CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-142

ADMINISTRATIVE DOCUMENTS
CORRESPONDENCE

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service

Food and Drug Administration
Rockville MD 20857

K. Blatt

OCT 13 1999

NDA 21-142

Connetics Corporation
Attention: Claire J. Lockey
Vice President, Regulatory Affairs
3400 West Bayshore Road
Palo Alto, CA 94303

Dear Ms. Lockey:

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

Name of Drug Product: Olux (clobetasol propionate foam) Foam, 0.05%

Therapeutic Classification: Standard (S)

Date of Application: July 28, 1999

Date of Receipt: July 29, 1999

Our Reference Number: NDA 21-142

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on September 27, 1999 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be May 29, 2000 and the secondary user fee goal date will be July 29, 2000.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within 120 days of receipt of your pediatric drug development plan, we will notify you of the pediatric studies that are required under section 21 CFR 314.55.

If you believe that this drug qualifies for a waiver of the study of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov.cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will proceed with the pediatric drug development plan that you submit, and notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

U.S. Postal Service:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatologic and Dental Drug Products, HFD-540
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatologic and Dental Drug Products, HFD-540
9201 Corporate Blvd.
Rockville, Maryland 20850-3202

If you have any questions, contact Kalyani Bhatt, Project Manager, at 301-827-2020.

Sincerely,

/S/

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

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

HFD-340
Kallyana

Food and Drug Administration
Rockville MD 20857

MAR 31 2000

Dale E. Martin, M.D.
Skin Surgery Medical Group, Inc.
5222 Balboa Avenue, 6th Floor
San Diego, California 92117

Dear Dr. Martin:

Between January 13 and 14, 2000, Ms. Diane VanLeeuwen, representing the Food and Drug Administration (FDA), met with you to review your conduct of a clinical study (Protocol # CPCD.C.002) of the investigational drug clobetasol propionate foam 0.05%, performed for Connetics Corporation. This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate clinical studies on which drug approval may be based and to assure that the rights and welfare of the human subjects of those studies have been protected.

From our evaluation of the inspection report, the documents submitted with that report, we conclude that you did not adhere to all pertinent federal regulations and/or good clinical investigational practices governing your conduct of clinical investigations and the protection of human subjects. We note that at the conclusion of the inspection, Ms. VanLeeuwen presented and discussed with your staff your failure to perform the study according to the relevant protocol in that you enrolled subjects #166 and #167 despite not meeting the entry criteria for plaque thickness. We acknowledge your response and your promise to make corrections/changes in your procedures to ensure that the findings noted above is not repeated in any ongoing or future studies.

We appreciate the cooperation shown Investigator VanLeeuwen during the inspection. Should you have any questions or concerns about any aspect of the clinical testing of investigational drugs, please contact me at (301)594-1032.

Sincerely,

/S/

Antoine El-Hage, Ph.D.
Branch Chief
Good Clinical Practice II, HFD-47
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, MD 20855

CFN: 3002905730
Field Classification: NAI
Headquarters Classification:
__ _1) NAI
__X__2)VAI-no response required
_____3)VAI-response requested

Deficiencies noted:
____ inadequate consent form
____ inadequate drug accountability records
__X__ failure to adhere to protocol
_____ inadequate records
_____ failure to report ADRS in the case report form
_____ Other (specify) failure to report ADRS to the IRB

cc:
HFA-224
HFD-540 Review Div. Dir.
HFD-540/ MO/Huene
HFD-540/ PM/Kalyani
HFD-540/Doc. Rm. NDA # 21-142
HFD-45 r/f
HFD-47 c/r/s GCP file# 10002
HFD-47/Carreras/Currier
HFR-PA250/Kozick
HFR-PA250/Koller
HFR-PA2565/VanLeeuwen

r/d:JAC:3/10/00
f/c:mb:3/31/00

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Note to Rev. Div. M.O.

DEPARTMENT OF HEALTH & HUMAN SERVICES

HFD-540
Kalyani

Food and Drug Administration
Rockville MD 20857

David Fivenson, M.D.
Henry Ford Hospital System
2799 West Grand Boulevard
Detroit, Michigan 48202

Dear Dr. Fivenson:

Between November 30 and December 2, 1999, Ms. Leslie A. Paul, representing the Food and Drug Administration (FDA), met with you to review your conduct of a clinical study (Protocol # CPCD.C.002) of the investigational drug clobetasol propionate foam 0.05%, performed for Connetics Corporation. This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate clinical studies on which drug approval may be based and to assure that the rights and welfare of the human subjects of those studies have been protected.

From our evaluation of the inspection report, the documents submitted with that report and your December 6, 1999, written response to the items listed on the Form FDA 483, we conclude that you did not adhere to all pertinent federal regulations and/or good clinical investigational practices governing your conduct of clinical investigations and the protection of human subjects. We note that at the conclusion of the inspection, Ms. Paul presented and discussed with you her findings. The discussion included: 1) failure to provide your IRB with a safety update on subject #045; and 2) non-performance of protocol required physical examination. We acknowledge your responses and your promise to make corrections/changes in your procedures to ensure that the findings noted above are not repeated in any ongoing or future studies.

We appreciate the cooperation shown Investgator Paul during the inspection. Should you have any questions or concerns about any aspect of the clinical testing of investigational drugs, please contact me at (301)594-1032.

Sincerely,

/S/

Antoine El-Hage, Ph.D.
Branch Chief
Good Clinical Practice II, HFD-47
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, MD 20855

CFN: 3002867519
Field Classification: VAI
Headquarters Classification:
__ _1) NAI
__X__2)VAI-no response required
_____3)VAI-response requested

Deficiencies noted:
____ inadequate consent form
____ inadequate drug accountability records
__X__ failure to adhere to protocol
____ inadequate records
__X__ failure to report ADRS in the case report form
__X__ Other (specify) failure to report ADRS to the IRB

cc:
HFA-224
HFD-540 Review Div. Dir.
HFD-540/ MO/Huene
HFD-540/ PM/Kalyani
HFD-540/Doc. Rm. NDA # 21-142
HFD-45 r/f
HFD-47 c/r/s GCP file# 09952
HFD-47/Carreras/Currier
HFR-CE752/Dempster
HFR-CE750/Mundo
HFR-CE750/Paul

r/d:JAC:2/9/00
f/c:mb:3/28/00

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Note to Rev. Div. M.O.

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

FINAL EVALUATION OF CLINICAL INVESTIGATOR INSPECTIONS.

DATE: March 9 , 2000

NDA 21-142
HFD-540
SPONSOR: Connetics Corporation
Product: Olux Foam 0.05% (clobetasol propionate foam 0.05%,)
Chemical Type: 4
Potential: S
Indications : [redacted]

Project Manager: Kalyani Bhatt
Medical Officer: Phyllis Huene

I. Background:

These routine inspections were part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate clinical studies on which NDA 21-142 approval may be based and to assure that the rights and welfare of the human subjects of those studies were protected. These inspections were conducted in accordance with CP 7348.811, Clinical Investigators, in addition to concentrate in comparing source documents, CRFs , and data listings in regard to primary endpoints, adverse drug events reporting and discontinued subjects in these protocols. Sites selected in corroboration between division medical officer, Dr. Huene and DSI reviewer, Dr. Jose Carreras.

