CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-470

ADMINISTRATIVE DOCUMENTS

13. PATENT INFORMATION

Pursuant to 21 CFR 314. 53(a), (b) and (c)(1) and (2), the undersigned declares that the patent identified below covers the Method of Use of Azelaic Acid Gel, 15%, the subject of NDA 21-470 or which approval is being sought.

Type of Patent	U.S. Patent Number	Patent Owner	Expiration Date
Method of Use*	4,713,394	Thornfeldt	January 17, 2006

*A method for the treatment of skin, suffering from a condition selected from a group consisting of nonacne inflammatory dermatoses, comprising applying to the affected area a therapeutically effective amount of azelaic acid.

Berlex Laboratories has an exclusive license from Neutrogena under Thornfeldt, U.S. Patent 4,713,394, for the use of azelaic acid for the treatment of certain skin conditions that include nonacne inflammatory dermatoses.

BERLEX LABORATORIES, INC.

Ted Ikeda

Ted Ikeda
General Counsel Intellectual Properties

January 29, 2002
Date

14. PATENT CERTIFICATION

A patent certification pursuant to 21 U.S.C. 355(b)(2) or (j)(2)(A) is not applicable to the New Drug Application for Azelaic Acid Gel, 15%, the subject of NDA 21-470.

BERLEX LABORATORIES, INC.

Ted Ikeda

Ted Ikeda
General Counsel Intellectual Properties

January 29, 2002
Date

Request for Three Years Marketing Exclusivity

Pursuant to 21 U.S.C. 21 U.S.C. 355(c)(3)(D)(iii) and 355(j)(4)(D)(iii), and with reference to 21 CFR 314.50(j)(1) and 314.108(b)(4)(iv), Berlex Laboratories, Inc. hereby requests a period of three years marketing exclusivity for Azelaic Acid Gel, 15%, the subject of NDA 21-470. This request for a three-year exclusivity period is based upon the following criteria:

1. The Food and Drug Administration has not previously approved the Azelaic Acid Gel, 15%, the subject of NDA 21-470.

2. The results of the two new clinical investigations included in NDA 21-470 that support a finding of substantial evidence of effectiveness of Azelaic Acid Gel, 15% for the treatment of moderate, papulopustular facial rosacea.

   A. Study 304342, "A 12-week, randomized, double-blind, multicenter study comparing the clinical efficacy and safety of Azelaic Acid 15% gel (SH H 655 BA, Finevin Gel) with its vehicle in patients with moderate, papulopustular facial rosacea". Report A03125 for Study 304342 can be found in N21-470/clinstat/papulopustularrosacea/A03125.pdf.

   B. Study 304344, "A 12-week, randomized, double-blind, multicenter study comparing the clinical efficacy and safety of Azelaic Acid 15% gel (SH H 655 BA, Finevin Gel) with its vehicle in patients with moderate, papulopustular facial rosacea". Report A03126 for Study 304344 can be found in N21-470/clinstat/papulopustularrosacea/A03126.pdf.

3. A determination that the two aforementioned clinical investigations are essential to the approval of Azelaic Acid Gel, 15%, the subject of NDA 21-470, for the treatment of moderate, papulopustular facial rosacea. Berlex Laboratories, Inc. certifies that there are not sufficient published studies or publicly available reports of clinical investigations to support the approval of NDA 21-470, other than these clinical investigations that were sponsored by Berlex Laboratories, Inc. under IND —

4. Berlex Laboratories, Inc. submitted IND — for Azelaic Acid Gel, 15% to the Food and Drug Administration on November 27, 2000 for review by the Division of Dermatologic and Dental Drug Products, HFD-540.

EXCLUSIVITY SUMMARY for NDA # 21-470 SUPPL # _____
Trade Name FINACEA Gel, 15% Generic Name azelaic acid
Applicant Name Berlex Laboratories, Inc. HFD- 540
Approval Date 12/24/02

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain 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 an original NDA? YES/_X_/ NO /___/

   b) Is it an effectiveness supplement? YES /___/ NO /_X_/

      If yes, what type(SE1, SE2, etc.)? _____

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

      YES /_X_/ NO /___/

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

      _____

      _____

      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:

      _____

      _____

   d) Did the applicant request exclusivity?

      YES /_X__/ NO /___/

7If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

3 years

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

YES /___/ NO /_X_/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /___/ NO /_X_/

If yes, NDA # _____ Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

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

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

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

YES /_X_/ NO /___/

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

NDA # 21-428, AZELEX (azelaic acid) Cream, 20%

NDA # _____ _____

NDA # _____ _____

2. Combination product.

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

YES /___/ NO /_X_/

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

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

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

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

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /_X_/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

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.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

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

YES /_X_/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

_____

_____

(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 /_X_/ 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 /_X_/

If yes, explain: _____

_____

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

YES /___/ NO /_X_/

If yes, explain: _____

_____

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

Investigation #1, Study Rpt# A03125

Investigation #2, Study Rpt# A03126

Investigation #3, Study # _____

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

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

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

If you have answered "yes" for one or more

investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ Study # _____
NDA # _____ Study # _____
NDA # _____ Study # _____

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

Investigation #1 YES /___/ NO /_X_/

Investigation #2 YES /___/ NO /_X_/

Investigation #3 YES /___/ NO /___/

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

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

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

Investigation #_1_, Study # _A03125_____

Investigation #_2_, Study # _A03126_____

Investigation #__, Study # _____

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 # _____ YES /_X_/ NO /___/ Explain: _____

Investigation #2

IND # _____ YES /_X_/ NO /___/ Explain: _____

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

Investigation #1

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

Investigation #2

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

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

YES /___/ NO /_X_/

If yes, explain: _____

_____

_____

/S/ _____ 12/10/02

Signature of Preparer Date

Title: Frank H. Cross, Jr., M.A., CDR
Senior Regulatory Management Officer

/S/ 12/20/02

Signature of ~~Office or Division~~ Director Date

cc:
Archival NDA 21-470
HFD-540/Division File
HFD-540/Cross
HFD-093/Mary Ann Holovac
HFD-104/PEDS/T.Crescenzi

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

PEDIATRIC PAGE

(Complete for all APPROVED original applications and efficacy supplements)

NDA/BLA # : 21-470 Supplement Type (e.g. SE5): _____ Supplement Number: _____

Stamp Date: March 21, 2002 Action Date: January 21, 2003

HFD -540 Trade and generic names/dosage form: FINACEA (azelaic acid) Gel, 15%

Applicant: Berlex Laboratories, Inc. Therapeutic Class: _____

Indication(s) previously approved: None

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

Number of indications for this application(s): 1

Indication #1: topical application in the treatment of inflammatory papules and pustules of mild to moderate rosacea.

