product name as Olux E Aerosol Foam. The product name should be corrected to Primolux.

Please submit your response no later than COB Friday, October 20, 2006.

Please call if you have questions.

Margo Owens
Project Manager

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FACSIMILE TRANSMITTAL SHEET

Date: October 17, 2006

To: Darlene O'Banion/Ed Smith
Connetics Corporation

Phone: (650) 843-2829
Fax: (650) 843-2802

From: Margo Owens, Project Manager
Phone: (301) 796-2110
Fax: (301) 796-9894 or 9895

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FDA Facsimile Memorandum

Date: October 17, 2006
To: Darlene O'Banion/Edward Smith
Regulatory Affairs
Connetics Corporation
From: Margo Owens, Project Manager
Subject: NDA 22-013 Primolux (clobetasol propionate) Foam, 0.05%

Ms. Obanion,

The Clinical Reviewer has the following information request for your NDA 22-013 Primolux (clobetasol propionate) Foam, 0.05%.

Clinical Information Request:

In the protocols for the Phase 3 studies, CPE.C.301 and 302, it is stated that study drug kits contained two cans of EF Clobetasol Foam or Vehicle Foam (study 301) or two cans of either EF Clobetasol Foam or Vehicle Foam or two tubes of Temovate Ointment (study 302). Did each study recipient receive one kit? How many grams of study drug were in the cans?

Please submit your response no later than COB Wednesday, October 18, 2006.

Please call if you have questions.

Margo Owens
Project Manager

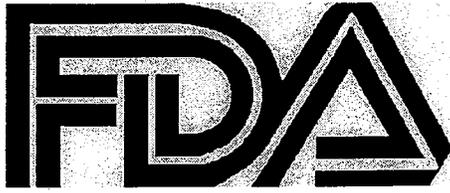
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Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: September 25, 2006

To: Darlene O'Banion	From: Margo Owens Project Manager
Company: Connetics Corporation	Division of Dermatologic & Dental Drug Products
Fax number: (650) 843-2802	Fax number: (301) 796-9894
Phone number: (650) 843-2829	Phone number: (301) 796-0966

Subject: NDA 22-013 Primolux (clobetasol propionate) Foam

Total no. of pages including cover: 13

Comments: The CMC reviewer has the following informational request. Please submit your response no later than Friday, Sept. 25, 2006.

Chemistry, Manufacturing and Controls Informational Request:

Drug product specification:

1. A test for 'Total Combined Yeasts and Molds Count' should be included in the microbial limits test with an acceptance criterion.
2. The acceptance criteria for each of the specified related substances should be revised to NMT ~~0.5%~~, because the proposed acceptance criterion of ~~0.5%~~ exceeds the ICH Q3B(R) recommended total daily intake (TDI) limit of 50 µg for qualification threshold. Otherwise, the proposed acceptance criteria for the specified related substances should be justified based on the safety data.
3. The acceptance criterion for "any unspecified related substance" should be revised to NMT ~~0.5%~~, because the proposed acceptance criterion of 0.5% exceeds the ICH Q3B(R) recommended TDI limit of 20 µg for identification threshold.

Document to be mailed:

YES

NO

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Center for Drug Evaluation and Research
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: August 10, 2006

To: Darlene O'Banion	From: Margo Owens Project Manager
Company: Connetics Corporation	Division of Dermatologic & Dental Drug Products
Fax number: (650) 843-2802	Fax number: (301) 796-9894
Phone number: (650) 843-2829	Phone number: (301) 796-0966
Subject: NDA 22-013 Primolux (clobetasol propionate) Foam	

Total no. of pages including cover: 1 (2)

Comments:

Please submit timelines, including protocol submission, study initiation and completion and final report submission, for the dermal carcinogenicity and photocarcinogenicity studies to be conducted post-marketing.

Document to be mailed: YES NO

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Margo Owens
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MEMORANDUM OF TELECON

DATE: August 30, 2006

APPLICATION NUMBER: NDA 22-013, PRIMOLUX FOAM 0.05%

BETWEEN:

Name: Michael S. Eison, Ph.D., Vice President, Regulatory Affairs
Matt Foehr, Senior Vice President, Technical Operations
Darlene O'Banion, Senior. Manager Regulatory Affairs
Katy Morton, Senior. Director Regulatory Affairs, CMC
Phone: 650 739-2708
Representing: Connetics

AND

Name: Rao Puttagunta, Ph.D., Chemist
Shulin Ding, Ph.D., Pharmaceutical Assessment Lead
Linda Athey, Regulatory Project Manager for Quality
Division of Pre-Marketing Assessment II, Branch III

SUBJECT: Established name.

