CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-076

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

1.3.1 ADMINISTRATIVE DOCUMENTS

1.3.1.1 PATENT INFORMATION

U.S. Patent Application No. 10/762,652 "Stabilized Steroid Composition and Method for its Preparation" was filed by Ferndale Laboratories, Inc. on January 22, 2004 and is currently under review by the U.S. Patent and Trademark Office. This application covers the formulation, composition and method of preparation of the drug product, Locoid (hydrocortisone butyrate) Lotion, 0.1%. The patent certification statement will be amended as soon as the patent issues.

1.3.1.2 PATENT CERTIFICATION

In the opinion and to the best knowledge of Ferndale Laboratories, Inc., there are currently no patents that claim the drug or drug product on which investigations that are relied upon in this application were conducted or that claim a use of such drug or drug product.

Signed: _____ Date: 6/26/06

Richard A. Hamer, Vice President, Regulatory/
Clinical Affairs and Quality Assurance

N-020 C NEW CORRESP

Department of Health and Human Services
Food and Drug Administration

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

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

Form Approved: OMB No. 0910-0513
Expiration Date: 7/31/06
See OMB Statement on Page 3.

NDA NUMBER
22-076

ORIGINAL

NAME OF APPLICANT / NDA HOLDER
Ferndale Laboratories, Inc.

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

TRADE NAME (OR PROPOSED TRADE NAME)
Locoid (hydrocortisone butyrate) Lotion, 0.1%

ACTIVE INGREDIENT(S)
Hydrocortisone Butyrate

STRENGTH(S)
0.1% w/w

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DOSAGE FORM
Lotion

CDER Wilke Oak DR 1

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA application, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. The information submitted in the declaration form submitted upon or after approval will be the *only* information relied upon by FDA for listing a patent in the Orange Book.

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

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

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

1. GENERAL

a. United States Patent Number	b. Issue Date of Patent	c. Expiration Date of Patent
d. Name of Patent Owner	Address *(of Patent Owner)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant/holder does not reside or have a place of business within the United States) ☞	Address *(of agent or representative named in 1.e.)*	
	City/State	
	ZIP Code	FAX Number *(if available)*
	Telephone Number	E-Mail Address *(if available)*

f. Is the patent referenced above a patent that has been submitted previously for the approved NDA or supplement referenced above? ☐ Yes ☐ No

g. If the patent referenced above has been submitted previously for listing, is the expiration date a new expiration date? ☐ Yes ☐ No

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

2. Drug Substance (Active Ingredient)

2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
2.2 Does the patent claim a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
2.3 If the answer to question **2.2** is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b).	☐ Yes	☐ No
2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in **2.3**.		
2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.)	☐ Yes	☐ No
2.6 Does the patent claim only an intermediate?	☐ Yes	☐ No
2.7 If the patent referenced in **2.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

3. Drug Product (Composition/Formulation)

3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
3.2 Does the patent claim only an intermediate?	☐ Yes	☐ No
3.3 If the patent referenced in **3.1** is a product-by-process patent, is the product claimed in the patent novel? (An answer is required only if the patent is a product-by-process patent.)	☐ Yes	☐ No

4. Method of Use

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

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?	☐ Yes	☐ No
4.2 Claim Number *(as listed in the patent)*	Does the patent claim referenced in **4.2** claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement? ☐ Yes ☐ No	
4.2a If the answer to **4.2** is "Yes," identify with specificity the use with reference to the proposed labeling for the drug product.	Use: *(Submit indication or method of use information as identified specifically in the proposed labeling.)*	

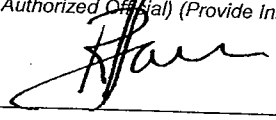
5. No Relevant Patents

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

6. Declaration Certification

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

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

6.2 Authorized Signature of NDA Applicant/Holder or Patent Owner *(Attorney, Agent, Representative or other Authorized Official) (Provide Information below)*	Date Signed
	11/2/06

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

Check applicable box and provide information below.

☑ NDA Applicant/Holder	☐ NDA Applicant's/Holder's Attorney, Agent (Representative) or other Authorized Official
☐ Patent Owner	☐ Patent Owner's Attorney, Agent (Representative) or Other Authorized Official

Name Richard Hamer	
Address 780 West 8 Mile Rd	City/State Ferndale, MI
ZIP Code 48220	Telephone Number (248) 548-0900
FAX Number *(if available)* (248) 548-9472	E-Mail Address *(if available)*

EXCLUSIVITY SUMMARY

NDA # 22-076 SUPPL # N/A HFD # 540

Trade Name Locoid Lotion, 0.1%

Generic Name hydrocortisone butyrate

Applicant Name Ferndale Laboratories, Inc.

Approval Date, If Known May 17, 2007

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES ☒ NO ☐

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

505(b)(1)

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

YES ☒ NO ☐

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

N/A

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

N/A

d) Did the applicant request exclusivity?

YES ☒ NO ☐

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

3 years and 6 months

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

YES ☐ NO ☒

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

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

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

YES ☐ NO ☒

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

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

1. Single active ingredient product.

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

YES ☒ NO ☐

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

NDA#	18-514	Locoid Cream, 0.1%
NDA#	20-769	Locoid Lipocream, 0.1%
NDA#	19-116	Locoid Solution, 0.1%
	18-652	Locoid Ointment, 0.1%
	76-654	Hydrocortisone Butyrate Cream, 0.1%
	76-842	Hydrocortisone Butyrate Ointment, 0.1%
	76-364	Hydrocortisone Butyrate Solution, 0.1%

2. Combination product.

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

YES ☐ NO ☒

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

NDA#

NDA#

NDA#

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

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

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

to PART II, Question 1 or 2 was "yes."

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

YES ☒ NO ☐

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

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

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

YES ☒ NO ☐

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

N/A

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

YES ☐ NO ☒

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

YES ☐ NO ☒

If yes, explain:

N/A

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

YES ☐ NO ☒

If yes, explain:

N/A

(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:

04-103, 03-074, 01-029, 02-043, 02-044, 04-108, 01-036, 03-097, 04-101

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

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

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

Investigation #1 YES ☐ NO ☒

Investigation #2 YES ☐ NO ☒

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

N/A

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the

effectiveness of a previously approved drug product?