NAME	CITY	Protocol	CL
Jennie J. Muglia, M.D.	Providence, RI	CPCD.C.002	NAI
Dale E. Martin, M.D.	San Diego, CA	CPCD.C.002	VAI
David Fivenson, M.D.	Detroit, MI	CPCD.C.002	VAI

Key to Classifications
NAI = No deviation from regulations
VAI = Minor Deviation(s) from regulations

Site #1

Jennie J. Muglia, M.D.
Providence, RI
CPCD.C.002

This investigator enrolled 18 subjects in the study. All subjects completed the study.
D.O. investigator examined 8 subject records. Data audit did not reveal any significant discrepancies and/or deficiencies in the conduct of the study. The data collected from this site appears acceptable.

Site #2

Dale E. Martin, M.D.
San Diego, CA
CPCD.C.002

This investigator enrolled 18 subjects in this study. All subjects completed the study. The DO investigator audited all records. The inspectional findings are not significant to preclude the use of the data in support for this application.

Site #3
David Fivenson, M.D.
Detroit, MI
CPCD.C.002 VAI

This investigator enrolled 18 subjects in the study. All subjects completed the study.
D.O. investigator examined 7 subject records in depth and examined all 18 records for informed consent, study evaluations, laboratory tests, concomitant medications and adverse events. Data audit did not reveal any clinically significant discrepancies and/or deficiencies in the conduct of the study. The data collected from this site appears acceptable

OVERALL ASSESSMENT OF FINDINGS AND GENERAL RECOMMENDATIONS :

No objectionable conditions were found in the above sites which would preclude the use of their data submitted in support of pending NDA.

Jose A. Carreras, M.D.

cc:
NDA 21-112
Division File
HFD-47/Currier

HFD-47/GPC2/ Elhage

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

HFD-540
Kalyani

Food and Drug Administration
Rockville MD 20857

FEB 4 2000

Jennie J. Muglia, M.D.
Rhode Island Hospital Group Inc.
Jane Brown South
593 Eddy Street,
Providence, Rhode Island, 02903

Dear Dr. Muglia:

Between December 17 and 18, 1999, Ms. Constance DeSimone, representing the Food and Drug Administration (FDA), met with you to review your conduct of a clinical study (protocol # CPCD.C.002) of the investigational drug Clobetasol Propionate foam 0.05%, performed for Connetics Corporation. This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate clinical studies on which drug approval may be based and to assure that the rights and welfare of the human subjects of those studies have been protected.

From our evaluation of the inspection report and the documents submitted with that report, we conclude that you adhered to all pertinent federal regulations and/or good clinical investigational practices governing your conduct of clinical investigations and the protection of human subjects.

We appreciate the cooperation shown Investigator DeSimone during the inspection. Should you have any questions or concerns about any aspect of the clinical testing of investigational drugs, please contact me at (301)594-1032.

Sincerely yours,

/s/

Antoine El-Hage, Ph.D.
Branch Chief
Good Clinical Practice Branch II, HFD-47
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, MD 20855

CFN: 3002873329

Field Classification: NAI
Headquarters Classification:
__X _1) NAI
_____2)VAI-no response required
_____3)VAI-response requested

cc:
HFA-224
HFD-540 Review Div. Dir.
HFD-540/ MO/Huene
HFD-540/ PM/Kalyani
HFD-540/Doc. Rm. NDA # 21-142
HFD-45 r/f
HFD-47 c/r/s GCP file# 09948
HFD-47/Carreras
HFD-47/Currier
HFR-NE252/Kraychuk
HFR-NE250/Levitt
HFR-NE250/DeSimone

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Note to Rev. Div. M.O.

connetics

FACSIMILE TRANSMISSION SHEET

Date: May 25, 2000

To: Kalyani Bhatt

Fax: (301) 827-2091

From: Dawn Parsell
Director, Regulatory Affairs

Subj: Information Request--Chemistry

No. of pgs. (2) including transmission sheet

Dear Kalyani:

This fax is in response to the Agency's faxed request for information (5/24/00) regarding our NDA #21-142. We plan to submit this information to our NDA, but wanted to provide it by fax for your convenience. The Agency's comments are in bold and our responses follow.

1. **Confirm that ICH conditions (25°C/60%RH, 30°C/60%RH, 40°C/75% RH) have been used and will be used in *all* the stability studies.**

   ICH conditions (25°C/60%RH, 30°C/60%RH, 40°C/75% RH) have been used and will be used in all the stability studies.

2. **Specify in future reports of stability data the ICH conditions actually used (not just the temperature).**

   Future reports of stability data will specify the ICH conditions actually used (*e.g.*, both temperature and humidity).

3. **Please explain what is meant by "types" in the subordinant clause "if the product is packaged in multiple sizes and types" (vol. 1.2, page 04 0331, second paragraph).**

   Type refers to the characteristics of the container/closure (e.g., materials of construction of the can and valve). Our product is packaged in an [redacted] aluminum can with an inverted valve, a spout actuator and a clear cover cap. Any post-approval changes to the type of packaging will be reported as per 21CFR 314.70 and any applicable FDA Guidance documents.

4. **In all future stability testing, the protocol should also provide for storing the can in both the upright and inverted positions.**

   All future stability testing will be performed in both the upright and inverted positions until sufficient data has been generated to demonstrate that the product in maximum contact with the primary pack does not have a significantly greater impact on drug product quality than the upright orientation as per the draft FDA Guidance document "Stability Testing of Drug Substances and Drug Products."

If you have any further questions on these issue, please contact me at (650) 843-2809.

Sincerely,

Dawn Parsell

Dawn Parsell, Ph.D.
Director, Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

3400 W. Bayshore Road, Palo Alto, CA 94303. Telephone (650) 843-2800. Fax (650) 857-1193.

connetics

FACSIMILE TRANSMISSION SHEET

Date: May 24, 2000

To: Kalyani Bhatt

Fax: (301) 827-2091

From: Dawn Parsell
Director, Regulatory Affairs

Subj: Draft Labeling

No. of pgs. (9) including transmission sheet

Dear Kalyani:

Pursuant to our conversation earlier today, attached is a copy of our revised draft labeling. We have incorporated all of the changes suggested by the Agency with the following exceptions:

1. The item code "L00702" was added back. This is our contract manufacturer's item code for the package insert, and it is necessary for the receipt and control of the component.