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

X 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
X Disease/condition does not exist in children
☐ Too few children with disease to study
☐ There are safety concerns
X Other: The indication sought is not typically seen in subjects younger than 18 years.

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.____ yr. 0 Tanner Stage____

Max____ kg____ mo.____ yr. 11 Tanner Stage____

Reason(s) for partial waiver:

☐ Products in this class for this indication have been studied/labeled for pediatric population
☐ Disease/condition does not exist in children
☐ 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._____	Tanner Stage_____
Max_____	kg_____	mo._____	yr._____	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}

(S)

Regulatory Project Manager

(S)
12/20/02

cc: NDA 21-470
HFD-950/ Terrie Crescenzi
HFD-960/ Grace Carmouze
(revised 9-24-02)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960
301-594-7337

Request for a Waiver from the Requirement to Assess the Safety and Effectiveness of New Drugs in Pediatric Patients

Berlex Laboratories requests a full waiver from the requirement to submit data adequate to assess the safety and efficacy of the drug product for the claimed indication in all relevant pediatric subpopulations in accordance with 21 CFR §314.55(c)(2)(ii). Additionally, the Sponsor certifies that it believes that necessary studies are impossible or highly impractical because, e.g., the number of such patients is so small or geographically dispersed.

NDA number: 21-470

Sponsor: Berlex Laboratories, Inc.
Attn: John Hegarty
340 Changebridge Rd.
P.O. Box 1000
Montville, NJ 07045

Product Name:

FINACEA™ (azelaic acid gel) 15%

Indication, dosage and administration:

Twice daily topical application for the treatment of inflammatory papules and pustules of rosacea.

Age ranges included in pediatric waiver:

Ages 0 to 18 years

Reason for waiving pediatric studies:

Studies are impossible or highly impractical because the number of patients is so small or geographically dispersed.

Justification for waiving pediatric studies:

Rosacea, a chronic inflammatory facial skin disorder, is a common disease affecting approximately 13 million people in the U.S. (1). It occurs primarily in middle-aged adults, peaking between the ages of 40 and 50 years. Rosacea is rare in children; some case reports exist in the literature (2).

For more specific numbers on the incidence of rosacea in children the following sources were searched:

- National Health Data System (NHDS)
- National Ambulatory Medical Care Survey (NAMCS)
- National Hospital Ambulatory Medical Care Survey (NHAMCS)

Likewise, an extensive literature search in epidemiology/incidence/prevalence databases delivered only articles documenting that the disease is rare in a pediatric population, but no specific data.

In the IMS National Disease and Therapeutics Index (NDTI) database, updated as of September 2001, the number of patient visits is captured, reflecting the population size of patients seeking treatment for rosacea. This database does not control for multiple visits of the same patient. The age categories do not exactly reflect the Pediatric Rule definitions of subcategories within the pediatric population (21 CFR 314.55(a) and 601.27 (a)), but the following age categories: 0-2; 3-9; 10-19 years. In these categories, based on the average number of diagnosis over the past 3 years (ending 9/01), 5700 patient visits age 0-2 years, 1000 patient visit for age 3-9 years, and 9700 patient visits for age 10-19, were recorded.

With this information background, the sponsor believes that there is not a substantial number of pediatric patients with the disease.

References:

(1) In Acne and Rosacea. G. Plewig, A.M. Kligman, eds. 3rd edition, Springer, Berlin. p.456

(2) Levy ML, Dermatologic Clinics 16, 593-608 (1998)

Item 19 – Financial Information

Pursuant to 21 CFR 54, Berlex Laboratories, Inc. is providing certification for the investigators who participated in the 4 following covered clinical studies:

One Phase 3 study conducted in the U.S. identified as Report A03125 (Protocol 304342) "A 12-week, randomized, double-blind multicenter study comparing the clinical efficacy and safety of azelaic acid 15% gel with its vehicle in patients with moderate, papulopustular facial rosacea" (FDA Form 3454 – Attachment 1)

One Phase 3 study conducted in the U.S. identified as Report A03126 (Protocol 304344) "A 12-week, randomized, double-blind multicenter study comparing the clinical efficacy and safety of azelaic acid 15% gel with its vehicle in patients with moderate, papulopustular facial rosacea" (FDA Form 3454 – Attachment 2)

Two Phase 1 studies conducted in the U.S. identified as Report A04832 (Protocol 305182) "A 21-day, vehicle-controlled, observer-blind study to evaluate the local tolerability of azelaic acid, 15% gel in healthy volunteers, using a cumulative irritant patch test design", and Report A04766 (Protocol 305181) "A randomized, vehicle-controlled, observer-blind study to evaluate the sensitizing potential of topically applied azelaic acid, 15% gel in 200 healthy volunteers, using a human repeat insult patch test design" (FDA Form 3454 – Attachment 3)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form approved: OMB No. 0910-0396
Expiration Date: 3/31/02

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if applicable)) submitted in support of this application, I certify to one of the statement below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