Investigation #1 YES ☐ NO ☒

Investigation #2 YES ☐ NO ☒

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

N/A

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

04-103, 03-074, 01-029, 02-043, 02-044, 04-108, 01-036, 03-097, 04-101

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

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

Investigation #1

IND # 64,845 YES ☒ ! NO ☐
! Explain:

Investigation #2

IND # 64,845 YES ☒ ! NO ☐
! Explain:

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

Investigation #1	!
	!
YES ☐	! NO ☐
Explain:	! Explain:
N/A	
Investigation #2	!
	!
YES ☐	! NO ☐
Explain:	! Explain:
N/A	

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

YES ☐ NO ☒

If yes, explain:

N/A

==========

Name of person completing form: Melinda Bauerlien, M.S.
Title: Regulatory Project Manager
Date: May 15, 2007

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

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

/s/

Stanka Kukich
5/18/2007 11:14:28 AM
sign off for Dr. Susan Walker, Division Director

1.3.1.9 STATEMENTS OF CLAIMED EXCLUSIVITY

Pursuant to the provisions of Section 505 (c)(3)(D) (iii) of the Federal Food, Drug and Cosmetic Act, Ferndale Laboratories claims an exclusivity period of three years and six months from the date of approval of this application.

PEDIATRIC PAGE

(Complete for all filed original applications and efficacy supplements)

NDA/BLA # : 22-076 Supplement Type (e.g. SE5): N/A Supplement Number: N/A

Stamp Date: July 20, 2006 PDUFA Goal Date: May 20, 2007

HFD-540 Trade and generic names/dosage form: Locoid (hydrocortisone butyrate) Lotion, 0.1%

Applicant: Ferndale Laboratories Therapeutic Class: 3

Does this application provide for new active ingredient(s), new indication(s), new dosage form, new dosing regimen, or new route of administration? *

- X Yes. Please proceed to the next question.
- ☐ No. PREA does not apply. Skip to signature block.

** SE5, SE6, and SE7 submissions may also trigger PREA. If there are questions, please contact the Rosemary Addy or Grace Carmouze.*

Indication(s) *previously approved* (please complete this section for supplements only): N/A

Each indication covered by current application under review must have pediatric studies: *Completed, Deferred, and/or Waived.*

Number of indications for this application(s): 1

Indication #1: topical treatment of mild to moderate atopic dermatitis in patients 3 months of age and older.

Is this an orphan indication?

- ☐ Yes. PREA does not apply. Skip to signature block.
- X No. Please proceed to the next question.

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

- ☐ Yes: Please proceed to Section A.
- X No: Please check all that apply: X Partial Waiver ___ Deferred X Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

Section A: Fully Waived Studies

Reason(s) for full waiver:

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

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

Section B: Partially Waived Studies

Age/weight range being partially waived (fill in applicable criteria below):

Min_____ kg_____ mo.__0____ yr.___0__ Tanner Stage_____
Max_____ kg_____ mo._less than 3 months____ yr._0____ Tanner Stage_____
Reason(s) for partial waiver:

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

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

Section C: Deferred Studies

Age/weight range being deferred (fill in applicable criteria below):

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 (fill in applicable criteria below):

Min _____ kg_____ mo.__3____ yr._____ Tanner Stage_____
Max_____ kg_____ mo._____ yr._less than 18____ Tanner Stage_____

Comments:

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

This page was completed by:

{See appended electronic signature page}

Melinda Bauerlien, M.S.
Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 10/10/2006)

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

/s/

Kenneth A Katz
5/17/2007 10:34:03 AM

Markham Luke
5/17/2007 10:38:00 AM

Stanka Kukich
5/17/2007 12:37:35 PM

1.3.1.3 DEBARMENT CERTIFICATION

Ferndale Laboratories, Inc. hereby certifies that the services of any persons debarred under Section 306(a) or (b) have not and will not be used in any capacity in connection with this application.

Signed: _____ Date: 6/26/06

Richard A. Hamer, Vice President, Regulatory/
Clinical Affairs and Quality Assurance

MEMORANDUM OF TELECON

DATE: May 10, 2007

APPLICATION NUMBER: NDA 22-076
Locoid (hydrocortisone butyrate) topical lotion/cream

BETWEEN:

Name: Richard Hamer
Phone: 888-247-1961
Representing: Ferndale Laboratories, Inc.
Leon Dupuis
Sarah Saxton
Brookfield Attendees:
John Wall
David Moonay

AND

Name: Stanka Kukich, M.D./DDDP
Christy Cottrell/DDDP
Kenneth Katz, M.D./DDDP
Markham Luke, M.D., Ph.D./DDDP
Elaine Morefield, Ph.D./ONDQA
Moo-Jhong Rhee, Ph.D./ONDQA
Shulin Ding, Ph.D./ONDQA
Tarun Mehta, M.Sc./ONDQA
Linda Athey/ONDQA

SUBJECT: Dosage Form Cream vs. Lotion and Amount Undeliverable

1.0 BACKGROUND

NDA 22-076 was submitted by Ferndale Laboratories, Inc. (Ferndale) on June 26, 2006, stamped on June 28, 2007, to the Division of Dermatology and Dental Products for Locoid (hydrocortisone butyrate) topical lotion, proposed for the relief c [redacted] atopic dermatitis in patients 3 months of age and older. A teleconference was requested by FDA to address the following issues: dosage form nomenclature and the amount of product that can be delivered from the package. The teleconference occurred on May 10, 2007.

b(4)

2.0 DISCUSSION

FDA stated that it was misleading to label a product as a lotion when it should be a cream and that there was a concern about the patient receiving enough of the product because of the difficulty in removing the product from the bottle.

FDA stated that the product dosage form should be classified as a cream not a lotion. The consistency of the product is a semisolid because it does not flow when poured. In addition, it exhibits a yield value that is distinctly large enough to prevent pouring and thus it meets the definition of a cream rather than a lotion. A lotion should be a liquid. Both British pharmacopeia and USP follow this definition.

The sponsor stated that all through their formulation development (IND and NDA application) for this project, they intended to make a lotion, and the formulation had not been changed since year 2001. Because the dosage form definition in the CDER Data Standards Manual was not updated for creams and lotions until June 21, 2006, the sponsor believed that this NDA should be evaluated and approved using the previous standard not the current one.