BACKGROUND:

Connetics would like to use ' _____' as the dosage form in the drug product established name "Primolux™ (clobetasol propionate) _____, 0.05%".

CALL: The T-con took place at the request of the reviewing chemist, Rao Puttagunta, and concurrence of the Branch Chief. Dr. Rao Puttagunta told the firm that the revised drug product established name was not acceptable for its proposed dosage form "_____" . The drug product established name proposed in the original submission, Primolux™ (clobetasol propionate) foam, 0.05%, was acceptable. Dr. Shulin Ding explained that the addition of the word " _____" as a modifier for the dosage form ' _____' was unacceptable because " _____" was not a recognized topical dosage form in CDER Data Standards Manual, whereas "foam" was a recognized topical dosage form. Furthermore, the use of such a modifier to a dosage form in the established name would normally not be considered by the Agency unless the modifier carried pharmacokinetic significance (i.e., change the pharmacokinetic profile of the active ingredient). Since the firm had not provided any pharmacokinetic information to support its proposal, the addition of the word " _____" to the dosage form was not accepted.

The firm noted that CDER Data Standards Manual listed many dosage form names. Dr. Ding responded that only selective dosage form names listed in the Manual could be used in the drug product established name.

The firm wishes to add the modifier to the trade name. Dr. Ding responded that the acceptability of a trade name was reviewed and determined by the Division of Medication Errors and Technical Support (DMETS). If the firm wanted to change the trade name, a formal amendment should be submitted.

Connetics stated that there are other products with a modifier description in the trade name and will send references showing this. The sponsor agreed to change the dosage form back to the original submitted one and the established name would be, "Trade NameTM (clobetasol propionate) foam, 0.05%".

The meeting ended amicable. The sponsor will submit an amendment to the file and send an electronic copy to Linda Athey, FDA's Regulatory Health Project Manager for Quality.

{See appended electronic signature page}

Linda Athey
Regulatory Health Project Manager for Quality

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Linda D Mullins-Athey
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PROJECT MANAGER FOR QUALITY

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**Food and Drug Administration
Center for Drug Evaluation and Research
Office of Drug Evaluation III**

FACSIMILE TRANSMITTAL SHEET

DATE: August 10, 2006

To: Darlene O'Banion	From: Margo Owens Project Manager
Company: Connetics Corporation	Division of Dermatologic & Dental Drug Products
Fax number: (650) 843-2802	Fax number: (301) 796-9894
Phone number: (650) 843-2829	Phone number: (301) 796-0966
Subject: NDA 22-013 Primolux (clobetasol propionate) Foam	

Total no. of pages including cover: 1

Comments:

Please submit timelines, including protocol submission, study initiation and completion and final report submission, for the dermal carcinogenicity and photocarcinogenicity studies to be conducted post-marketing.

Document to be mailed: YES NO

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Margo Owens
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Linda D Mullins-Athey
8/8/2006 11:10:49 AM
PROJECT MANAGER FOR QUALITY

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ATTACHMENT

MEMO OF FILING MEETING

DATE: 5/3/06

BACKGROUND: Primolux (clobetasol propionate) Foam, 0.05% is a 505(b)(2) NDA application for the treatment of inflammatory and pruritic manifestation of corticosteroid-responsive dermatoses. This application submitted in eCTD format. The reference listed drug is Temovate Ointment, 0.05%, NDA 19-323. The following applications are cross-referenced in this NDA:

Currently approved - NDA 20-934, Luxiq; NDA 21-142, Olux Foam, and NDA 50-801, Evoclin. Under review - NDA 21-978, Desonide Foam. The Package Insert for NDA 21-644 Clobex Shampoo is also referenced.

ATTENDEES: Shulin Ding, Ph.D., Carmen Booker, Ph.D., Sue Chih Lee, Ph.D., Dennis Bashaw, Pharm.D., Patricia Brown, M.D., Jill Lindstrom, M.D., Kathleen Fritsch, Ph.D., Mohamed Aloh, Ph.D.