☒ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator has a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	Charles Birbara, MD, Worchester, MA	Sooji Lee-Rugh, MD, Arlington, VA
	Leslie Capin, MD, Parker, CO	Mark Ling, MD, Newnan, GA
	Boni Elewski, MD, Birmingham, AL	John Proffitt, MD, Shawnee, KS
	Michael Heffernan, MD, St. Louis, MO	Daniel Stewart, DO, Clinton Twp., MI
	Terry Jones, MD, Byran, TX	Diane Thiboutot, MD, Hershey, PA
	Lewis Kaminester, MD, North Palm Beach, FL	Jonathan Weiss, MD, Snelville, GA
	Kean Lawlor, MD, Seattle, WA	

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Ruth Thieroff-Ekerdt, M.D.	Director, Clinical Development Dermatology
FIRM / ORGANIZATION: Berlex Laboratories, Inc.	
SIGNATURE: R. Thieroff-Ekerdt	DATE: 02-27-02

Paperwork Reduction Act Statement

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. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

FORM FDA 3454 (3/99)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form approved: OMB No. 0910-0396
Expiration Date: 3/31/02

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if applicable)) submitted in support of this application, I certify to one of the statement below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox.

☒ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator has a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigators		
	Toni Funicella, MD, Austin, TX	Robert Matheson, MD, Portland, OR
	Michael Gold, MD, Nashville, TN	Thomas Nigra, MD, Washington, DC
	Adelaide Hebert, MD, Houston, TX	David Pariser, MD, Norfolk, VA
	Joanne Herzog, MD, Birmingham, AL	Elyse Rafal, MD, Stony Brook, NY
	Irving Katz, MD, Minneapolis, MN	Toivo Rist, MD, Knoxville, TN
	Steven E. Kempers, MD, Fridley, MN	Kimberly Stone, MD, Aurora, CO
	Michael Maloney, MD, Denver, CO	Eduardo Tschen, MD, Albuquerque, NM

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Ruth Thieroff-Ekerdt, M.D.	Director, Clinical Development Dermatology
FIRM / ORGANIZATION Berlex Laboratories, Inc.	
SIGNATURE R. Thieroff-Ekerdt	**DATE** 02-27-02

Paperwork Reduction Act Statement

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. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

FORM FDA 3454 (3/99)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Food and Drug Administration

CERTIFICATION: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

Form approved: OMB No. 0910-0396
Expiration Date: 3/31/02

TO BE COMPLETED BY APPLICANT

With respect to all covered clinical studies (or specific clinical studies listed below (if applicable)) submitted in support of this application, I certify to one of the statement below as appropriate. I understand that this certification is made in compliance with 21 CFR part 54 and that for the purposes of this statement, a clinical investigator includes the spouse and each dependent child of the investigator as defined in 21 CFR 54.2(d).

Please mark the applicable checkbox

☒ (1) As the sponsor of the submitted studies, I certify that I have not entered into any financial arrangement with the listed clinical investigators (enter names of clinical investigators below or attach list of names to this form) whereby the value of compensation to the investigator could be affected by the outcome of the study as defined in 21 CFR 54.2(a). I also certify that each listed clinical investigator required to disclose to the sponsor whether the investigator has a proprietary interest in this product or a significant equity in the sponsor as defined in 21 CFR 54.2(b) did not disclose any such interests. I further certify that no listed investigator was the recipient of significant payments of other sorts as defined in 21 CFR 54.2(f).

Clinical Investigator

☐ (2) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that based on information obtained from the sponsor or from participating clinical investigators, the listed clinical investigators (attach list of names to this form) did not participate in any financial arrangement with the sponsor of a covered study whereby the value of compensation to the investigator for conducting the study could be affected by the outcome of the study (as defined in 21 CFR 54.2(a)); had no proprietary interest in this product or significant equity interest in the sponsor of the covered study (as defined in 21 CFR 54.2(b)); and was not the recipient of significant payments of other sorts (as defined in 21 CFR 54.2(f)).

☐ (3) As the applicant who is submitting a study or studies sponsored by a firm or party other than the applicant, I certify that I have acted with due diligence to obtain from the listed clinical investigators (attach list of names) or from the sponsor the information required under 54.4 and it was not possible to do so. The reason why this information could not be obtained is attached.

NAME	TITLE
Ruth Thieroff-Ekerdt, M.D.	Director, Clinical Development Dermatology
FIRM / ORGANIZATION: Berlex Laboratories, Inc.	
SIGNATURE: R. Thieroff-Ekerdt	DATE: 02-27-02

Paperwork Reduction Act Statement

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. Public reporting burden for this collection of information is estimated to average 1 hour per response, including time for reviewing instructions, searching existing data sources, gathering and maintaining the necessary data, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information to the address to the right:

Department of Health and Human Services
Food and Drug Administration
5600 Fishers Lane, Room 14C-03
Rockville, MD 20857

FORM FDA 3454 (3/99)

Certification Under Section 306(k)(1) of the FD & C Act

Berlex Laboratories, Inc. 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 NDA 21-470 for Azelaic Acid Gel, 15%.

BERLEX LABORATORIES, INC.

Joan Mutascio
Associate, Regulatory Submissions
and Information

Feb 14, 2002
Date

17. 1. FIELD COPY PROVISION CERTIFICATION

A Field Copy to this New Drug Application for Azelaic Acid Gel, 15%, NDA 21-470, has been provided to the FDA District Office, 120 North Center Drive, North Brunswick, New Jersey 08902, in accord with 21 CFR 314.50(k)(3). The undersigned certifies that the Field Copy provided to the District Office is a true copy of the technical section contained in the Archival and Review copies of the NDA 21-470 submitted to the Food and Drug Administration, Rockville, MD 20857.

BERLEX LABORATORIES, INC.