We have made the following additional changes to the labeling:

1. The name of the product is written in all capital letters (OLUX) rather than with an initial capital (Olux) every time it appears in the labeling.
2. On line 66 a typographical error was corrected by removing the word "from."
3. On line 72 a paragraph break was inserted prior to the sentence beginning "In a controlled..."
4. The [redacted] in addition to the word [redacted], was removed from the package insert, the patient information leaflet, the container label and the carton label.
5. In the "DO NOT:" section on page 2 of the patient information leaflet, the editorial comment in square brackets was removed.
6. In the "DO:" section on page 2 of the patient information leaflet, the word "part" was changed to "parts."

In addition, the Agency's comments on our current container and carton labeling for Luxiq™ (betamethasone valerate) Foam, 0.12% were taken into consideration as they pertain to the labeling for OLUX Foam. Specifically:

1. The drug name and strength will be located more towards the center on the label and will be given greater prominence.
2. The trade dress will be modified such that there can be no confusion with the Controlled Substances Symbol which is overlayed on scheduled drugs.
3. The "Rx Only" statement will be moved to the primary display panel.
4. All inactive ingredients will be listed on both the container and the carton in alphabetical order.

5. The prominence of the net quantity statement will be diminished such that it is not more prominent than the product strength.
6. The '

This information is provided to you via fax for your convenience. We will also formally submit it to our NDA. Thank you very much for your assistance.

Sincerely,

Dawn Parsell

Dawn Parsell, Ph.D.
Director, Regulatory Affairs

3400 W. Bayshore Road, Palo Alto, CA 94303. Telephone (650) 843-2800. Fax (650) 857-1193.

APPEARS THIS WAY
ON ORIGINAL

Number of Pages Redacted 8

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Draft Labeling
(not releasable,

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard, HFD-540
Rockville, MD 20850

FACSIMILE TRANSMISSION

DATE: May 24, 2000 Number of Pages 2

TO: Claire J. Lockey/Dawn Parsell
COMPANY: Connetics Corporation
FAX #: 1-650-857-1193

MESSAGE: NDA 21-142 Olux Foam 0.05%.
Please see the Chemistry information request regarding the stability data.

FROM: Kalyani Bhatt,
TITLE: Project Manager
PHONE #: 301-827-2049
FAX #: 301-827-2075/2091

1. Confirm that ICH conditions (25°C/60%RH, 30°C/60%RH, 40°C/75%RH) have been used and will be used in ***all*** the stability studies.

2. Specify in future reports of stability data the ICH conditions actually used (not just the temperatures).

3. Please explain what is meant by "types" in the subordinate clause "if the product is packaged in multiple sizes and types" (vol. 1.2, page 04 0331, second paragraph).

4. In all future stability testing, the protocol should also provide for storing the can in both the upright and inverted positions.

cc:
NDA 21-142
HFD-540/Div. File
HFD-540/DeCamp
HFD-540/Turujman
HFD-540/Bhatt

APPEARS THIS WAY
ON ORIGINAL

connetics®
CORPORATION

May 24, 2000

Jonathan K. Wilkin, M.D.
Director, Division of Dermatologic & Dental Drug Products
Food and Drug Administration
Attention: Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

NC

RE: NDA #21-142 OLUX™ (clobetasol propionate) Foam, 0.05%

12.1 Change in Company's Authorized Representative

Dear Dr. Wilkin:

We are requesting that the name of our company's authorized representative and official designated correspondent for the above-referenced NDA be changed from Claire J. Lockey to Katrina J. Church.

If you have any questions regarding this submission, please contact Dawn Parsell at (650) 843-2809.

Thank you for your cooperation.

Sincerely,

Katrina J. Church
Senior Vice President, Legal Affairs
General Counsel and Secretary

cc: Claire J. Lockey

3400 West Bayshore Road • Palo Alto, CA 94303 • USA • Telephone: (650) 843-2800 • Facsimile: (650) 843-2899

connetics®
CORPORATION

NDA ORIG AMENDMENT

May 23, 2000

Jonathan K. Wilkin, M.D.
Director, Division of Dermatologic & Dental Drug Products
Food and Drug Administration
Attention: Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

B2

RE: NDA #21-142 OLUX™ (clobetasol propionate) Foam, 0.05%

11.1 Response to Request for CMC Information and Change to Draft Labeling

Dear Dr. Wilkin:

Pursuant to the Agency's request (telephone conference dated 5/11/00 and 5/12/00) regarding modification of the "Dosage and Administration" section of the Package Insert of OLUX (clobetasol propionate) Foam, 0.05% (OLUX Foam), attached is a revised Package Insert and Patient Information Leaflet (see Attachment 1) that includes a common reference (a golf ball) to the maximum amount of product to be applied per day if the patient is to not exceed the maximum recommended weekly dose of clobetasol propionate (50 g/week). This reference is included in both the "Dosage and Administration" section of the Package Insert and the "How to apply OLUX foam" section of the Patient Information Leaflet.

In response to the Agency's request for additional stability data on the four OLUX lots submitted in our NDA, we have provided tables that include 17.5 months of real time (25°C/60%RH) stability data (Attachment 2). Tables 2, 3, 5, 6, and 7 are not included because these tests were not scheduled to be performed at the 18-month time point. Based on this data, we propose that the finished dosage form in the marketed package will bear a 2.0-year (24-month) expiry date. This date will appear on the immediate container and on the outer carton.

Please do not hesitate to call Dawn Parsell at (650) 843-2809 if you need any additional information regarding this submission.

Sincerely,

Katrina J. Church
Senior Vice President, Legal Affairs
General Counsel and Secretary

ORIGINAL

3400 West Bayshore Road • Palo Alto, CA 94303 • USA • Telephone: (650) 843-2800 • Facsimile: (650) 843-2899

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard, HFD-540
Rockville, MD 20850

FACSIMILE TRANSMISSION

DATE: May 22, 2000 Number of Pages 2

TO: Claire J. Lockey/Dawn Parsell
COMPANY: Connetics Corporation
FAX #: 1-650-~~843-2899~~ 857-1193

MESSAGE: NDA 21-142 Olux Foam 0.05%.
Please find additional comments from the Office of Post Marketing Drug Risk Assessment

FROM: Kalyani Bhatt,
TITLE: Project Manager
PHONE #: 301-827-2049
FAX #: 301-827-2075/2091

NDA 21-142
Olux Foam, 0.05%

OPDRA's recommendations:

CONTAINER LABEL:

1. Please note that the "ASHP Guidelines on Preventing Medication Errors in Hospitals", AJHP, Volume 50, February 1993, notes that important information such as drug name and strength should have the greatest prominence. *"Olux"and the established name* should be relocated to appear more central on the label and its prominence should be increased.

2. The large logo "C" which appears over the majority of the primary panel may be confused with a Controlled Substance Symbol © which is overlayed on scheduled drugs as required by the DEA.

3. The "Rx Only" statement should be moved to the primary display panel.

4 In accordance with 21CFR 201.100(b)(1)all inactive ingredient names must be listed on the label if the product is not for oral use. The ingredients should be listed in alphabetical order.