ASSIGNED REVIEWERS (including those not present at filing meeting) :

<u>Discipline</u>	<u>Reviewer</u>	<u>Review Date</u>
Medical:	Patricia Brown, M.D.	November 1, 2006
Secondary Medical:	Jill Lindstrom, M.D.	
Statistical:	Kathleen Fritsch, Ph.D.	November 1, 2006
Pharmacology:	Carmen Booker, Ph.D.	October 13, 2006
Statistical Pharmacology:	n/a	
Chemistry:	Rao Puttagunta, Ph.D.	Mid-November
Environmental Assessment (if needed):		
Biopharmaceutical:	Sue Chih Lee, Ph.D.	Mid-November
Microbiology, sterility:	n/a	
Microbiology, clinical:	n/a	
DSI:	n/a	
Regulatory Project Management:	Margo Owens	
Other Consults:	n/a	

English or English translation? YES NO

If no, explain:

CLINICAL REFUSE TO
 FILE FILE

- Clinical site inspection needed? YES NO
- Advisory Committee Meeting needed? YES, NO

NDA 22-013 Primolux (clobetasol propionate) Foam, 0.05%

- 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 YES NO

CLINICAL MICROBIOLOGY FILE REFUSE TO
N/A FILE

STATISTICS FILE REFUSE TO
N/A FILE

BIOPHARMACEUTICS REFUSE TO
FILE FILE

- Biopharm. inspection needed?
YES NO

PHARMACOLOGY FILE REFUSE TO
N/A FILE

- GLP inspection needed?
YES NO

CHEMISTRY REFUSE TO
FILE FILE

- Establishment(s) ready for inspection?
YES NO
- Microbiology
YES NO

ELECTRONIC SUBMISSION:

Any comments: This application was submitted in eCTD format.

REGULATORY CONCLUSIONS/DEFICIENCIES:

(Refer to 21 CFR 314.101(d) for filing requirements.)

- The application is unsuitable for filing. Explain why:
- The application, on its face, appears to be well-organized and indexed. The application appears to be suitable for filing.
 - No filing issues have been identified.
 - Filing issues to be communicated by Day 74. List (optional):
Biostatistics

- 1) In the psoriasis study, the incorrect IGA scale was initially distributed to the sites. The Application will be asked to provide more information on this issue.
- 2) The Applicant will be asked to provide more specific information on the protocol deviations identified in the pivotal studies.
- 3) The Applicant will be asked to provide their rationale for changing the inclusion criteria during the course of the pivotal studies.

ACTION ITEMS:

1. If RTF, notify everybody who already received a consult request of 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. Convey document filing issues/no filing issues to applicant by Day 74.

Margo Owens
Regulatory Project Manager, HFD-540

Jill Lindstrom, M.D.
Acting Deputy Division Director, HFD-540

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

/s/

Margo Owens
5/24/2006 01:30:23 PM
CSO

Jill Lindstrom
5/24/2006 02:58:16 PM
MEDICAL OFFICER

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ACTION PACKAGE CHECKLIST

Application Information

BLA # NDA # 22-013	BLA STN# NDA Supplement # n/a	If NDA, Efficacy Supplement Type n/a
Proprietary Name: Olux-E Established Name: clobetasol propionate Dosage Form: Foam, 0.05%		Applicant: Connetics Corporation
RPM: Margo Owens		Division: Dermatology and Dental Products Phone # 301-796-2110
<p>NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" type="checkbox"/> 505(b)(2)</p> <p>Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)</p> <p>(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). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p>		<p>505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)):</p> <p>Temovate (clobetaol propionate) Ointment, 0.05% - NDA 19-323</p> <p>Provide a brief explanation of how this product is different from the listed drug. Different dosage form</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct.</p> <p><input checked="" type="checkbox"/> Confirmed <input type="checkbox"/> Corrected Date: 12/4/2007</p>
❖ User Fee Goal Date		1/16/2007
❖ Action Goal Date (if different)		
❖ Actions		
• Proposed action		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA <input type="checkbox"/> CR
• Previous actions (specify type and date for each action taken)		<input checked="" type="checkbox"/> None
❖ Advertising (approvals only) Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed (indicate dates of reviews)		<input checked="" type="checkbox"/> Requested in AP letter <input type="checkbox"/> Received and reviewed