Joan Mutascio
Associate, Regulatory Submissions
& Information

February 8, 2002
Date

17. 2. FIELD COPY CONTENT CERTIFICATION

The undersigned certifies that this Field Copy of the New Drug Application for Azelaic Acid, 15%, NDA 21-470, is a true copy of the technical section contained in the Archival and Review copies of NDA 21-470 submitted to the Food and Drug Administration, Rockville, MD 20857.

BERLEX LABORATORIES, INC.

Joan Mutascio
Associate, Regulatory Submissions
& Information

February 8, 2002
Date

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: December 24, 2002 Number of Pages (including cover sheet) – 1

TO: John Hegarty, Regulatory Associate
COMPANY: Berlex Laboratories
FAX #: 973-487-2016

MESSAGE: For your NDA 21-470, Finacea (azelaic acid) Gel, 15%, we have the following information request from the Biopharmaceutics Reviewer:

Although not a requirement for approval, the Agency strongly recommends the Applicant to develop an in vitro release test and specifications so as to facilitate future formulation changes.

Thank you.

FROM: Frank H. Cross, Jr., M.A., CDR
TITLE: Senior Regulatory Management Officer
PHONE #: 301-827-2063
FAX #: 301-827-2075/2091

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: December 24, 2002 Number of Pages (including cover sheet) – 21

TO: John Hegarty, Regulatory Associate
COMPANY: Berlex Laboratories
FAX #: 973-487-2016

MESSAGE: Please find attached to this facsimile transmission a copy of our Action Letter for your NDA 21-470, Finacea (azelaic acid) Gel, 15%.

Thank you.

FROM: Frank H. Cross, Jr., M.A., CDR
TITLE: Senior Regulatory Management Officer
PHONE #: 301-827-2063
FAX #: 301-827-2075/2091

BERLEX

Facsimile
Transmittal Sheet

FROM: Susan Kummerer	TELEPHONE: (973) 487-2078
ADDRESS: ✘ 340 Changebridge Road, P. O. 1000, Montville, NJ 07045-1000 ❑ 300 Fairfield Road, Wayne, NJ 07470-4100	
FAX NUMBER: ✘ Drug Regulatory Affairs (973) 487-2016 ❑ Wayne Headquarters (973) 942-1610	
TO: Cdr. Frank Cross Sr. Regulatory Management Officer Division of Dermatologic and Dental Drug Products	Telephone: (301) 827-2063
SUBJECT: NDA 21-470 FINACEA™ (azelaic acid) Gel, 15% Response to FDA Request for Information (Carton/Container Labeling)	FAX NUMBER: (301) 827-2091 DATE: December 24, 2002 TOTAL NUMBER OF PAGES (INCLUDING COVER SHEET): 3

Dear Cdr. Cross,

Please see the attached letter regarding our discussions about carton and container labeling.

This submission will be sent in electronic format to the CDER Central Document Room on 1 diskette.

Sincerely,

BERLEX LABORATORIES

Susan Kummerer

Susan Kummerer
Director
Drug Regulatory Affairs

SK/finacea/003

BERLEX

UPS DELIVERY

Drug Development & Technology
Division of Berlex Laboratories, Inc.

340 Changebridge Road
P.O. Box 1000
Montville, NJ 07045-1000
Telephone: (973) 487-2000

December 24, 2002

Jonathan Wilkin, MD, Director
Division of Dermatologic and Dental Drug Products – HFD-540
Office of Drug Evaluation V
Center for Drug Evaluation & Research
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857-1706

Re: NDA 21-470
FINACEA™ (azelaic acid) Gel, 15%
OTHER: RESPONSE TO FDA REQUEST FOR INFORMATION
CARTON LABELING

Dear Dr. Wilkin:

Reference is made to NDA 21-470, submitted on March 20, 2002, for Finacea™ (azelaic acid) Gel, 15%. Further reference is made to a telephone conversation on December 23, 2002, between your representative, Cdr. Frank Cross, and the undersigned regarding carton and container labeling.

Additional reference is made to the electronic mail message sent to the Division on December 23, 2002, in which the Sponsor notified the Division of our intent to include the expiration date and lot number on the both the cartons and container for the marketed product and the product samples. This letter confirms that we will include the expiration date and lot number on all cartons and containers.

Since NDA 21-470 was submitted in electronic format, this submission was prepared in electronic format in accordance with the *Guidance for Industry Providing Regulatory Submissions in Electronic Format - NDAs*, issued by the Center for Drug Evaluation and Research in January 1999. This submission contains 1 floppy diskette that has been scanned for viruses using Trend Office Scan, Version 3.54.

Please call the undersigned at (973) 487-2078, if you have any questions concerning this application.

Sincerely,

BERLEX LABORATORIES

Susan Kummerer
Director
Drug Regulatory Affairs

SK005

BERLEX

Facsimile
Transmittal Sheet

FROM: John Hegarty	TELEPHONE: (973) 487-2166
ADDRESS: ✘ 340 Changebridge Road, P. O. 1000, Montville, NJ 07045-1000 ❑ 300 Fairfield Road, Wayne, NJ 07470-4100	
FAX NUMBER: ✘ Drug Regulatory Affairs (973) 487-2016 ❑ Wayne Headquarters (973) 942-1610	
TO: Cdr. Frank Cross Sr. Regulatory Management Officer Division of Dermatologic and Dental Drug Products	Telephone: (301) 827-2063
SUBJECT: NDA 21-470 FINACEA™ (azelaic acid) Gel, 15% Response to FDA Request for Information: Agreement With Labeling	FAX NUMBER: (301) 827-2075 DATE: December 23, 2002 TOTAL NUMBER OF PAGES (INCLUDING COVER SHEET): 3

Dear Cdr. Cross,

Please see the attached letter.

This submission will be sent in electronic format to the CDER Central Document Room on 1 diskette.

Sincerely,

BERLEX LABORATORIES

John Hegarty

John Hegarty
Regulatory Associate
Drug Regulatory Affairs

JJH/Fax/Finacea087

BERLEX

TELEFAX AND UPS DELIVERY

Drug Development & Technology
Division of Berlex Laboratories, Inc.