5. The *net quantity statement* should not have greater prominence than the product strength. It is recommended that the prominence of the product strength be increased and the net quantity not be highlighted.

CARTON AND PACKAGE INSERT LABELING:

See comments above, as applicable.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard, HFD-540
Rockville, MD 20850

FACSIMILE TRANSMISSION

DATE: May 22, 2000 Number of Pages 13

TO: Claire J. Lockey/Dawn Parsell
COMPANY: Connetics Corporation
FAX #: 1-650-843-2899

MESSAGE: NDA 21-142, Olux Foam 0.05%.
The following draft label, draft container label is enclosed. Please find revised draft labeling for Olux Foam 0.05% for your comments.

FROM: Kalyani Bhatt,
TITLE: Project Manager
PHONE #: 301-827-2049
FAX #: 301-827-2075/2091

Number of Pages Redacted 12

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Draft Labeling
(not releasable,

connetics®
CORPORATION

FACSIMILE TRANSMITTAL SHEET

DATE: MAY 12, 2000

To: Kalyani Bhatt
Company: FDA/Div. Of Dermatologic and Dental Drug Products
Fax number: 301-827-2075
Telephone number: 301-827-2049

From: Dawn Parsell
Sender's telephone: 650-843-2809
Total Pages *including cover*: 12

Re: NDA #21-142 OLUX (Clobetasol Propionate Foam 0.05%)

Dear Kalyani,
This fax is in response to the Agency's telephone requests for information (5/11/00 and 5/12/00) regarding our NDA #21-142. We plan to submit this information to our NDA, but wanted to provide it by fax for your convenience.

Revised Draft Labeling: Attached is revised draft labeling containing the addition of the phrase "up to a maximum of a golf-ball-sized dollop" to the Dosage and Administration section of the package insert and to the "How to Apply OLUX" section of the patient information leaflet as requested by the Agency.

Revised Container and Carton Trade Dress: We propose that the background color of the OLUX can and carton be [redacted] nat was previously submitted. This will allow easy differentiation between the OLUX packaging and the current Luxiq packaging, which has a navy blue to light green gradated background.

In the future, we plan to [redacted]. When this change is made, the packaging for the two products will be even more dissimilar.

If this proposal is acceptable to the Agency, we can provide new color mock-ups of the proposed OLUX can and carton labeling early next week.

Best regards,
Dawn
Dawn Parsell
Director, Regulatory Affairs

3400 W. Bayshore Rd. Palo Alto, CA 94303

Number of Pages Redacted 11

❖❖❖

Draft Labeling
(not releasable,

connetics®
CORPORATION

FACSIMILE TRANSMITTAL SHEET

DATE:

To: Kalyani Bhatt

From: Dawn Parsell

Company: FDA/Div. Of Dermatologic and Dental Drug Products

Sender's telephone: 650-843-2809

Fax number: 301-827-2075

Total Pages *including cover*: 1

Telephone number: 301-827-2049

Re: NDA #21-142 Clobetasol Propionate Foam 0.05% (Clobetasol foam)

Dear Kalyani,
This fax is in response to the Agency's telephone request for information (5/11/00) regarding our NDA #21-142. We plan to submit this information to our NDA, but wanted to provide it by fax for your convenience.

Revised Expiration Dating Period: We propose that " ". This date will appear on the immediate container and on the outer carton.

We also wish to clarify that the stability data we faxed to you yesterday, which contained 17.5 months of data from Clobetasol Foam lots 8D971, 8D972, 8D973 and 8D976, is data from our ongoing stability study conducted at 25C/60%RH.

Best regards,
Dawn Parsell
Dawn Parsell
Director, Regulatory Affairs

CONFIDENTIALITY NOTICE

Rev 5.12.00

3400 W. Bayshore Rd. Palo Alto, CA 94303

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

Division of Dermatologic and Dental Drug Products

Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard, HFD-540
Rockville, MD 20850

FACSIMILE TRANSMISSION

DATE: May 12, 2000 Number of Pages 2

TO: Claire J. Lockey/Dawn Parsell
COMPANY: Connetics Corporation
FAX #: 1-650-843-2899

MESSAGE: The following information is requested regarding NDA 21-142, Olux Foam for the proposed labeling.

FROM: Kalyani Bhatt,
TITLE: Project Manager
PHONE #: 301-827-2049
FAX #: 301-827-2075/2091

1. The section in "DOSAGE AND ADMINISTRATION" fails to clarify how the patient would ascertain that the recommended dosage (3.5 g) was dispensed from the can in the absence of an analytical balance. The applicant should be requested to propose a simple way for the patient to determine when the recommended dosage is dispensed. One possibility would be by the volume of foam dispensed. In such a case the amount could be approximated by an easily recognized object, such as the size of a golf ball.

2. The proposed color and pattern on the carton and container (can) of Olux foam are identical to those of Luxiq foam, which might cause inadvertent mix ups if the two products were stored side-by-side. The applicant should be requested to provide a distinguishing feature that would avert such a mix-up.

cc:
NDA 21-142/Div. File
Decamp/HFD-540
Turujman/HFD-540
Bhatt/HFD-540

connetics®
CORPORATION

FACSIMILE TRANSMITTAL SHEET

☐ CONFIRMATION COPY WILL BE SENT ONLY IF THIS BOX IS CHECKED

DATE: MAY 11, 2000

TO: KALYANI BHATT
COMPANY: FDA
DIVISION OF DERMATOLOGY AND DENTAL DRUG PRODUCTS

FROM: DAWN PARSELL
SENDER'S TELEPHONE:: 650-843-2809

FAX NUMBER: 301-827-2075
TELEPHONE NUMBER: 301-827-2049

TOTAL PAGES *INCLUDING COVER*: 14

RE: NDA #21-142 OLUX™ (CLOBETASOL PROPIONATE) FOAM, 0.05%

☐ URGENT ☐ PLEASE REVIEW ☐ PER OUR CONVERSATION

NOTES/COMMENTS:

Dear Kalyani,

Please find attached tables that provide 17.5 months of real time (25 °C) stability data for the four lots of Clobetasol Propionate Foam, 0.05% presented in our NDA #21-142. Tables 2, 3, 5, 6, and 7 are not included because these tests were not scheduled to be performed at the 18-month time point. We will formally submit this information to our NDA, but wanted to provide it to you via fax for your convenience. If you have any further questions, please do not hesitate to call me at (650) 843-2809.