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❖ Application Characteristics	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): 3	
NDAs, BLAs and Supplements: <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> CMA Pilot 1 <input type="checkbox"/> CMA Pilot 2 <input type="checkbox"/> Orphan drug designation	
NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies	BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies
NDAs and NDA Supplements: <input type="checkbox"/> OTC drug Other: Other comments:	
❖ Application Integrity Policy (AIP)	
<ul style="list-style-type: none"> Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> This application is on the AIP <ul style="list-style-type: none"> Exception for review (<i>file Center Director's memo in Administrative Documents section</i>) OC clearance for approval (<i>file communication in Administrative Documents section</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> No <input checked="" type="checkbox"/> Yes <input type="checkbox"/> Not an AP action
❖ Public communications (approvals only)	
<ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> Press Office notified of action 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	<input checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

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<p>❖ Exclusivity</p>	
<ul style="list-style-type: none"> • NDAs: Exclusivity Summary (approvals only) (<i>file Summary in Administrative Documents section</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> • Is approval of this application blocked by any type of exclusivity? <ul style="list-style-type: none"> • NDAs/BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> • NDAs: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? (<i>Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.</i>) • NDAs: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (<i>Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.</i>) • NDAs: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? (<i>Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.</i>) 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # and date exclusivity expires: <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA # and date exclusivity expires: <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA # and date exclusivity expires: <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA # and date exclusivity expires:
<p>❖ Patent Information (NDAs and NDA supplements only)</p>	
<ul style="list-style-type: none"> • Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> • Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. • [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	21 CFR 314.50(i)(1)(i)(A) <input checked="" type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input checked="" type="checkbox"/> (ii) <input type="checkbox"/> (iii) <input type="checkbox"/> No paragraph III certification Date patent will expire
<ul style="list-style-type: none"> • [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). (<i>If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (Summary Reviews).</i>) • [505(b)(2) applications] For each paragraph IV certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. <p>Answer the following questions for each paragraph IV certification:</p> <p>(1) Have 45 days passed since the patent owner's receipt of the applicant's</p>	<input type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified <input type="checkbox"/> Yes <input type="checkbox"/> No

notice of certification?

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "Yes," skip to question (4) below. If "No," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (5).

- (5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced

<p>within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.</i></p>	
Summary Reviews	
❖ Summary Reviews (e.g., Office Director, Division Director) (indicate date for each review)	Pharm/Tox Supervisory memo - 11/20/06 Clinical Team Leader - 1/12/07
❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) (indicate date)	n/a
Labeling	
❖ Package Insert	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	n/a
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	1/13/07
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	3/14/06
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	n/a
❖ Patient Package Insert	
<ul style="list-style-type: none"> • Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	n/a
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	n/a
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	n/a
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable 	n/a
❖ Medication Guide	
<ul style="list-style-type: none"> • Most recent division-proposed labeling (only if generated after latest applicant submission of labeling) 	n/a
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version) 	n/a
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	n/a
<ul style="list-style-type: none"> • Other relevant labeling (e.g., most recent 3 in class, class labeling) 	n/a
❖ Labels (full color carton and immediate-container labels)	
<ul style="list-style-type: none"> • Most-recent division-proposed labels (only if generated after latest applicant submission) 	
<ul style="list-style-type: none"> • Most recent applicant-proposed labeling 	12/20/06

❖ Labeling reviews and minutes of any labeling meetings (<i>indicate dates of reviews and meetings</i>)	<input checked="" type="checkbox"/> DMETS Reviews- 9/22/06; 1/8/2007. <input type="checkbox"/> DSRCS n/a <input checked="" type="checkbox"/> DDMAC Reviews: 9/22/06, 1/8/2007 <input type="checkbox"/> SEALD n/a <input type="checkbox"/> Other reviews n/a <input type="checkbox"/> Memos of Mtgs none
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Administrative Documents

❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) (<i>indicate date of each review</i>)	RPM Filing Review/Memo of Filing - 5/24/06 Revised RPM Filing Review - 505B2 Clearance - 1/4/2007
❖ NDA and NDA supplement approvals only: Exclusivity Summary (<i>signed by Division Director</i>)	<input checked="" type="checkbox"/> Included
❖ AIP-related documents <ul style="list-style-type: none"> • Center Director's Exception for Review memo • If AP: OC clearance for approval 	n/a n/a
❖ Pediatric Page (all actions)	<input checked="" type="checkbox"/> Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent. (<i>Include certification.</i>)	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Postmarketing Commitment Studies	<input type="checkbox"/> None
<ul style="list-style-type: none"> • Outgoing Agency request for post-marketing commitments (<i>if located elsewhere in package, state where located</i>) 	8/10/06
<ul style="list-style-type: none"> • Incoming submission documenting commitment 	9/11/06
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	Faxes; - 8/10/06; 9/25/06; 10/17/06; 10/19/06; 10/26/06; 11/13/06; 11/15/06. Telecon- 8/7/06
❖ Internal memoranda, telecons, email, etc.	n/a
❖ Minutes of Meetings	n/a
<ul style="list-style-type: none"> • Pre-Approval Safety Conference (<i>indicate date; approvals only</i>) 	n/a
<ul style="list-style-type: none"> • Pre-NDA/BLA meeting (<i>indicate date</i>) 	<input type="checkbox"/> No mtg 12/14/05
<ul style="list-style-type: none"> • EOP2 meeting (<i>indicate date</i>) 	<input type="checkbox"/> No mtg 11/29/04
<ul style="list-style-type: none"> • Other (e.g., EOP2a, CMC pilot programs) 	11/24/06 Guidance meeting
❖ Advisory Committee Meeting	<input checked="" type="checkbox"/> No AC meeting
<ul style="list-style-type: none"> • Date of Meeting 	
<ul style="list-style-type: none"> • 48-hour alert or minutes, if available 	
❖ <u>Federal Register</u> Notices, DESI documents, NAS/NRC reports (if applicable)	

CMC/Product Quality Information

❖ CMC/Product review(s) (<i>indicate date for each review</i>)	12/11/06; 12/13/06; 12/15/06; 1/11/07
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ BLAs: Product subject to lot release (APs only)	<input type="checkbox"/> Yes <input type="checkbox"/> No
Environmental Assessment (check one) (original and supplemental applications)	

<ul style="list-style-type: none"> <input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(all original applications and all efficacy supplements that could increase the patient population) 	12/11/06
<ul style="list-style-type: none"> <input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>) 	n/a
<ul style="list-style-type: none"> <input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>) 	n/a
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) (<i>indicate date of each review</i>)	n/a
❖ Facilities Review/Inspection	<input checked="" type="checkbox"/> Not a parenteral product
❖ NDAs: Facilities inspections (include EER printout)	Date completed: 12/14/06 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation

<ul style="list-style-type: none"> ❖ BLAs: Facility-Related Documents <ul style="list-style-type: none"> Facility review (<i>indicate date(s)</i>) Compliance Status Check (approvals only, both original and supplemental applications) (<i>indicate date completed, must be within 60 days prior to AP</i>) 	<input type="checkbox"/> Requested <input type="checkbox"/> Accepted <input type="checkbox"/> Hold
❖ NDAs: Methods Validation	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed

Nonclinical Information

❖ Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	11/2/06
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
ECAC/CAC report/memo of meeting	n/a
Nonclinical inspection review Summary (DSI)	<input checked="" type="checkbox"/> None requested

Clinical Information

❖ Clinical review(s) (<i>indicate date for each review</i>)	1/10/07
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	1/10/07
❖ Clinical consult reviews from other review disciplines/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Microbiology (efficacy) reviews(s) (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not needed
❖ Safety Update review(s) (<i>indicate location/date if incorporated into another review</i>)	1/10/07
❖ Risk Management Plan review(s) (including those by OSE) (<i>indicate location/date if incorporated into another review</i>)	n/a
❖ Controlled Substance Staff review(s) and recommendation for scheduling (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not needed
❖ DSI Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> None requested
<ul style="list-style-type: none"> Clinical Studies^{III} Bioequivalence Studies Clin Pharm Studies 	
❖ Statistical Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 11/6/06
❖ Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None 10/24/06

Appendix A to Action Package Checklist

1 NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy 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).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's Office of Regulatory Policy representative.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-013

Connetics Corporation
Attention: Michael S. Eisen, Ph.D.
Vice President, Regulatory Affairs
3160 Porter Drive
Palo Alto, CA 94304

Dear Dr. Eisen:

Please refer to your March 14, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Primolux (clobetasol propionate) Foam, 0.05%

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 May 16, 2006 in accordance with 21 CFR 314.101(a).