340 Changebridge Road
P.O. Box 1000
Montville, NJ 07045-1000
Telephone: (973) 487-2000

December 23, 2002

Jonathan Wilkin, MD, Director
Division of Dermatologic and Dental Drug Products – HFD-540
Office of Drug Evaluation V
Center for Drug Evaluation & Research
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857-1706

Re: NDA 21-470
FINACEA™ (azelaic acid) Gel, 15%
OTHER: RESPONSE TO FDA REQUEST FOR INFORMATION (TRADENAME)

Dear Dr. Wilkin:

Reference is made to NDA 21-470, submitted on March 20, 2002, for Finacea™ (azelaic acid) Gel, 15%. Reference is also made to telephone conversations on December 18, 19, and 20, 2002, between your representatives and the undersigned regarding our proposed tradename Finacea™.

The following sentence contains confidential business information that should not be publicly disclosed.

As a result of these conversations, Berlex has initiated the activities as outlined in our December 19, 2002, letter regarding our [redacted] s for [redacted]

Since NDA 21-470 was submitted in electronic format, this submission was prepared in electronic format in accordance with the *Guidance for Industry Providing Regulatory Submissions in Electronic Format - NDAs*, issued by the Center for Drug Evaluation and Research in January 1999. This submission contains 1 floppy diskette that has been scanned for viruses using Trend Office Scan, Version 3.54.

Please call the undersigned at (973) 487-2078, if you have any questions concerning this application.

Sincerely,

BERLEX LABORATORIES

Susan Kummerer
Director
Drug Regulatory Affairs

SK003

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: December 23, 2002 Number of Pages (including cover sheet) – 1

TO: John Hegarty, Regulatory Associate
COMPANY: Berlex Laboratories
FAX #: 973-487-2016

MESSAGE: For your NDA 21-470, Finacea (azelaic acid) Gel, 15%, we have the following information request from the CMC Reviewer:

With regard to your proposed revised Carton/Container labeling submitted earlier today, December 23, 2002, please confirm that the expiration date will be printed on the carton of the marketed product and on the free samples supplied to physicians.

Thank you.

FROM: Frank H. Cross, Jr., M.A., CDR
TITLE: Senior Regulatory Management Officer
PHONE #: 301-827-2063
FAX #: 301-827-2075/2091

BERLEX

Facsimile
Transmittal Sheet

FROM: John Hegarty	TELEPHONE: (973) 487-2166
ADDRESS: ✘ 340 Changebridge Road, P. O. 1000, Montville, NJ 07045-1000 ❑ 300 Fairfield Road, Wayne, NJ 07470-4100	
FAX NUMBER: ✘ Drug Regulatory Affairs (973) 487-2016 ❑ Wayne Headquarters (973) 942-1610	
TO: Cdr. Frank Cross Sr. Regulatory Management Officer Division of Dermatologic and Dental Drug Products	Telephone: (301) 827-2063
SUBJECT: NDA 21-470 FINACEA™ (azelaic acid) Gel, 15% Response to FDA Request for Information: Agreement With Labeling	FAX NUMBER: (301) 827-2075 DATE: December 23, 2002 TOTAL NUMBER OF PAGES (INCLUDING COVER SHEET): **15**

Dear Cdr. Cross,

Please see the attached letter regarding our agreement with the revised labeling received from the Division via telefax on Friday December 20, 2002 at 1813 hours. Also attached are the revised carton and tube labels, which were sent to you this morning via e-mail in PDF format with password protection. Each of the carton and tube labels herein is immediately followed by an enlarged version.

This submission will be sent in electronic format to the CDER Central Document Room on 1 diskette.

Sincerely,

BERLEX LABORATORIES

John Hegarty

John Hegarty
Regulatory Associate
Drug Regulatory Affairs

JJH/Fax/Finacea086

BERLEX

UPS DELIVERY

Drug Development & Technology
Division of Berlex Laboratories, Inc.

340 Changebridge Road
P.O. Box 1000
Montville NJ 07045-1000
Telephone: (973) 487-2000

December 23, 2002

Jonathan Wilkin, MD, Director
Division of Dermatologic and Dental Drug Products – HFD-540
Office of Drug Evaluation V
Center for Drug Evaluation & Research
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857-1706

Re: NDA 21-470
FINACEA™ (azelaic acid) Gel, 15%
OTHER: RESPONSE TO FDA REQUEST FOR INFORMATION AGREEMENT WITH LABELING

Dear Dr. Wilkin:

Reference is made to NDA 21-470, submitted on March 20, 2002, for Finacea™ (azelaic acid) Gel, 15%. Reference is also made to labeling for NDA 21-470 proposed by the Division on December 20, 2002. Further reference is made to a telephone conversation on December 20, 2002, between representatives of the Division and the Sponsor regarding this labeling.

Based on this conversation, Berlex Laboratories, Inc. agrees with the revised labeling, received Friday December 20, 2002 at 1816 hours which is provided herewith in Item 2. Additionally, Berlex is providing revised carton and tube labels in Item 2 as requested by the Division.

Since NDA 21-470 was submitted in electronic format, this submission was prepared in electronic format in accordance with the *Guidance for Industry Providing Regulatory Submissions in Electronic Format - NDAs*, issued by the Center for Drug Evaluation and Research in January 1999. This submission contains 1 floppy diskette that has been scanned for viruses using Trend Office Scan, Version 3.54.

Please call the undersigned at (973) 487-2078, if you have any questions concerning this application.

Sincerely,

BERLEX LABORATORIES

Susan Kummerer

Susan Kummerer
Director
Drug Regulatory Affairs

SK004

21 pages redacted from this section of the approval package consisted of draft labeling

Cross Jr, Frank H

From: Cross Jr, Frank H

Sent: Monday, December 23, 2002 2:36 PM

To: Ferguson, Shirnette D

Cc: Gautam Basak, Mamta; Decamp II, Wilson H; Turujman, Saleh; Wilkin, Jonathan K; Kozma-Fornaro, Mary J

Subject: RE: 21-470

Thanks for your help, Shirnette.