FDA responded that even though the sponsor's intent was to make a lotion, the product they made was a cream. FDA also stated that the concept of lotions being a liquid is not a recent one, and has always been widely accepted by the pharmaceutical industry as evidenced by the lotion definition given in British Pharmacopeia and USP<1151>. Furthermore, the update on June 21, 2006 in the CDER Data Standards Manual was not a change in FDA's definition for creams and lotions but an addition of information to enhance the clarity of the definitions.

With regard to the amount of undeliverable product, the FDA explained that in an FDA test, there was about 20% of the product left in the lotion bottle which may be impossible for the patient to retrieve. If physicians prescribe a specific amount of medication and patients are unable to get the full amount from the bottle, this could lead to inadequate treatment. FDA requested that the sponsor perform a "use test" to measure the amount of product left in the bottle. The sponsor responded that phase 3 trials were conducted with the product packaged in the similar lotion bottle.

The teleconference was concluded by a re-iteration of the Agency's concerns with the dosage form name and the potentially large undeliverable amount in dispensing. The Agency asked the sponsor to address the concerns. The Sponsor's response should be received by the FDA by early the week of May 14th because the user fee goal date is May 20, 2007.

{See appended electronic signature page}

Stanka Kukich, M.D.
Deputy Director

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

/s/

Linda D Mullins-Athey
5/22/2007 02:12:31 PM
PROJECT MANAGER FOR QUALITY

Stanka Kukich
5/30/2007 02:45:13 PM
MEDICAL OFFICER

FERNDALE LABORATORIES INC

DUPLICATE

VIA COURIER

NDA 22-076

March 23, 2007

N-600 (L)
NEW CORRESP

RECEIVED
MAR 2 7 2007
CDER CDR

Susan Walker, M.D.
Director
Division of Dermatology & Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Rd.
Beltsville MD 20705-1266
Attn: Melinda Bauerlien, Regulatory Project Manager

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MAR 2 7 2007
CDER White Oak DR 1

Re: NDA 22-076 Response to 3/22/07 Information Request

Dear Dr. Walker:

Please refer to our July 20, 2006 new drug application submitted under section 505(b) (1) of the Federal Food, Drug and Cosmetic Act for Locoid® (hydrocortisone butyrate) Lotion, 0.1%, as amended. Reference is also made to your facsimile memorandum of March 22, 2007 requesting a commitment to conduct a nonclinical post-marketing study with the subject product.

As requested, we hereby commit to conduct a 2-year dermal carcinogenicity study with Locoid (hydrocortisone butyrate) Lotion, 0.1% in accordance with the following schedule:

90-day dose range-finding study:	By June 1, 2008
Study protocol submission:	By December 1, 2008
Study start date:	By September 1, 2009
Final report submission:	By March 1, 2013

Should you have any questions or concerns, please do not hesitate to contact me by phone (248.548.0900 X433), fax (248.548.4790) or e-mail (rhamer@ferndalelabs.com).

Sincerely,

Richard A. Hamer
Vice President, Regulatory/Clinical Affairs
and Quality Assurance

NDA 22-076

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

FACSIMILE TRANSMITTAL SHEET

Date: March 22, 2007

To: Richard Hamer
Vice President, Regulatory/Clinical Affairs and Quality Assurance
Ferndale Laboratories, Inc.
Phone: (248) 548-0900
Fax: (248) 548-0708

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

This transmission includes 3 pages (including this page)

FDA Facsimile Memorandum

Date: March 22, 2007

To: Richard Hamer
Vice President, Regulatory/Clinical Affairs and Quality Assurance
Ferndale Laboratories, Inc.
Phone: (248) 548-0900
Fax: (248) 548-0708

From: Margo Owens, Project Manager

Subject: NDA 22-076 Locoid Lotion

Mr. Hamer,

The Pharmacology/Toxicology Reviewer has the following information request for your NDA 22-076 Locoid (hydrocortisone butyrate) Lotion.

Pharmacology/Toxicology Information Request:
It is recommended that the following nonclinical Post-marketing commitment be conducted for Locoid lotion.

1. Conduct a 2-year dermal carcinogenicity study with Locoid (hydrocortisone butyrate) lotion.

90-day dose range-finding study:	By June 1, 2008
Study protocol submission:	By December 1, 2008
Study start date:	By September 1, 2009
Final report submission:	By March 1, 2013

Please submit officially to your NDA, your commitment to conduct a 2-year dermal carcinogenicity study for Locoid Lotion to include the protocol submission, study initiation and completion and final report submission dates as outlined above.

Please call if you have questions.

Margo Owens
Project Manager

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/s/

Margo Owens
3/22/2007 02:18:15 PM
CSO

MEMORANDUM OF TELECONFERENCE

Sponsor Name:	Ferndale Laboratories, Inc.
Application Number:	NDA 22-076
Product Name:	Locoid (hydrocortisone butyrate) topical lotion/cream
Teleconference Date and Time:	February 26, 2007 0930 ET
FDA Attendees:	Office of New Drug Quality Assessment Shulin Ding, PhD, Pharmaceutical Assessment Lead Tarun Mehta, M.Sc, Review Chemist Scott N. Goldie, PhD, Regulatory Health Project Manager for Quality Division of Dermatology and Dental Products Stanka Kukich, MD, Deputy Division Director Kenneth Katz, MD; Medical Officer
Ferndale Attendees:	Leon Dupuis, VP Operations Richard A. Hamer, VP, Regulatory/Clinical Affairs & Quality Assurance Sarah Saxton, RA Manager- CMC

1.0 BACKGROUND

NDA 22-076 was submitted by Ferndale Laboratories, Inc. (Ferndale) on June 28, 2006, stamped on May 20, 2007, to the Division of Dermatology and Dental Products for Locoid (hydrocortisone butyrate) topical lotion, proposed for the relief [redacted] of atopic dermatitis in patients 3 months of age and older. A CMC teleconference was requested by FDA to discuss the following issues: dosage form nomenclature, trade name, particle size distribution, and homogeneity. The teleconference occurred on February 26, 2007. The CMC draft comments on these issues were e-mailed to Ferndale on February 20, 2007 to assist the company in preparation of the teleconference.

b(4)

2.0 DISCUSSION

2.1 Labeling Issue:

2.1.1 ***Background:*** Incorrect Dosage form: Upon examining your drug product received in 2oz packaging, we concluded that the proposed drug product name, Locoid® (hydrocortisone butyrate) Lotion, 0.1% does not describe your dosage form correctly. Lotion is not a correct term for your proposed drug product. Based on the experiments with the sample product, we are not able to pour the product from bottle unless we squeeze the product out of bottle; product does not show Newtonian flow behavior. The product was set on a smooth sloping surface for over an hour and did not show any sign of flowing or changing its original shape. Lotion should have low stress yield, enough to conform to shape (i.e. to be spread out or roll off on sloping surface) with gravitational force at room temperature.