Best regards,

Dawn

Dawn Parsell
Director, Regulatory Affairs

3400 W. Bayshore Rd. Palo Alto, CA 94303

TABLE 1: APPEARANCE

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	pass	8D973	0	pass
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	pass		3	pass
	6	pass		6	pass
	9	pass		9	pass
	12	pass		12	pass
	17.5	pass		17.5	pass
8D972	0	pass	8D976	0	pass
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	pass		3	pass
	6	pass		6	pass
	9	pass		9	pass
	12	pass		12	pass
	17.5	pass		17.5	pass

TABLE 4A: LEAK TEST—AVERAGE (%)

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	0.15	8D973	0	0.25
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.28		3	0.26
	6	0.26		6	0.33
	9	0.09		9	0.09
	12	0.35		12	0.41
	17.5	0.23		17.5	0.25
8D972	0	0.19	8D976	0	0.27
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.25		3	0.31
	6	0.28		6	0.20
	9	0.08		9	0.11
	12	0.42		12	0.50
	17.5	0.22		17.5	0.23

TABLE 4B: LEAK TEST—MAXIMUM (%)

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	0.19	8D973	0	0.30
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.33		3	0.29
	6	0.41		6	0.49
	9	0.13		9	0.12
	12	0.47		12	0.61
	17.5	0.28		17.5	0.31
8D972	0	0.21	8D976	0	0.34
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.30		3	0.34
	6	0.38		6	0.26
	9	0.11		9	0.17
	12	0.55		12	0.60
	17.5	0.26		17.5	0.27

TABLE 8: ETHANOL CONTENT (%w/w)

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	60.8	8D973	0	60.3
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	62.5		3	60.9
	6	60.5		6	60.6
	9	62.6		9	64.2
	12	59.4		12	59.9
	17.5	59.2		17.5	59.0
8D972	0	60.4	8D976	0	60.8
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	61.5		3	61.5
	6	60.9		6	60.3
	9	63.2		9	61.5
	12	60.1		12	60.5
	17.5	59.2		17.5	59.4

TABLE 9: pH

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	6.0	8D973	0	6.0
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	6.3		3	6.2
	6	6.3		6	6.2
	9	6.4		9	6.3
	12	6.3		12	6.1
	17.5	6.5		17.5	6.3
8D972	0	6.0	8D976	0	6.0
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	6.2		3	6.2
	6	6.2		6	6.3
	9	6.3		9	6.3
	12	6.1		12	6.2
	17.5	6.3		17.5	6.3

TABLE 10: CLOBETASOL PROPIONATE CONTENT (%w/w)

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	0.0507	8D973	0	0.0502
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0501		3	0.0500
	6	0.0498		6	0.0508
	9	0.0520		9	0.0531
	12	0.0496		12	0.0500
	17.5	0.0483		17.5	0.0479
8D972	0	0.0504	8D976	0	0.0512
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0497		3	0.0500
	6	0.0508		6	0.0494
	9	0.0508		9	0.0528
	12	0.0500		12	0.0501
	17.5	0.0480		17.5	0.0479

TABLE 11: PEAK A (area %)

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	0.0000	8D973	0	0.0000
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0139		3	0.0471
	6	0.0899		6	0.0684
	9	0.2955		9	0.1526
	12	0.0000		12	0.0000
	17.5	0.2185		17.5	0.2023
8D972	0	0.0000	8D976	0	0.0000
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0101		3	0.0601
	6	0.0805		6	0.0856
	9	0.2866		9	0.2887
	12	0.0198		12	0.0000
	17.5	0.2083		17.5	0.2403

TABLE 12: PEAK C (area %)

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	0.1653	8D973	0	0.0253
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.1800		3	0.0028
	6	0.1180		6	0.0059
	9	0.1561		9	0.0127
	12	0.0593		12	0.0634
	17.5	0.1027		17.5	0.0000
8D972	0	0.0343	8D976	0	0.0135
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0096		3	0.0027
	6	0.0003		6	0.0175
	9	0.0145		9	0.0096
	12	0.0544		12	0.0807
	17.5	0.0252		17.5	0.0000

TABLE 13: PEAK D (area %)

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	0.0000	8D973	0	0.0000
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0000		3	0.0020
	6	0.0097		6	0.0139
	9	0.0427		9	0.0593
	12	0.0968		12	0.0013
	17.5	0.0125		17.5	0.0000
8D972	0	0.0000	8D976	0	0.0000
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0000		3	0.0000
	6	0.0137		6	0.0229
	9	0.0722		9	0.0406
	12	0.0060		12	0.0039
	17.5	0.0000		17.5	0.0000

TABLE 14: PEAK E (area %)

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	0.1070	8D973	0	0.0330
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0268		3	0.0337
	6	0.0750		6	0.0443
	9	0.0293		9	0.0069
	12	0.1708		12	0.0870
	17.5	0.0448		17.5	0.0292
8D972	0	0.0670	8D976	0	0.1320
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0000		3	0.1308
	6	0.0565		6	0.1300
	9	0.0161		9	0.0722
	12	0.1206		12	0.1522
	17.5	0.0271		17.5	0.0681

TABLE 15: PEAK H (area %)

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	0.0000	8D973	0	0.0000
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0000		3	0.0000
	6	0.0299		6	0.0226
	9	0.0059		9	0.0018
	12	0.0000		12	0.0000
	17.5	0.0214		17.5	0.0000
8D972	0	0.0000	8D976	0	0.0000
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0000		3	0.0000
	6	0.0315		6	0.0282
	9	0.0000		9	0.0030
	12	0.0000		12	0.0000
	17.5	0.0076		17.5	0.0156

TABLE 16: PEAK I (area %)

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	0.0025	8D973	0	0.0000
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0346		3	0.0321
	6	0.1053		6	0.1016
	9	0.1546		9	0.1463
	12	0.2768		12	0.2587
	17.5	0.0000		17.5	0.2415
8D972	0	0.0000	8D976	0	0.0013
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0346		3	0.0390
	6	0.1219		6	0.1269
	9	0.1676		9	0.1620
	12	0.2775		12	0.2838
	17.5	0.0000		17.5	0.2852

TABLE 17: PEAK J (area %)

Lot Number	Time	25°C	Lot Number	Time	25°C
8D971	0	0.0270	8D973	0	0.1185
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0000		3	0.0000
	6	0.0000		6	0.0000
	9	0.0207		9	0.0000
	12	0.0000		12	0.0000
	17.5	0.2727		17.5	0.0000
8D972	0	0.0433	8D976	0	0.1383
	1	not performed		1	not performed
	2	not performed		2	not performed
	3	0.0000		3	0.0000
	6	0.0000		6	0.0061
	9	0.0000		9	0.0000
	12	0.0000		12	0.0168
	17.5	0.2617		17.5	0.0000

connetics

FACSIMILE TRANSMISSION SHEET

Date: April 27, 2000

To: Kalyani Bhatt

Fax: (301) 827-2075

From: Dawn Parsell
Director, Regulatory Affairs

Subj: Draft Labeling – Geriatric Use Statement

No. of pgs. (15) including transmission sheet

Dear Kalyani:

Pursuant to our conversation earlier today, attached is a copy of our submission regarding the Geriatric Use statement in our draft labeling. This submission is being sent to Document Control via Fed Ex today.

Thank you very much for your assistance.