Frank

-----Original Message-----
From: Ferguson, Shirnette D
Sent: Monday, December 23, 2002 2:35 PM
To: Cross Jr, Frank H
Subject: 21-470

I have given the above reference application an acceptable overall recommendation. Although, when you look in the status folder at the Schering facilities the last Compliance status shows pending, these facilities have an acceptable recommendation in the milestone folder. Therefore, the overall recommendation is acceptable.

Cross Jr, Frank H

From: Turujman, Saleh
Sent: Monday, December 23, 2002 5:47 PM
To: Cross Jr, Frank H
Cc: Decamp II, Wilson H; Wilkin, Jonathan K; Kozma-Fornaro, Mary J; Gautam Basak, Mamta
Subject: RE: 21-470 Carton/container label, acceptable; satisfactory cGMP; Recommend APPROVAL

Hello Frank:

The chemistry reviewer's recommendation for this NDA was "APPROVABLE". There were two residual CMC issues to be evaluated to change the recommendation to "approval": carton/container labeling and the EES recommendation. I have reviewed the resubmitted carton/container labeling of the 3 sizes (3 gm, 30 gm and 50 gm), amended by the sponsor as requested by the chemistry reviewer. With the confirmation by the sponsor that the expiration date [and the lot number] will appear on both the tubes and cartons for the marketed product and the free physician samples, the resubmitted labeling of the carton/container is acceptable from a CMC point of view. As per Shirnette Ferguson's e-mail to you, the Office of Compliance has confirmed an overall recommendation of acceptable for this application. Both issues are therefore resolved.

The CMC recommendation for this NDA is APPROVAL.

I will be in tomorrow to sign the action letter for chemistry.

Thank you for all your help today.

Saleh

-----Original Message-----
From: Cross Jr, Frank H
Sent: Monday, December 23, 2002 3:42 PM
To: Turujman, Saleh
Cc: Decamp II, Wilson H; Wilkin, Jonathan K; Kozma-Fornaro, Mary J; Gautam Basak, Mamta
Subject: RE: 21-470

Hi Saleh,

Will do.

Applicant will be sending later today by e-mail, fax tomorrow and official submission mailed in tomorrow.

Is all else with Carton/Container lbl okay?

How about inspections since EES said Acceptable" as of today, i.e., will a memo for both of these items be forthcoming?

Thanks again for all of your help.

Frank

-----Original Message-----
From: Turujman, Saleh
Sent: Monday, December 23, 2002 3:17 PM
To: Cross Jr, Frank H
Cc: Decamp II, Wilson H; Wilkin, Jonathan K; Kozma-Fornaro, Mary J; Gautam Basak, Mamta
Subject: RE: 21-470

Frank:

Could you ask the sponsor to "confirm" that the expiration date will be printed on the carton of the marketed product and on the free samples supplied to physicians.

Thanks,

Saleh

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: December 20, 2002 Number of Pages (including cover sheet) – 17

TO: John Hegarty, Regulatory Associate
COMPANY: Berlex Laboratories
FAX #: 973-487-2016

MESSAGE: Please find attached to this facsimile transmission our draft labeling for your NDA 21-470, FINACEA™ (azelaic acid) Gel, 15%.

Please submit final color proof copies of your proposed Carton and Container Labeling revised per the attached draft sample Carton and Container Labeling.

Thank you.

FROM: Frank H. Cross, Jr., M.A., CDR
TITLE: Senior Regulatory Management Officer
PHONE #: 301-827-2063
FAX #: 301-827-2075/2091

16 pages redacted from this section of the approval package consisted of draft labeling

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: December 20, 2002 Number of Pages (including cover sheet) – 4

TO: John Hegarty, Regulatory Associate
COMPANY: Berlex Laboratories
FAX #: 973-487-2016

MESSAGE: Please find attached to this facsimile transmission our minutes of our December 18, 2002, CMC teleconference regarding your NDA 21-470, FINACEA™ (azelaic acid) Gel, 15%.

Thank you.

FROM: Frank H. Cross, Jr., M.A., CDR
TITLE: Senior Regulatory Management Officer
PHONE #: 301-827-2063
FAX #: 301-827-2075/2091

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: December 20, 2002 Number of Pages (including cover sheet) – 3

TO: John Hegarty, Regulatory Associate
COMPANY: Berlex Laboratories
FAX #: 973-487-2016

MESSAGE: Please find attached to this facsimile transmission our minutes of our December 18, 2002, teleconference regarding your NDA 21-470, FINACEA™ (azelaic acid) Gel, 15%.

Thank you.

FROM: Frank H. Cross, Jr., M.A., CDR
TITLE: Senior Regulatory Management Officer
PHONE #: 301-827-2063
FAX #: 301-827-2075/2091

BERLEX

Facsimile
Transmittal Sheet

FROM: Susan Kummerer	TELEPHONE: (973) 487-2078
ADDRESS: ✗ 340 Changebridge Road, P. O. 1000, Montville, NJ 07045-1000 ☐ 300 Fairfield Road, Wayne, NJ 07470-4100	
FAX NUMBER: ✗ Drug Regulatory Affairs (973) 487-2016 ☐ Wayne Headquarters (973) 942-1610	
TO: Cdr. Frank Cross Sr. Regulatory Management Officer Division of Dermatologic and Dental Drug Products	Telephone: (301) 827-2063
SUBJECT: NDA 21-470 FINACEA™ (azelaic acid) Gel, 15% Response to FDA Request for Information (Tradename)	FAX NUMBER: (301) 827-2091 DATE: December 19, 2002 TOTAL NUMBER OF PAGES (INCLUDING COVER SHEET): 3

Dear Cdr. Cross,

Please see the attached letter regarding our discussions about our tradename.