Refer to following definition for lotion and cream from CDER Data Standard Manual.

According to CDER Data Standard Manual, lotion by definition is "An emulsion, liquid[1] dosage form. This dosage form is generally for external application to the skin.[2]

[1] A liquid is pourable; it flows and conforms to its container at room temperature. It displays Newtonian or pseudoplastic flow behavior.

[2] Previously the definition of a lotion was "The term, lotion has been used to categorize many topical suspensions, solutions, and emulsions intended for application to the skin." The current definition of a lotion is restricted to an emulsion.

The proposed drug product meets the characteristics of cream dosage. Please refer to definition by CDER Data Standard Manual.

An emulsion, semisolid[3] dosage form, usually containing > 20% water and volatiles 5 and/or < 50% hydrocarbons, waxes, or polyols as the vehicle. This dosage form is generally for external application to the skin or mucous membranes.

[3] A semisolid is not pourable; it does not flow or conform to its container at room temperature. It does not flow at low shear stress and generally exhibits plastic flow behavior.

2.1.1 ***Meeting Discussion:*** FDA stated that based on the rheological data provided in the NDA and the experiments performed on the drug product samples received with the December 21, 2006, submission, the nomenclature for the proposed drug product is incorrectly listed as a lotion. FDA stated that the drug product should instead be classified as a cream dosage form. Ferndale asked for CDER's definition for lotion and how the experiments were conducted. FDA reiterated the definition given in the draft comments which had been e-mailed to the company prior to the teleconference, and acknowledged that the experiments performed were not standard tests. Ferndale indicated its disagreement with FDA's position on this issue, and stated that Cutivate lotion (NDA 21-152, approved in year 2005) was similar to the proposed product in appearance, feel and rheological characteristics. FDA recommended and Ferndale Laboratories committed to submit samples and rheograms of Cutivate lotion and the two marketed Locoid creams for the Agency to review. Ferndale could also submit scientific justification for its position with references for the Agency to consider.

2.1.2 Trade name issue: (for cream as a dosage)

Background: Ferndale Laboratories Inc. is currently marketing approved Locoid (hydrocortisone butyrate) cream, 0.1%.The use of the same trade name for two different indications is not permitted. A second trade name must be approved to use cream as a dosage form,

2.1.2 ***Meeting Discussion:*** This discussion was tabled pending the submissions associated with 2.1.1.

2.2 Particle size distribution:

Background: Please provide a new regulatory method for measuring the particle size distribution. There is an adequate amount of data provided for the particle size. However, the test method suggests that samples were diluted with 90% water and mechanically mixed for about 5 minutes. By performing this way, practically, all the agglomeration can be destroyed and will produce results which may not represent for the true particle size distribution. Therefore, this method of testing is not deemed acceptable, unless justified. Furthermore, microscopic data are not deemed conclusive. Please provide an alternate or modified method for examining agglomeration and particle size distribution.

Meeting Discussion: FDA recommended that appropriate scientific justification be submitted to the NDA to justify Ferndale's measurement of particle size distribution. FDA stated that the current analytical method was biased and did not reflect the true particle size. Ferndale indicated that they were developing a new particle size method, and would take the recommendations under advisement.

FDA recommended that Ferndale generate data on particle size for in-process samples. FDA suggested that Ferdnale should measure particle size of samples taken from the scale-up process after the [redacted], which comprised of [redacted] (Lines 32 and 33 of batch record MPR 0872-60). It is preferable to analyze the samples as they are collected from vessel without any dilution or mechanical aid. Ferndale acknowledged FDA's recommendation and indicated that they would take it under advisement. b(4)

FDA recommended that Ferndale add particle size distribution testing at release and on stability for the first three commercial scale validation batches. FDA indicated that upon generating adequate data the specification can be revised. Ferndale acknowledged FDA's recommendation and agreed to collect the particle size data for the first three commercial validation batches.

2.3 Homogeneity:

Background: In accordance with ICH Q6A: Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances, a test for homogeneity of the drug product should be included with the bulk batch testing and an adequate sampling plan.

Meeting Discussion: FDA recommended that Ferndale add homogeneity to the bulk batch testing protocol with an adequate sampling plan. Ferndale acknowledged FDA's recommendations and agreed to submit a bulk product homogeneity testing plan to amend the NDA.

2.4 Expiry Testing:

Meeting Discussion: FDA noted that 1 batch of the three stability batches submitted for the physicians sample package size appeared to be failing the acceptance criteria at [redacted] months. Ferndale acknowledged this observation and indicated that they planned to submit a request for 24 months expiry dating to the NDA. FDA recommended that this occur as soon as possible. b(4)

2.5 Labeling:

Meeting Discussion: FDA asked when Ferndale planned to submit the revised labeling. Ferndale replied that FDA would receive the revised labeling on Monday, February 26, 2007, and responses to other outstanding queries by the end of the week of February 26, 2007. As of March 12, 2007, FDA has not yet received responses to the outstanding inquiries.