Sincerely,

Dawn Parsell

Dawn Parsell, Ph.D.

3400 W. Bayshore Road, Palo Alto, CA 94303. Telephone (650) 843-2800. Fax (650) 857-1193.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on last page

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

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

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Connetics Corporation	April 27, 2000
TELEPHONE NO. *(Include Area Code)* 650/843-2800	FACSIMILE (FAX) Number *(Include Area Code)* 650/843-2899
APPLICANT ADDRESS *(Number, Street, City, State, County, and ZIP Code or Mail Code, and U.S. License number if previously issued)*: 3400 West Bayshore Road, Palo Alto, CA 94303	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) NDA 21-142

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Clobetasol Propionate, USP	OLUX™ Foam

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(if any)*: (11β,16β)-21-chloro-9-fluoro-11-hydroxy-16-methyl-17 (1-oxopropoxy)-pregna-1,4-diene-3,20-dione

CODE NAME *(if any)*:

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Aerosol Foam	0.05%	Topical

(PROPOSED) INDICATION(S) FOR USE:

APPLICATION INFORMATION

APPLICATION TYPE (check one)
X NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGIC LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b) (1) X 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

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

REASON FOR SUBMISSION
Financial Disclosure Statements

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

NUMBER OF VOLUMES SUBMITTED 1

THIS APPLICATION IS X PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

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.

Drug substance is manufactured by . Drug product is manufactured by CCL Pharmaceuticals (see Section 4.A.2.d); this site is ready for pre-approval inspection. Final product is released following approval by Connetics Corporation. The contact person for all sites is Claire J. Lockey, Vice President, Regulatory Affairs, Connetics Corporation, 3400 West Bayshore Road, Palo Alto, CA; (650) 843-2800.

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

Connetics Corporation (Clobetasol Propionate Foam, 0.05%), Palo Alto, CA 94303
NDA #20-934: Connetics Corporation [Luxiq™ (betamethasone valerate) foam, 0.12%], Palo Alto, CA 94303

FORM FDA 356h (4/97)

001

This application contains the following items: *(Check all that apply)*	
	1. Index
X	2. Labeling (check one) X Draft Labeling ☐ Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
	12. Case reports forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.5 (k) (3))
	18. User Fee Cover Sheet (Form FDA 3397)
	19. OTHER (Specify)

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 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 806, 610 and/or 809.
4. In the case of a prescription drug or biologic product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

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

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

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

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
	**Katrina J. Church** **Senior Vice President** **Legal Affairs & General Counsel**	**4/27/00**

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
3400 West Bayshore Road, Palo Alto, CA 94303	**650/843-2800**

Number of Pages Redacted 11

❖❖❖

Draft Labeling
(not releasable

connetics®
CORPORATION

AMENDMENT
BL

April 27, 2000

Jonathan K. Wilkin, M.D.
Director, Division of Dermatologic & Dental Drug Products
Food and Drug Administration
Attention: Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

RE: NDA #21-142 OLUX™ (clobetasol propionate) Foam, 0.05%

10.1 Response to Request for Change to Draft Labeling
- **Geriatric Use Statement**

Dear Dr. Wilkin:

Pursuant to the Agency's request (fax correspondence dated 4/25/00) regarding a Geriatric Use statement in the labeling of OLUX (clobetasol propionate) Foam, 0.05% (OLUX Foam). attached is a revised Package Insert and Patient Information Leaflet that includes a Geriatric Use subsection. Our clinical trials did not include sufficient numbers of subjects aged 65 and over to determine whether elderly subjects respond differently from younger subjects when treated with OLUX Foam. Accordingly, the labeling statement presented in 21 CFR 201.57(f)(10)(ii)(A) has been incorporated into the OLUX Foam Package Insert.

Please do not hesitate to call Dawn Parsell at (650) 843-2809 if you need any additional information regarding this submission.

Sincerely,

Katrina J. Church
Senior Vice President
Legal Affairs and General Counsel

ORIGINAL

Number of Pages Redacted 1

❖❖❖

Draft Labeling
(not releasable,

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

Division of Dermatologic and Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard, HFD-540
Rockville, MD 20850

FACSIMILE TRANSMISSION

DATE: April 25, 2000

Number of Pages 1
(Including cover sheet)

TO: Claire J. Lockey/Dawn Parsell
COMPANY: Connetics Corporation
FAX #: 1-650-843-2899

MESSAGE: For NDA 21-142 Olux Foam (clobetasol propionate) submitted July 29, 1999.
Please provide a Geriatric Use statement for the labeling . The regulations for this information is cited in the 21 CFR 201.57.

FROM: Kalyani Bhatt,
TITLE: Project Manager
PHONE #: 301-827-2049
FAX #: 301-827-2075/2091

CC:
NDA 21-142/Div. File
Huene/HFD-540
Okun/HFD-540
Bhatt/HFD-540

CORPORATION

March 21, 2000

NEW

Jonathan K. Wilkin, M.D.
Director, Division of Dermatologic & Dental Drug Products
Food and Drug Administration
Attention: Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

RE: NDA #21-142 OLUX™ (clobetasol propionate) Foam, 0.05%

NC

9.1 Financial Disclosure Statements

Dear Dr. Wilkin:

This submission is in response to the following information request that we received from the Medical Officer via facsimile on March 13, 2000:

Please submit the proper Financial Disclosure Form, and list the studies and investigators to which their disclosure statement applies.

Pursuant to this request and in accordance with an agreement with Linda Carter (CDER), the following documents are attached:

- Form FDA 3454
- Financial disclosure statement regarding proprietary interest in clobetasol propionate foam, 0.05%
- List of clinical studies and investigators for the three clinical studies that were submitted in the above-referenced NDA

Please do not hesitate to call Dawn Parsell at (650) 843-2809 or me at (650) 843-2889 if you need any additional information regarding this submission.

Sincerely,

Claire J. Lockey
Vice President
Regulatory Affairs
and Quality Assurance

ORIGINAL

9.1
3/21/00

FORM FDA 356h

ATTACHMENTS

West Bayshore Road • Palo Alto, CA 94303 • USA • Telephone: (650) 843-2800 • Facsimile: (650) 843-2899

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

Division of Dermatologic and Dental Drug Products

Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard, HFD-540
Rockville, MD 20850

FACSIMILE TRANSMISSION

DATE: March 13, 2000

Number of Pages 2
(Including cover sheet)

TO: Claire J. Lockey/Dawn Parsell
COMPANY: Connetics Corporation
FAX #: 1-650-843-2899

MESSAGE: Please find information requests from the Medical Officer for your original NDA 21-142 Olux Foam (clobetasol propionate) submitted July 29, 1999.