This submission will be sent in electronic format to the CDER Central Document Room on 1 diskette.

Thanks for communicating!
Susan

Sincerely,

BERLEX LABORATORIES

Susan Kummerer

Susan Kummerer
Director
Drug Regulatory Affairs

SK/finacea/003

BERLEX

TELEFAX AND UPS OVERNIGHT

Drug Development & Technology
Division of Berlex Laboratories, Inc.

340 Changebridge Road
P.O. Box 1000
Montville, NJ 07045-1000
Telephone: (973) 487-2000

December 19, 2002

Jonathan Wilkin, MD, Director
Division of Dermatologic and Dental Drug Products – HFD-540
Office of Drug Evaluation V
Center for Drug Evaluation & Research
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857-1706

Re: **NDA 21-470**
FINACEA™ (azelaic acid) Gel, 15%
OTHER: RESPONSE TO FDA REQUEST FOR INFORMATION (TRADENAME)

Dear Dr. Wilkin:

Reference is made to NDA 21-470, submitted on March 20, 2002, for Finacea™ (azelaic acid) Gel, 15%. Reference is also made to telephone conversations on December 18 and 19, 2002, between your representative Cdr. Frank H. Cross, and the undersigned regarding our proposed tradename Finacea™.

The following paragraph contains confidential business information that should not be publicly disclosed.

As a result of those conversations, Berlex is prepared to engage in activities aimed at having [redacted]. This process would entail a [redacted]

Since NDA 21-470 was submitted in electronic format, this submission was prepared in electronic format in accordance with the *Guidance for Industry Providing Regulatory Submissions in Electronic Format - NDAs*, issued by the Center for Drug Evaluation and Research in January 1999. This submission contains 1 floppy diskette that has been scanned for viruses using Trend Office Scan, Version 3.54.

Please call the undersigned at (973) 487-2078, if you have any questions concerning this application.

Sincerely,

BERLEX LABORATORIES

Susan Kummerer

Susan Kummerer
Director
Drug Regulatory Affairs

SK002

9 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

Teleconference Date: December 18, 2002 Time: 1300 Location: N229
Meeting ID: 9707

NDA 21-470, TRADEMARK (azelaic acid) Gel, 15%

Indication: Topical Treatment of Inflammatory Papules and Pustules ——— of Rosacea

SUBJECT: CMC Teleconference - Omission of universal test/criteria from product specification

Applicant: Berlex Laboratories, Inc.

Meeting Chair: Wilson DeCamp, Ph.D.

Meeting Recorder (Project Manager): Frank Cross, Jr., M.A., CDR

FDA Attendees, titles and offices:

Wilson DeCamp, Ph.D., Chemistry Team Leader, DNDCIII, HFD-830
Frank Cross, Jr., M.A., CDR, Senior Regulatory Management Officer, DDDDP, HFD-540

Applicant Attendees, titles and offices:

Jeffrey Farkas, Manager, Quality Systems
Sue Kummerer, Director, Regulatory Affairs
John Hegarty, Regulatory Associate

Agency:

We initiated the telephone call to advise the Applicant of an omission in the product specification. Specifically, no test/criterion is proposed for impurities in the drug product. This test is required by ICH guidance Q6A.

We proposed that the Applicant prepare to respond promptly after our action on the NDA to modify the calculations for the test for the content of azelaic acid and benzoic acid (as provided in Section 4.2.6.3, report number ———). This modification should require the calculation of the percentage corresponding to any observed peak, following the principles used for the calculation of the content of azelaic acid and benzoic acid. Per ICH guidance Q3B and the general notices in USP 25, any related substance exceeding 0.1% should be reported on the COA.

This change should be submitted as an amendment (or supplement, as appropriate) to the NDA as soon as possible after receipt of our action letter. If submitted as a supplement, a CBE-0 category is appropriate.

Applicant:

The Applicant thanked the Agency for the teleconference and will make the requested NDA submission as advised.

The teleconference ended amicably.

Signature, minutes preparer: _____

Concurrence Chair (or designated signatory): _____

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

/s/

Wilson H. DeCamp
12/18/02 04:06:20 PM
concur

Teleconference Date: December 18, 2002 Time: 1100 Location: N229
Meeting ID: 9706

NDA 21-470, TRADEMARK (azelaic acid) Gel, 15%

Indication: Topical Treatment of Inflammatory Papules and Pustules [redacted] of Rosacea

Applicant: Berlex Laboratories, Inc.

Meeting Chair: Frank Cross, Jr., M.A., CDR

Meeting Recorder (Project Manager: Frank Cross, Jr., M.A., CDR

FDA Attendees, titles and offices:

Frank Cross, Jr., M.A., CDR, Senior Regulatory Management Officer, DDDDP, HFD-540

Applicant Attendees, titles and offices:

John Hegarty, Regulatory Associate

Agency:

Regarding NDA 21-470, TRADEMARK (azelaic acid) Gel, 15%, the Division of Medication Errors and Technical Support does not recommend the use of the proprietary name, FINACEA™. In reviewing the proprietary name, FINACEA™, the primary concern was related to the proprietary name FINEVIN™, which already exists in the U.S. marketplace. FINEVIN™ has potential for look-alike confusion with FINACEA™.

The Office of Drug Safety will be unable to review Applicant's proposed new TRADEMARK(s) for this NDA before the PDUFA date. The Applicant is recommended to submit its proposed new TRADEMARK(s) after receiving our Action Letter for this NDA.

The Agency will review the Applicant's proposed new TRADEMARK(s) for this NDA as rapidly as possible and get back to the Applicant with its comments.

Applicant:

The Applicant asked if there is a possibility for further discussion.

Agency:

A teleconference may be requested after the Applicant receives the Action Letter for this NDA 21-470.

The Applicant thanked the Agency for today's teleconference.