3.0 CONCURRENCE:

{See appended electronic signature page}

Scott N. Goldie, Ph.D.
Regulatory Health Project Manager for Quality
Division of Pre-Marketing Assessment I
Office of New Drug Quality Assessment

{See appended electronic signature page}

Shulin Ding Ph.D.
Pharmaceutical Assessment Lead
Division of Pre-Marketing Assessment II
Office of New Drug Quality Assessment

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/s/

Scott Goldie
3/16/2007 03:43:45 PM
PROJECT MANAGER FOR QUALITY

Shulin Ding
3/16/2007 04:12:41 PM
CHEMIST

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

REQUEST FOR SEALD CONSULTATION

TO *(Division/Office)*:
Study Endpoints and Label Development Team (SEALD)
CDER/OND-IO White Oak Bldg 22, Mail Drop 6411

FROM *(Division/Office)*: Melinda Bauerlien, M.S.
Regulatory Project Manager
Division of Dermatology and Dental Products

DATE of REQUEST	NDA/BLA/IND NO	SERIAL NO/SUPPL. NO	TYPE OF DOCUMENT	DATE OF DOCUMENT
March 12, 2007	22-076		NDA	June 26, 2006

NAME OF DRUG	MEETING DATES FOR SUBMISSION	CLASSIFICATION OF DRUG	REQUESTED COMPLETION DATE
Locoid Lotion	Internal: Sponsor:		April 12, 2007

NAME OF SPONSOR or INVESTIGATOR (for investigator Initiated INDs): Ferndale LAboratories

DRUG DEVELOPMENT PHASE & MILESTONE

- ☐ pre-IND/pre-BBIND
- ☐ PHASE II
- ☐ PHASE III
- ☐ PRE-NDA/BLA MEETING

- ☒ NDA/BLA/sNDA/SBLA REVIEW
- ☐ NDA/BLA SAFETY/EFFICACY UPDATE
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ NDA/BLA/sNDA/SBLA RESUBMISSION REVIEW
- ☐ ADVISORY COMMITTEE MEETINGS
- ☐ LABELING (INITIAL OR REVISION)
- ☐ ADVERTISING REVIEW

- ☐ OTHER (Specify)

STUDY ENDPOINT OR LABELING To BE REVIEWED

STUDY ENDPOINT REVIEW		LABELING REVIEW
☐ TYPE A MEETING PACKAGE ☐ CLINICAL HOLD/DISPUTE RESOLUTION ☐ SPA RESPONSE ☐ TYPE B MEETING PACKAGE ☐ PRE-IND MEETING ☐ END OF PHASE II/Pre-PHASE III ☒ PRE-NDA/BLA ☐ TYPE C MEETING PACKAGE	☐ SPECIAL PROTOCOL ASSESSMENT REVIEW ☐ STANDARD PROTCOL REVIEW ☐ PROGRESS REPORT ☐ STATISTICAL ANALYSIS PLAN REVIEW ☐ ENDPOINT DEVELOPMENT/VALIDATION DOSSIER ☐ NDA / BLA REVIEW ☐ AC MEETING	☐ PROPOSED LABELING ☐ FINAL PRINTED LABELING ☐ LABELING REVISION ☐ DRUG ADVERTISING ☐ OTHER (SPECIFY):

CONSULT REVIEW REQUESTED

The applicant proposes [redacted] *Please assess the appropriateness of the instrument used to measure this patient-reported outcome in the pivotal study (04-103)."* b(4)

Study report attached.

We have a labeling meeting scheduled for 3/26 and anticipate getting the label to the sponsor in early April.

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Melinda Bauerlien, M.S.	☐ INTEROFFICE MAIL ☐ HAND-CARRIED ☒ E-MAIL
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

Melinda Bauerlien
3/12/2007 12:27:39 PM

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

FACSIMILE TRANSMITTAL SHEET

DATE: March 6, 2007

To: Richard Hamer	**From:** Melinda Bauerlien, M.S. Project Manager
Company: Ferndale Laboratories	Division of Dermatology & Dental Products
Fax number: (248) 548-4790	**Fax number:** (301) 796-9895
Phone number: (248) 548-0900 x 433	**Phone number:** (301) 796-2110

Subject: NDA 22-076

Total no. of pages including cover: 3

Comments: Clinical request for information. Please respond as soon as possible.

For study 04-101, please provide the mean, standard deviation, median, and minimum and maximum values for compliance and weight of medication used. Please list the compliance and weight of medication used for each of the seven subjects who experienced adrenal suppression.

Document to be mailed: ☐ YES ☑ NO

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/s/

Melinda Bauerlien
3/6/2007 01:47:53 PM
CSO

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

FACSIMILE TRANSMITTAL SHEET

DATE: February 21, 2007

To: Richard Hamer	**From:** Melinda Bauerlien, M.S. Project Manager
Company: Ferndale Laboratories	Division of Dermatology & Dental Products
Fax number: (248) 548-4790	**Fax number:** (301) 796-9895
Phone number: (248) 548-0900 x 433	**Phone number:** (301) 796-2110

Subject: NDA 22-076

Total no. of pages including cover: 3

Comments: Clinical request for information. Please respond as soon as possible.

Document to be mailed: ☐ YES ☑ NO

NDA 22-076

Clinical request for information

For study 03-074, please identify normal ranges used to assess blood pressure, pulse, temperature, and respiratory rate and identify subjects (by number) whose values for any of these measurements were outside of the normal range at any time point.

Trade Name Group request for information

Per the tradename reviewer please provide

1) a working sample so they can thoroughly evaluate the packaging configuration for this product.

2) the carton labeling for the trade sizes (2 fl oz and 4 fl oz)/

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/s/

Melinda Bauerlien
2/21/2007 11:17:54 AM
CSO

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

FACSIMILE TRANSMITTAL SHEET

DATE: February 7, 2007

To: Richard Hamer	**From:** Melinda Bauerlien, M.S. Project Manager
Company: Ferndale Laboratories	Division of Dermatology & Dental Products
Fax number: (248) 548-4790	**Fax number:** (301) 796-9895
Phone number: ()	**Phone number:** (301) 796-2110

Subject: NDA 22-076

Total no. of pages including cover: 2

Comments: Please respond to the following request for information as soon as possible

Document to be mailed: ☐ YES ☑ NO

NDA 22-076 Request for Information

For studies 02-043 and 02-044:

Please provide an analysis that shows the proportion of subjects in each study who experienced each level of irritancy at any time during the study for each test article, both for "actual" and "converted' scores.

Please provide an explanation of the difference between "actual" and "converted" scores in each study.

Please provide an explanation of what the codes for hydrocortisone butyrate and vehicle mean (e.g., #R6539), and which codes correspond to the to-be-marketed formulation containing HCB and the vehicle for that formulation for which the applicant has submitted the NDA.

For study 04-101:

Please provide an analysis that (1) shows the proportion of subjects in the study who experienced an abnormal vital sign (systolic or diastolic blood pressure, pulse, respiration rate, or temperature) at each evaluation point in the study; (2) identifies the subject number of any subject who experienced an abnormal vital sign at any evaluation point in the study; and (3) lists the normal values of each vital sign for each age group.