FROM: Kalyani Bhatt,
TITLE: Project Manager
PHONE #: 301-827-2049
FAX #: 301-827-2075/2091

Please find comments as follows:

1. Please submit the proper Financial Disclosure Form, and list the studies and investigators to which their disclosure statement applies.

connetics®
CORPORATION

February 16, 2000

Ms. Kalyani Bhatt
Division of Dermatologic & Dental Drug Products
Food and Drug Administration
9201 Corporate Boulevard
HFD 540, Room N241
Rockville, MD 20850

RE: NDA #21-142 OLUX™ (clobetasol propionate) Foam, 0.05%

Desk Copies of Draft Container Label, Carton Label and Package Insert

Dear Kalyani,

Please find enclosed three additional desk copies of the full color mock-ups of the draft container and carton labeling and the draft package insert for our OLUX Foam product (submitted to NDA #21-142 on 2/4/00). For your convenience, we have also included the cover letter from our NDA Amendment (8.1; 2/16/00) clarifying the slight differences between this labeling and that submitted in our original NDA (7/28/99).

Please do not hesitate to call me at (650) 843-2809 if you need any additional information.

Sincerely,

Dawn Parsell, Ph.D.
Associate Director, Regulatory Affairs

3400 West Bayshore Road • Palo Alto, CA 94303 • USA • Telephone: (650) 843-2800 • Facsimile: (650) 843-2899

connetics®
CORPORATION

February 16, 2000

Jonathan K. Wilkin, M.D.
Director, Division of Dermatologic & Dental Drug Products
Food and Drug Administration
Attention: Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

RE: NDA #21-142 OLUX™ (clobetasol propionate) Foam, 0.05%

8.1 Explanation of Changes to Draft Container Label, Carton Label, and Package Insert/Patient Information Leaflet

Dear Dr. Wilkin:

On 2/4/00, at the request of Kalyani Bhatt, we submitted full color mock-ups of the draft container and carton labeling and the draft package insert/patient information leaflet for our OLUX Foam product. Pursuant to a conversation with Olga Cintron on 2/10/00, this submission clarifies slight differences between this labeling and that submitted in our original NDA (7/28/99). With the following exceptions, the text of the labeling in the 2/4/00 submission is identical to that in the original NDA submission:

Container Label

- [redacted]
- [redacted]

Carton Label

- [redacted]
- [redacted]

Package Insert and Patient Information Leaflet

- [redacted]
- [redacted]

Please do not hesitate to call Dawn Parsell at (650) 843-2809 or me at (650) 843-2889 if you need any additional information regarding this submission.

Sincerely,

Claire J. Lockey
Vice President, Regulatory Affairs

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

Division of Dermatologic and Dental Drug Products

Office of Drug Evaluation V
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard, HFD-540
Rockville, MD 20850

FACSIMILE TRANSMISSION

DATE: February 8, 2000 Number of Pages 2 (Including coversheet)

TO: Thomas W. Walton / Trudy A. Rumbaugh, M.D.
COMPANY: Allergan
FAX #: 1-714-246-4272

MESSAGE: Clinical comments regarding the electronic submission of NDA. 21-184

FROM: Kalyani Bhatt
TITLE: Project Manager
PHONE #: 301-827-2020
FAX #: 301-827-2075/2091

1. In the pre-NDA minutes (the meeting dated 6/14/99), the Sponsor has been advised (Clinical Item 1) the following:

   - "All safety data must be presented, including postmarketing data for marketed formulations, data from studies on indications not sought and on formulations not marketed, and data from ongoing studies not yet completed (domestic and foreign)."

   Concerning the present request for postmarketing data, this is what has originally been conveyed to the Sponsor as information needed for filing of the NDA [The above being part of the answer to the Sponsor's question: "Allergan is assembling a clinical package, as outlined in this document, including human dermal safety, clinical pharmacokinetics
   and two Phase 3 studies which we believe fully meet the requirements for fileability, review and approval. Does the FDA concur?"].

   The Integrated Summary of Safety gave postmarketing data of tazarotene gels up to 7/15/99 only with incidence of the most common events. The Applicant needs to –

a) clarify whether the information is from U.S. sources or ALL sources;
b) provide incidence of death, serious adverse events or discontinuations due to adverse events; and
c) provide incidence of pregnancies and outcomes of pregnancies encountered in users.
d) summarize safety data from postmarketing studies (e.g., summary tables on the safety data from the long list of studies in the annual reports of NDA 20-600 would be appropriate).

The Integrated Summary of Safety should also address the safety data of the oral tazarotene dosage forms.

2. We previously requested the following on 11/4/99:

   - p-values for adverse event data contrasting:
   - Tazarotene 0.1% cream versus vehicle cream
   - Tazarotene 0.1% cream versus Tazarotene 0.05% cream
   - Tazarotene 0.05% cream versus vehicle cream
     (ALL adverse events and treatment-related adverse events)

The Sponsor responded that they have not done so in order to save the medical reviewer time ["if all the p-values are reported, then this will produce volumes of paper for the medical reviewer to sift through.

The way it is done now is to save the medical reviewer time and effort."]. This reviewer thanks them for the consideration, but after
discussion with the statistician at that time, would still like to have the p-values for review because of their importance.

connetics®
CORPORATION

February 4, 2000

Jonathan K. Wilkin, M.D.
Director, Division of Dermatologic & Dental Drug Products
Food and Drug Administration
Attention: Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

RE: NDA #21-142 OLUX™
(clobetasol propionate) Foam, 0.05%

Draft Container Label, Carton Label, and Package Insert

Dear Dr. Wilkin:

This submission contains draft container and carton labeling and a draft package insert for our OLUX Foam product.

Please do not hesitate to call Dawn Parsell at (650) 843-2809 or me at (650) 843-2889 if you need any additional information.

Sincerely,

Claire J. Lockey
Vice President
Regulatory Affairs

3400 West Bayshore Road • Palo Alto, CA 94303 • USA • Telephone: (650) 843-2800 • Facsimile: (650) 843-2899

NEW DRUG APPLICATION #21-142

CLOBETASOL PROPIONATE FOAM, 0.05%

7.1 Draft Container Label, Carton Label and Package Insert

Desk Copy

Connetics Corporation
3400 West Bayshore Road
Palo Alto, CA 94303

(650) 843-2800
Fax: (650) 857-1193

Date: February 4, 2000

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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

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

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on last page.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Connetics Corporation	**February 4, 2000**
TELEPHONE NO. *(Include Area Code)* **650/843-2800**	FACSIMILE (FAX) Number *(Include Area Code)* **650/843-2899**
APPLICANT ADDRESS *(Number, Street, City, State, County, and ZIP Code or Mail Code, and U.S. License number if previously issued)*: **3400 West Bayshore Road, Palo Alto, CA 94303**	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) **NDA 21-142**

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Clobetasol Propionate, USP	**OLUX™ Foam**

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*: **(11β,16β)-21-chloro-9-fluoro-11-hydroxy-16-methyl-17 (1-oxopropoxy)-pregna-1,4-diene-3,20-dione** — CODE NAME *(If any)*:

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
Aerosol Foam	**0.05%**	**Topical**

(PROPOSED) INDICATION(S) FOR USE: [redacted]

APPLICATION INFORMATION

APPLICATION TYPE (check one): X NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94) ☐ BIOLOGIC LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE: ☐ 505 (b) (1) X 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

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

REASON FOR SUBMISSION: **Four-Month Safety Update Report**

PROPOSED MARKETING STATUS (check one): X PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED **1** — THIS APPLICATION IS X PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

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.