The teleconference ended amicably.

Signature, minutes preparer: _____

Concurrence Chair (or designated signatory): _____

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

/s/

Frank Cross
12/20/02 12:09:57 PM
CSO

BERLEX

Facsimile
Transmittal Sheet

FROM: John Hegarty	TELEPHONE: (973) 487-2166
ADDRESS: ✘ 340 Changebridge Road, P. O. 1000, Montville, NJ 07045-1000 ❑ 300 Fairfield Road, Wayne, NJ 07470-4100	
FAX NUMBER: ✘ Drug Regulatory Affairs (973) 487-2016 ❑ Wayne Headquarters (973) 942-1610	
TO: Cdr. Frank Cross Sr. Regulatory Management Officer Division of Dermatologic and Dental Drug Products	Telephone: (301) 827-2063
SUBJECT: NDA 21-470 FINACEA™ (azelaic acid) Gel, 15% Response to Proposed Phase 4 Commitments: Nonclinical Toxicology	FAX NUMBER: (301) 827-2075 DATE: December 17, 2002 TOTAL NUMBER OF PAGES (INCLUDING COVER SHEET): 3

Dear Cdr. Cross,

Please see the attached letter, which provides responses to the proposed Phase 4 Commitments – nonclinical toxicology, which we received from the Division via telefax on December 12 and December 17, 2002. This submission will be sent in electronic format to the CDER Central Document Room on 1 diskette.

Sincerely,

BERLEX LABORATORIES

John Hegarty

John Hegarty
Regulatory Associate
Drug Regulatory Affairs

JJH/Fax/Finacea081

BERLEX

TELEFAX AND UPS OVERNIGHT

Drug Development & Technology
Division of Berlex Laboratories, Inc.

340 Changebridge Road
P.O. Box 1000
Montville, NJ 07045-1000
Telephone: (973) 487-2000

December 17, 2002

Jonathan Wilkin, MD, Director
Division of Dermatologic and Dental Drug Products – HFD-540
Office of Drug Evaluation V
Center for Drug Evaluation & Research
U.S. Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857-1706

Re: NDA 21-470
FINACEA™ (azelaic acid) Gel, 15%
OTHER: PROPOSED PHASE 4 COMMITMENTS - NONCLINICAL

Dear Dr. Wilkin:

Reference is made to NDA 21-470, submitted on March 20, 2002 for FINACEA™ (azelaic acid) Gel, 15%. Reference is also made to the Division's facsimile transmission of December 12, 2002, which provided comments on our November 14, 2002 responses to the initial proposed nonclinical toxicology Phase 4 Commitments for NDA 21-470. Further reference is made to the Division's facsimile transmissions of December 12 and December 17, 2002, which provided revised proposed nonclinical toxicology Phase 4 Commitments. These proposed Phase 4 Commitments for NDA 21-470 are repeated below in **bold** text followed by our responses in unbold text.

Commitment Category: NON-CLINICAL TOXICOLOGY

1. **The Applicant commits to conduct a study to determine the photoco-carcinogenic potential associated with azelaic acid 15% gel.**
   - **Protocol submission: Within 4 months of the date of the Approval Letter for this NDA**
   - **Study Start: Within 6 months of the date of the approval of the protocol**
   - **Final Report Submission: Within 12 months after the study completion**

Berlex Laboratories, Inc. agrees to this Phase 4 Commitment.

2. **The Applicant commits to conducting an alternative, dermal carcinogenicity study in transgenic mice (Tg.AC assay) with the azelaic acid 15% gel.**

   - **Protocol submission: Within 5 months of the date of the Approval Letter for this NDA**
   - **Study Start: Within 6 months of the date of the approval of the protocol**
   - **Final Report Submission: Within 12 months after the study completion**

Berlex Laboratories, Inc. agrees to this Phase 4 Commitment.

Since NDA 21-470 was submitted in electronic format, this submission was prepared in electronic format in accordance with the *Guidance for Industry Providing Regulatory Submissions in Electronic Format - NDAs*, issued by the Center for Drug Evaluation and Research in January 1999. This submission contains 1 floppy diskette that has been scanned for viruses using Trend Office Scan, Version 3.54.

Please call the undersigned at (973) 487-2166, if you have any questions concerning this application.

Sincerely,

BERLEX LABORATORIES

John Hegarty

John Hegarty
Regulatory Associate
Drug Regulatory Affairs

JJH080

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: December 17, 2002 Number of Pages (including cover sheet) – 1

TO: John Hegarty, Regulatory Associate
COMPANY: Berlex Laboratories
FAX #: 973-487-2016

MESSAGE: Please review the following proposed Phase 4 Commitment for your NDA 21-470, Finacea (azelaic acid) Gel, 15%. If acceptable, please submit your commitment to the same.

Commitment Category: NON-CLINICAL TOXICOLOGY

1. The applicant commits to conduct a study to determine the photoco-carcinogenic potential associated with azelaic acid 15% gel.

Protocol submission: Within 4 months of the date of the Approval Letter for this NDA

Study Start: Within 6 months of the date of the approval of the protocol

Final Report Submission: Within 12 months after the study completion

Thank you.

FROM: Frank H. Cross, Jr., M.A., CDR
TITLE: Senior Regulatory Management Officer
PHONE #: 301-827-2063
FAX #: 301-827-2075/2091

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: December 17, 2002 Number of Pages (including cover sheet) – 4

TO: John Hegarty, Regulatory Associate
COMPANY: Berlex Laboratories
FAX #: 973-487-2016

MESSAGE: Please find attached to this facsimile transmission our minutes of our December 2, 2002, CMC teleconference regarding your NDA 21-470, Finacea (azelaic acid) Gel, 15%.

Thank you.

FROM: Frank H. Cross, Jr., M.A., CDR
TITLE: Senior Regulatory Management Officer
PHONE #: 301-827-2063
FAX #: 301-827-2075/2091