Table 14.4.1.2, Mod 5, Vol 20 indicates that 7 subjects experienced adrenal suppression. However, Table 14.4.4.1, Mod 5, Vol 20 lists the number of subjects experiencing adrenal suppression as 2. Please clarify this discrepancy.

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/s/

Melinda Bauerlien
2/7/2007 01:38:52 PM
CSO

FERNDALE LABORATORIES INC

DUPLICATE

N-0000-C

VIA COURIER: 1Z 459 858 22 1004 5340

NEW CORRESP

NDA 22-076

January 31, 2007

Susan Walker, M.D.
Director
Division of Dermatology & Dental products
Office of Drug Evaluation III
Center for Drug Evaluation and Research
Food and Drug Administration
5901-B Ammendale Rd.
Beltsville, MD 20705-1266
Attn: Melinda Bauerlien, Regulatory Project Manager

Re: NDA 22-076 Safety Update Report

Dear Dr. Walker:

Please refer to our July 20, 2006 new drug application submitted under section 505(b)(1) of the Federal Food, Drug and Cosmetic Act for Locoid® (hydrocortisone butyrate) Lotion, 0.1%. Reference is also made to your facsimile letter of January 25, 2007, requesting submission of a safety update report to this application.

In accordance with the provisions of 21 CFR 314.50 (d)(5)(vi)(b), please be advised that we have no additional safety data to report. All available data was included in the original application and no additional data has become available since submission.

If you have any questions or concerns, please do not hesitate to contact me by phone 248.548.0900 Ext. 433, by fax at 248.548.4790 or by e-mail at rhamer@ferndalelabs.com.

Sincerely,

Richard A. Hamer
Vice President, Regulatory/Clinical Affairs and
Quality Assurance

G:\RA\Products\Locoid Lotion\Locoid Lotion (Crelo)\NDA 22-076\01-31-07 - Safety Update Report.doc

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

FACSIMILE TRANSMITTAL SHEET

DATE: January 25, 2007

To: Richard Hamer	**From:** Melinda Bauerlien, M.S. Project Manager
Company: Ferndale Laboratories	Division of Dermatology & Dental Products
Fax number: (248) 548-9472	**Fax number:** (301) 796-9895
Phone number: ()	**Phone number:** (301) 796-2110

Subject: NDA 22-076

Total no. of pages including cover: 2

Comments: Please submit a safety update to this NDA as soon as possible

Document to be mailed: ☐ YES ☑ NO

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/s/

Melinda Bauerlien
1/25/2007 01:47:23 PM
CSO

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

FACSIMILE TRANSMITTAL SHEET

DATE: January 11, 2007

To: Richard Hamer	**From:** Melinda Bauerlien, M.S. Project Manager
Company: Ferndale Laboratories	Division of Dermatology & Dental Products
Fax number: (248) 548-9472	**Fax number:** (301) 796-9895
Phone number: ()	**Phone number:** (301) 796-2110

Subject: NDA 22-076

Total no. of pages including cover: 4

Comments: Clinical, PK and label request for information. Please provide a response by January 18, 2007 for the first 2 items and as soon as possible on the label changes.

Document to be mailed: ☐ YES ☑ NO

NDA 22-076 Clinical request for information

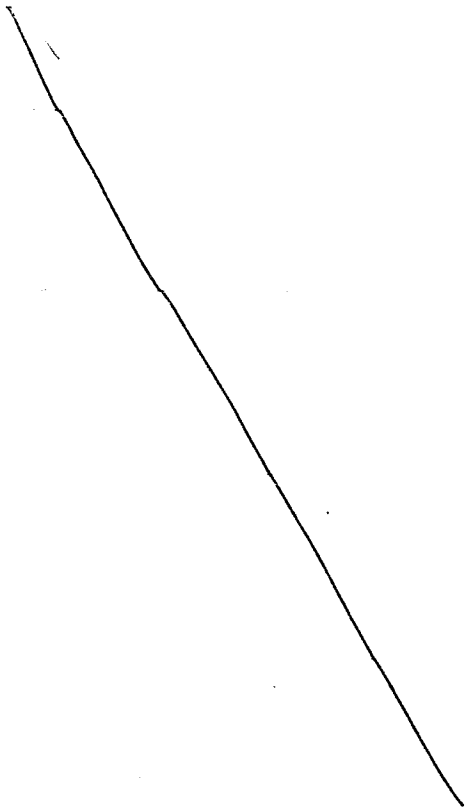
For each of Study 03-074 and 04-103, please provide the subject number, adverse event, and assessment of causality of that AE for each subject who discontinued prematurely due to an AE.

Clinical Pharmacology request for information

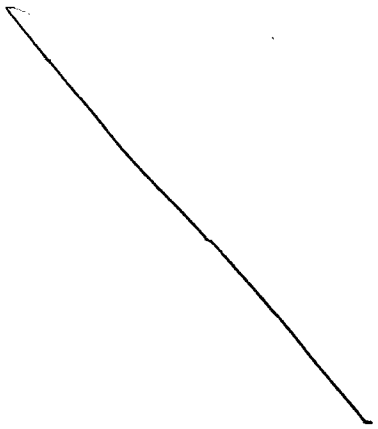
Please send us an electronic version (preferably MS Word) of study reports for studies 01-036 and 03-097.

Comments on the Label – SPL format

Highlights:



b(4)



b(4)

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/s/

Melinda Bauerlien
1/11/2007 08:40:12 AM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-076

Ferndale Laboratories
Attention: Richard Hamer, Vice President, Regulatory/Clinical Affairs
780 West Eight Mile Road
Ferndale, Michigan 48220

Dear Mr. Hamer:

Please refer to your July 20, 2006, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Locoid® (hydrocortisone butyrate) Lotion, 0.1%.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on September 18, 2006, in accordance with 21 CFR 314.101(a).

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

1. Uncertainty in the correctness of the name of the proposed dosage form, lotion.

2. Uncertainty in the formulation(s) used in clinical, toxicology, and stability studies.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

We also request that you submit the following information:

1. To assist in our review of this issue, please provide drug product samples (6 units for each packaging configuration), and the rheograms (viscosity versus shear rate and shear stress versus shear rate) of the to-be-marketed formulation.