); this site is ready for pre-approval inspection. Drug product is manufactured by CCL Pharmaceuticals (see Section 4.A.2.d); this site is ready for pre-approval inspection. Final product is released following approval by Connetics Corporation. The contact person for all sites is Claire J. Lockey, Vice President, Regulatory Affairs, Connetics Corporation, 3400 West Bayshore Road, Palo Alto, CA; (650) 843-2800.

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

Connetics Corporation (Clobetasol Propionate Foam, 0.05%), Palo Alto, CA 94303
NDA #20-934: Connetics Corporation [Luxiq™ (betamethasone valerate) foam, 0.12%], Palo Alto, CA 94303

This application contains the following items: *(Check all that apply)*	
	1. Index
X	2. Labeling (check one) X Draft Labeling ☐ Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g. 21 CFR 314.50 (d) (1), 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e) (1), 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g. 21 CFR 314.50 (e) (2) (i), 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g. 21 CFR 314.50 (d) (2), 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g. 21 CFR 314.50 (d) (3), 21 CFR 601.2)
	7. Clinical Microbiology (e.g. 21 CFR 314.50 (d) (4))
	8. Clinical data section (e.g. 21 CFR 314.50 (d) (5), 21 CFR 601.2)
	9. Safety update report (e.g. 21 CFR 314.50 (d) (5) (vi) (b), 21 CFR 601.2)
	10. Statistical section (e.g. 21 CFR 314.50 (d) (6), 21 CFR 601.2)
	11. Case report tabulations (e.g. 21 CFR 314.50 (f) (1), 21 CFR 601.2)
	12. Case reports forms (e.g. 21 CFR 314.50 (f) (2), 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b) (2) or (j) (2) (A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.5 (k) (3))
	18. User Fee Cover Sheet (Form FDA 3397)
	19. OTHER (Specify)

CERTIFICATION

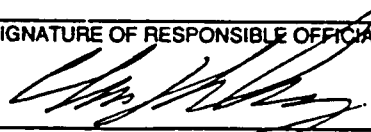
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. 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 210 and 211, 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR 201, 606, 610 and/or 809.
4. In the case of a prescription drug or biologic product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in 21 CFR 314.70, 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

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

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

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

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
	Claire J. Lockey Vice President, Regulatory Affairs	2/4/00

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
3400 West Bayshore Road, Palo Alto, CA 94303	650/843-2800

Number of Pages Redacted 16+5=21

❖❖❖

Draft Labeling
(not releasable,

DA # 21-142 DOCUMENT ID/LETTER DATE July 28, 1999

PPLICANT NAME CONNETICS

DUCT NAME Olux FOAM (clobetasol propionate)

FORM MUST BE COMPLETED ASAP

YES User Fee Cover Sheet Validated?

NOTE TO DOCUMENT ROOM: PLEASE MAKE THE FOLLOWING CHANGES TO THE COMIS DATA ELEMENTS:

505 (b)(2) Submission

with:

(1) Comparative vasoconstriction study

(2) Comparative Phase III safety & efficacy study

(3) Comparative HPA axis Study

— 505(b)(2)

YES ~~NO~~ CLINICAL DATA?
[Check YES if contains study reports or literature reports of what are explicitly or implicitly represented by the applicant to be adequate and well-controlled trials. "Clinical data do not include data used to modify the labelling to add a restriction that would improve the safe use of the drug (e.g., to add an adverse reaction, contraindication or warning to the labeling).]

will reference Olux Lidex

REF IF NO CLINICAL DATA IN SUBMISSION, INDICATE IF CLINICAL DATA ARE CROSS REFERENCED IN ANOTHER SUBMISSION?
NDA 19302, 19323, 20337

YES NO NDA BEING SPLIT FOR ADMINISTRATIVE CONVENIENCE (OTHER THAN BUNDLING)? IF YES, list ALL NDA numbers, review divisions & indicate those for which application fees apply.

NDA #	DIVISION		
N_____	_____	FEE	NO FEE
N_____	_____	FEE	NO FEE

YES NO BUNDLING POLICY APPLIED CORRECTLY? NO DATA ENTRY REQUIRED FOR ELEMENT
[Check YES if application is properly designated as one application or is properly submitted as a supplement instead of an original application. Check NO if application should be split into more than one application or submitted as an original instead of a supplement. IF NO, list resulting NDA numbers, and review divisions.]

NDA #	DIVISION	NDA #	DIVISION
N_____	_____	N_____	_____

P S PRIORITY OR STANDARD?

/S/

CSO SIGNATURE/DATE SCSO CONCURRENCE SIGNATURE/DATE

COPY DISTRIBUTION: ORIGINAL TO ARCHIVAL AFTER DATA ENTRY, ONE COPY EACH TO DIVISION FILE AND CDER, ASSOCIATE DIRECTOR FOR POLICY HFD-5

cc: S HFD540

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

Form Approved: OMB No. 0910-0297
Expiration Date: 04-30-01

USER FEE COVER SHEET

See instructions on reverse side before completing this form.

APPLICANT'S NAME AND ADDRESS

Connetics Corporation
3400 West Bayshore Road
Palo Alto, CA 94303
Contact person: Claire J. Lockey, V.P., Regulatory Affairs

2. TELEPHONE NUMBER *(include area code)*

(650) 843-2800

3. PRODUCT NAME

OLUX™ (clobetasol propionate) Foam, 0.05%

4. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL? 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:

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO (APPLICATION NO. CONTAINING THE DATA).

5. USER FEE I.D. NUMBER

N/A

6. LICENSE NUMBER / NDA NUMBER

21-142

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT *(See item 7, reverse side before checking box.)*

☒ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

FOR BIOLOGICAL PRODUCTS ONLY

☐ WHOLE BLOOD OR BLOOD COMPONENT FOR TRANSFUSION

☐ A CRUDE ALLERGENIC EXTRACT PRODUCT

☐ AN APPLICATION FOR A BIOLOGICAL PRODUCT FOR FURTHER MANUFACTURING USE ONLY

☐ AN "IN VITRO" DIAGNOSTIC BIOLOGICAL PRODUCT LICENSED UNDER SECTION 351 OF THE PHS ACT

☐ BOVINE BLOOD PRODUCT FOR TOPICAL APPLICATION LICENSED BEFORE 9/1/92

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?

☐ YES ☒ NO *(See reverse side if answered YES)*

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment.

Please DO NOT RETURN this form to this address.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
	Vice President, Regulatory Affairs	**July 16, 1999**

FORM FDA 3397 (5/98)