In our filing review, we have identified the following potential review issues:

1. The study report for Study 302 states that an incorrect Psoriasis Grading Scale was initially distributed to the sites, however the nature of the discrepancies with the correct scale and the logistics of the correction have not been adequately described.
2. Inadequate listings of protocol deviations have been provided for Subjects in Studies 301 and 302. Listing 16.2.2 provides only one protocol deviation per subject, even though the study reports indicate that some subjects had more than one reason for exclusion from the per protocol population. In addition, information on the per protocol exclusions has not been submitted electronically.
3. No rationale has been given for changing the inclusion criteria in Amendment 3 of Study 301 during the course of the study to remove the requirement of a pruritus score at baseline of at least 2.

We are providing the above comments to give you preliminary notice of potential 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. Issues may be added, deleted, expanded upon, or modified as we review the application.

We also request that you submit the following information:

1. For Study 302, please provide additional information regarding the errors in the Psoriasis Grading Scale originally sent to the sites. In particular please provide:
 - a. A comparison of the incorrect Psoriasis Grading Scale that was initially distributed to the sites with the correct version. In particular, describe any differences with what the sites originally received with what has been submitted in the NDA as Amendment 2 of Protocol 302.
 - b. The date the correct materials were sent to the investigators.
 - c. A scanned copy of the signature page of the final signed version of Protocol 302 with final signatures. If the signed copy is not identical in every way to the version submitted in the NDA as Amendment 2 to Protocol 302, submit the entire signed version of the protocol.
 - d. The listing of the 46 subjects who were evaluated under the incorrect scale including their scoring under both the incorrect and correct scale and the criteria used to map subjects from one scale to the other.
 - e. A description of how the inclusion criteria were not met for the five subjects who were found to be ineligible under the corrected grading scale and which subjects these were.
2. Please submit electronic datasets for Studies 301 and 302 containing all of the protocol deviations that led to exclusion from the per protocol population. Be sure to include all deviations for a given subject. If protocol deviations occurred that did not warrant exclusion from the per protocol population, indicate these as well.
3. For Study 301, please provide the rationale for changing the inclusion criteria regarding the needed level of pruritus at baseline while the study was ongoing. Also discuss the impact that a change in patient population might have on the conclusions of the study.

Please respond only to the above requests for additional information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

If you have any questions, call Margo Owens, Regulatory Project Manager, at (301) 796-2110.

Sincerely,

{See appended electronic signature page}

Jill Lindstrom, M.D.
Acting Deputy Division Director
Division of Dermatology and Dental
Products
Office of Drug Evaluation III
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/

Jill Lindstrom
5/25/2006 05:12:46 PM

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NDA REGULATORY FILING REVIEW
(Including Memo of Filing Meeting)

NDA # 22-013

Supplement #

Efficacy Supplement Type SE-

Trade Name: Primolux Foam

Established Name: _____ Clobetasol Propionate Foam

Strengths: 0.05%

Applicant: Connetics Corporation

Agent for Applicant: n/a

Date of Application: March 14, 2006

Date of Receipt: March 16, 2006

Date clock started after UN: n/s

Date of Filing Meeting: May 3, 2006

Filing Date: May 15, 2006

Action Goal Date (optional): January 17, 2007

User Fee Goal Date: January 17, 2007

Indication(s) requested:

Type of Original NDA: (b)(1) (b)(2)
OR
Type of Supplement: (b)(1) (b)(2)

NOTE:

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. 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), complete Appendix B.

(2) If the application is a supplement to an NDA, please indicate whether the NDA is a (b)(1) or a (b)(2) application:

NDA is a (b)(1) application OR NDA is a (b)(2) application

Therapeutic Classification: S

P

Resubmission after withdrawal?

Resubmission after refuse to file?

Chemical Classification: (1,2,3 etc.) 3

Other (orphan, OTC, etc.)

Form 3397 (User Fee Cover Sheet) submitted: YES NO

User Fee Status: Paid Exempt (orphan, government)
Waived (e.g., small business, public health)

NOTE: If the NDA is a 505(b)(2) application, and the applicant did not pay a fee in reliance on the 505(b)(2) exemption (see box 7 on the User Fee Cover Sheet), confirm that a user fee is not required. The applicant is required to pay a user fee if: (1) the product described in the 505(b)(2) application is a new molecular entity or (2) the applicant claims a new indication for a use that has not been approved under section 505(b). Examples of a new indication for a use include a new indication, a new dosing regime, a new patient population, and an Rx-to-OTC switch. The best way to determine if the applicant is claiming a new indication for a use is to compare the applicant's proposed labeling to labeling that has already been approved for the product described in the application. Highlight the differences between the proposed and approved labeling.

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