2. Please provide a table which correlates formulation number and lot numbers of drug substance and drug product to clinical/toxicology/stability studies, and a table which describes the formulation composition of all formulations.

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

If you have any questions, call Melinda Bauerlien, Regulatory Project Manager, at (301) 796-0906.

Sincerely,

{See appended electronic signature page}

Susan Walker, M.D.
Director
Division of Dermatology & Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

Susan Walker
10/2/2006 12:38:33 PM

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

FACSIMILE TRANSMITTAL SHEET

DATE: August 23, 2006

To: Richard Hamer	**From:** Melinda Bauerlien, M.S. Project Manager
Company: Ferndale Laboratories	Division of Dermatology & Dental Products
Fax number: (248) 548-8427)	**Fax number:** (301) 796-9895
Phone number: (248) 0900 ext. 433	**Phone number:** (301) 796-2110

Subject: NDA 22-076 Statistical Request for Information

Total no. of pages including cover: 2

Comments: Please provide the data sets for the NDA as soon as possible.

Document to be mailed: ☐ YES ☑ NO

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/s/

Melinda Bauerlien
8/23/2006 11:13:50 AM
CSO

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

REQUEST FOR CONSULTATION

TO *(Office/Division)*: Division of Medication Errors and Technical Support (DMETS)

FROM *(Name, Office/Division, and Phone Number of Requestor)*:
Melinda Bauerlien, M.S.
Project Manager
Division of Dermatology and Dental Products

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
November 29, 2006		22-076	new NDA	July 20, 2006

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Locoid (hydrocortisone butyrate) Lotion, 0.1%			March 1, 2007

NAME OF FIRM: Ferndale Laboratories, Inc.

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE / ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END-OF-PHASE 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☐ SAFETY / EFFICACY
- ☒ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: Please review the tradename Locoid. The Package Insert and carton and container labels are attached.

Please let me know if you need anything further.

SIGNATURE OF REQUESTOR
Melinda Bauerlien, M.S.
Project Manager 9-0906

METHOD OF DELIVERY (Check one)
☒ DFS ☐ EMAIL ☐ MAIL ☐ HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

13 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

X Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Administrative- 1

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/s/

Melinda Bauerlien
11/29/2006 11:27:52 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

PRESCRIPTION DRUG USER FEE COVER SHEET

Form Approved: OMB No. 0910-0297
Expiration Date: December 31, 2006.

See Instructions on Reverse Side Before Completing This Form

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

1. APPLICANT'S NAME AND ADDRESS

Ferndale Laboratories, Inc.
780 West eight Mile Road
Ferndale, MI 48220

2. TELEPHONE NUMBER *(Include Area Code)*

(248) 548-0900 x 433

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?
☒ YES ☐ NO

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).

3. PRODUCT NAME
Locoid (hydrocortisone butyrate) Lotion, 0.1%

6. USER FEE I.D. NUMBER

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)

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

☐ 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.)

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

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FORTHIS APPLICATION?
☐ YES ☒ NO
(See Item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

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

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
	VP, Regulatory/Clinical Affairs & QA	6/26/06

ACTION PACKAGE CHECKLIST

Application Information			
BLA # NDA # 22-076	BLA STN# NDA Supplement # N/A	If NDA, Efficacy Supplement Type N/A	
Proprietary Name: Locoid Established Name: hydrocortisone butyrate Dosage Form: Lotion, 0.1%		Applicant: Ferndale Laboratories, Inc.	
RPM: Melinda Bauerlien, M.S.		Division: DDDP	Phone # 301-796-2110

NDAs: NDA Application Type: ☒ 505(b)(1) ☐ 505(b)(2) Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2) (A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)	505(b)(2) NDAs and 505(b)(2) NDA supplements: Listed drug(s) referred to in 505(b)(2) application (NDA #(s), Drug name(s)): N/A Provide a brief explanation of how this product is different from the listed drug. N/A ☐ If no listed drug, check here and explain: N/A **Review and confirm the information previously provided in Appendix B to the Regulatory Filing Review. Use this Checklist to update any information (including patent certification information) that is no longer correct.** ☐ Confirmed ☐ Corrected Date: N/A

❖ User Fee Goal Date ❖ Action Goal Date (if different)	May 18, 2007 May 18, 2007
❖ Actions	
• Proposed action	☒ AP ☐ TA ☐ AE ☐ NA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☒ None
❖ Advertising *(approvals only)* Note: If accelerated approval (21 CFR 314.510/601.41), advertising must have been submitted and reviewed *(indicate dates of reviews)*	☒ Requested in AP letter ☐ Received and reviewed

❖ Application Characteristics

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only): 3

NDAs, BLAs and Supplements:
☐ Fast Track
☐ Rolling Review
☐ CMA Pilot 1
☐ CMA Pilot 2

☐ Orphan drug designation

NDAs: Subpart H
☐ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ Approval based on animal studies

NDAs and NDA Supplements:
☐ OTC drug

Other: N/A

Other comments: N/A

❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	☐ Yes ☒ No
• This application is on the AIP	☐ Yes ☒ No
• Exception for review *(file Center Director's memo in* Administrative Documents *section)*	☐ Yes ☒ No
• OC clearance for approval *(file communication in* Administrative Documents *section)*	☐ Yes N/A ☐ Not an AP action
❖ Public communications (approvals only)	
• Office of Executive Programs (OEP) liaison has been notified of action	☒ Yes ☐ No
• Press Office notified of action	☒ Yes ☐ No
• Indicate what types (if any) of information dissemination are anticipated	☒ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other

❖ Exclusivity	
• NDAs: Exclusivity Summary (approvals only) *(file Summary in* Administrative Documents *section)*	☒ Included
• Is approval of this application blocked by any type of exclusivity?	☒ No ☐ Yes
• NDAs/BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.*	☒ No ☐ Yes If, yes, NDA/BLA # and date exclusivity expires:
• NDAS: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
• NDAs: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? *(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)*	☒ No ☐ Yes If yes, NDA # and date exclusivity expires:
❖ Patent Information (NDAs and NDA supplements only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.	☒ Verified ☐ Not applicable because drug is an old antibiotic.
• Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.	21 CFR 314.50(i)(1)(*i*)(A) ☐ Verified N/A 21 CFR 314.50(i)(1) ☐ (ii) ☐ (iii)
• [505(b)(2) applications] If the application includes a **paragraph III** certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).	☐ No paragraph III certification Date patent will expire N/A
• [505(b)(2) applications] For **each paragraph IV** certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). *(If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (*Summary Reviews*)).*	☒ N/A (no paragraph IV certification) ☐ Verified
• [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation. Answer the following questions for **each** paragraph IV certification: (1) Have 45 days passed since the patent owner's receipt of the applicant's	☐ Yes ☐ No

notice of certification?

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

N/A

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

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

☐ Yes ☐ No

N/A

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

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

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

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

☐ Yes ☐ No

N/A

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

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

☐ Yes ☐ No

N/A

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

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

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

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

☐ Yes ☐ No

N/A

within the 45-day period). *If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below* (Summary Reviews). *If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007) and attach a summary of the response.*	
Summary Reviews	
❖ Summary Reviews (e.g., Office Director, Division Director) *(indicate date for each review)*	May 17, 2007 Team Leader
❖ BLA approvals only: Licensing Action Recommendation Memo (LARM) *(indicate date)*	N/A
Labeling	
❖ Package Insert	
• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	May 14, 2007
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	N/A
• Original applicant-proposed labeling	June 26, 2006
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	N/A
❖ Patient Package Insert	
• Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)	N/A
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	N/A
• Original applicant-proposed labeling	N/A
• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable	N/A
❖ Medication Guide	
• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)	N/A
• Most recent applicant-proposed labeling (only if subsequent division labeling does not show applicant version)	N/A
• Original applicant-proposed labeling	N/A
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	N/A
❖ Labels (**full color** carton and immediate-container labels)	
• Most-recent division-proposed labels (only if generated after latest applicant submission)	N/A
• Most recent applicant-proposed labeling	June 26, 2006

❖ Labeling reviews and minutes of any labeling meetings *(indicate dates of reviews and meetings)*	☒ DMETS March 5, 2007 ☐ DSRCS N/A ☒ DDMAC March 28, 2007 ☒ SEALD May 1, 2007 ☐ Other reviews ☐ Memos of Mtgs

Administrative Documents	
❖ Administrative Reviews (RPM Filing Review/Memo of Filing Meeting; ADRA) *(indicate date of each review)*	May 17, 2007
❖ NDA and NDA supplement approvals only: Exclusivity Summary *(signed by Division Director)*	☒ Included
❖ AIP-related documents • Center Director's Exception for Review memo • If AP: OC clearance for approval	 N/A N/A
❖ Pediatric Page (all actions)	☒ Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent. *(Include certification.)*	☒ Verified, statement is acceptable
❖ Postmarketing Commitment Studies	☐ None
• Outgoing Agency request for post-marketing commitments *(if located elsewhere in package, state where located)*	March 22, 2007
• Incoming submission documenting commitment	March 23, 2007
❖ Outgoing correspondence (letters including previous action letters, emails, faxes, telecons)	Yes
❖ Internal memoranda, telecons, email, etc.	N/A
❖ Minutes of Meetings	
• Pre-Approval Safety Conference *(indicate date; approvals only)*	March 26,2007
• Pre-NDA/BLA meeting *(indicate date)*	☐ No mtg January 5, 2006
• EOP2 meeting *(indicate date)*	☐ No mtg March 29, 2004
• Other (e.g., EOP2a, CMC pilot programs)	N/A
❖ Advisory Committee Meeting	☒ No AC meeting
• Date of Meeting	N/A
• 48-hour alert or minutes, if available	N/A
❖ Federal Register Notices, DESI documents, NAS/NRC reports (if applicable)	N/A

CMC/Product Quality Information	
❖ CMC/Product review(s) *(indicate date for each review)*	May 15, 2007
❖ Reviews by other disciplines/divisions/Centers requested by CMC/product reviewer *(indicate date for each review)*	☒ None
❖ BLAs: Product subject to lot release (APs only)	☐ Yes ☐ No N/A
❖ Environmental Assessment (check one) (original and supplemental applications)	
• ☒ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	May 15, 2007
• ☒ Review & FONSI *(indicate date of review)*	May 15, 2007
• ☒ Review & Environmental Impact Statement *(indicate date of each review)*	May 15, 2007
❖ NDAs: Microbiology reviews (sterility & apyrogenicity) *(indicate date of each review)*	N/A

	☒ Not a parenteral product
❖ Facilities Review/Inspection	
❖ NDAs: Facilities inspections (include EER printout)	Date completed: September 21, 2006 ☒ Acceptable ☐ Withhold recommendation

❖ BLAs: Facility-Related Documents • Facility review *(indicate date(s))* • Compliance Status Check (approvals only, both original and supplemental applications) *(indicate date completed, must be within 60 days prior to AP)*	N/A ☐ Requested ☐ Accepted ☐ Hold
❖ NDAs: Methods Validation	☒ Completed ☐ Requested ☐ Not yet requested ☐ Not needed
Nonclinical Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	March 12, 2007
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☒ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☒ No carc
❖ ECAC/CAC report/memo of meeting	N/A
❖ Nonclinical inspection review Summary (DSI)	☒ None requested
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	May 17, 2007
❖ Financial Disclosure reviews(s) or location/date if addressed in another review	May 17, 2007
❖ Clinical consult reviews from other review disciplines/divisions/Centers *(indicate date of each review)*	☒ None
❖ Microbiology (efficacy) reviews(s) *(indicate date of each review)*	☒ Not needed
❖ Safety Update review(s) *(indicate location/date if incorporated into another review)*	May 17, 2007
❖ Risk Management Plan review(s) (including those by OSE) *(indicate location/date if incorporated into another review)*	N/A
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date of each review)*	☒ Not needed
❖ DSI Inspection Review Summary(ies) *(include copies of DSI letters to investigators)*	☒ None requested
• Clinical Studies	N/A
• Bioequivalence Studies	N/A
• Clin Pharm Studies	N/A
❖ Statistical Review(s) *(indicate date for each review)*	☐ None March 26, 2007
❖ Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None May 4, 2007

Appendix A to Action Package Checklist

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

(1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.

(2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.

(3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

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

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

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

(1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).

(2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.

(3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

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

(1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).

(2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.

(3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

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