

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**22-087**

**ADMINISTRATIVE and CORRESPONDENCE**  
**DOCUMENTS**

## EXCLUSIVITY SUMMARY

NDA # 22-087

SUPPL # n/a

HFD # 540

Trade Name Vectical Ointment

Generic Name calcitriol

Applicant Name Galderma Laboratories, L.P.

Approval Date, If Known 23 January 2009

### 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.

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  NO

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

3 years

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

YES  NO

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# 18-044 Rocaltrol (calcitriol) Capsules, 0.25 mcg, 0.50 mcg  
NDA# 21-068 Rocaltrol (calcitriol) Solution, 1 mcg/mL  
NDA# 18-874 Calcijex (calcitriol) Injection, .001 mg/mL, .002 mg/mL

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:

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

YES  NO

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

YES  NO

If yes, explain:

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

YES  NO

If yes, explain:

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

Investigator #1 RD.06.SRE.18053

Investigator # 2 RD.06.SRE.18054

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:

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:

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"):

Investigator #1 RD.06.SRE.18053  
Investigator # 2 RD.06.SRE.18054

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 # 62, 151      YES       ! NO   
! Explain:

Investigation #2  
IND # 62, 151      YES       ! NO   
! Explain:

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

Investigation #1

YES

Explain:

!

!

! 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

If yes, explain:

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Name of person completing form: Emelia Annum

Title: Regulatory Project Manager

Date: 1-23-09

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

Title: Director

Division of Dermatology and Dental Products

Office of Drug Evaluation III

Center for Drug Evaluation and Research

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

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/s/

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Susan Walker

1/23/2009 05:18:39 PM

**PEDIATRIC PAGE**

(Complete for all filed original applications and efficacy supplements)

NDA/BLA#: 22-087

Supplement Number: n/a

NDA Supplement Type (e.g. SE5): n/a

Division Name: Division of Dermatology and Dental Products

PDUFA Goal Date: 1/27/09

Stamp Date: 12/27/2007

Proprietary Name: Vectical

Established/Generic Name: calcitriol

Dosage Form: Ointment, 3 mcg/g

Applicant/Sponsor: Galderna Laboratories, Inc.

Indication(s) previously approved (please complete this question for supplements and Type 6 NDAs only):

- (1) \_\_\_\_\_
- (2) \_\_\_\_\_
- (3) \_\_\_\_\_
- (4) \_\_\_\_\_

Pediatric use for each pediatric subpopulation must be addressed for each indication covered by current application under review. A Pediatric Page must be completed for each indication.

Number of indications for this pending application(s): 1

(Attach a completed Pediatric Page for each indication in current application.)

Indication: plaque psoriasis

Q1: Is this application in response to a PREA PMR?

Yes  Continue

No  Please proceed to Question 2.

If Yes, NDA/BLA#: \_\_\_\_\_

Supplement #: \_\_\_\_\_

PMR #: \_\_\_\_\_

Does the division agree that this is a complete response to the PMR?

Yes. Please proceed to Section D.

No. Please proceed to Question 2 and complete the Pediatric Page, as applicable.

Q2: Does this application provide for (if yes, please check all categories that apply and proceed to the next question):

(a) NEW  active ingredient(s) (includes new combination);  indication(s);  dosage form;  dosing regimen; or  route of administration?\*

(b)  No. PREA does not apply. Skip to signature block.

\* Note for CDER: SE5, SE6, and SE7 submissions may also trigger PREA.

Q3: Does this indication have orphan designation?

Yes. PREA does not apply. Skip to signature block.

No. Please proceed to the next question.

Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?

Yes: (Complete Section A.)

No: Please check all that apply:

Partial Waiver for selected pediatric subpopulations (Complete Sections B)

Deferred for some or all pediatric subpopulations (Complete Sections C)

Completed for some or all pediatric subpopulations (Complete Sections D)

Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)

Extrapolation in One or More Pediatric Age Groups (Complete Section F)

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL ([cdcrpmhs@fda.hhs.gov](mailto:cdcrpmhs@fda.hhs.gov)) OR AT 301-796-0700.

(Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

**Section A: Fully Waived Studies (for all pediatric age groups)**

Reason(s) for full waiver: (check, and attach a brief justification for the reason(s) selected)

- Necessary studies would be impossible or highly impracticable because:
  - Disease/condition does not exist in children
  - Too few children with disease/condition to study
  - Other (e.g., patients geographically dispersed): \_\_\_\_\_
- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)

Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

**Section B: Partially Waived Studies (for selected pediatric subpopulations)**

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

|                                     |         | Reason (see below for further detail): |               |                                     |   |                                    |                                 |
|-------------------------------------|---------|--|---------------|-------------------------------------|---|------------------------------------|---------------------------------|
|                                     |         | minimum                                | maximum       | Not feasible <sup>a</sup>           | Not meaningful therapeutic benefit <sup>b</sup> | Ineffective or unsafe <sup>c</sup> | Formulation failed <sup>d</sup> |
| <input checked="" type="checkbox"/> | Neonate | __ wk. 0 mo.                           | __ wk. 6 mo.  | <input checked="" type="checkbox"/> | <input type="checkbox"/>                        | <input type="checkbox"/>           | <input type="checkbox"/>        |
| <input checked="" type="checkbox"/> | Other   | __ yr. 6 mo.                           | 2 yr. __ mo.  | <input checked="" type="checkbox"/> | <input type="checkbox"/>                        | <input type="checkbox"/>           | <input type="checkbox"/>        |
| <input type="checkbox"/>            | Other   | __ yr. __ mo.                          | __ yr. __ mo. | <input type="checkbox"/>            | <input type="checkbox"/>                        | <input type="checkbox"/>           | <input type="checkbox"/>        |
| <input type="checkbox"/>            | Other   | __ yr. __ mo.                          | __ yr. __ mo. | <input type="checkbox"/>            | <input type="checkbox"/>                        | <input type="checkbox"/>           | <input type="checkbox"/>        |
| <input type="checkbox"/>            | Other   | __ yr. __ mo.                          | __ yr. __ mo. | <input type="checkbox"/>            | <input type="checkbox"/>                        | <input type="checkbox"/>           | <input type="checkbox"/>        |

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

Reason(s) for partial waiver (check reason corresponding to the category checked above, and attach a brief justification):

# Not feasible:

- Necessary studies would be impossible or highly impracticable because:
  - Disease/condition does not exist in children
  - Too few children with disease/condition to study
  - Other (e.g., patients geographically dispersed): \_\_\_\_\_

\* Not meaningful therapeutic benefit:

- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of

pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Δ Formulation failed:

- Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)

Justification attached.

*For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.*

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**Section C: Deferred Studies (for selected pediatric subpopulations).**

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

| Deferrals (for each or all age groups):   |               |               |                                     | Reason for Deferral                           |   |                          | Applicant Certification<br>† |
|---|---------------|---------------|-------------------------------------|---|---|--------------------------|------------------------------|
| Population  | minimum       | maximum       | Ready for Approval in Adults        | Need Additional Adult Safety or Efficacy Data | Other Appropriate Reason (specify below)* | Received                 |                              |
| <input type="checkbox"/> Neonate  | __ wk. __ mo. | __ wk. __ mo. | <input type="checkbox"/>            | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/> |                              |
| <input type="checkbox"/> Other  | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/>            | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/> |                              |
| <input checked="" type="checkbox"/> Other   | 2 yr. __ mo.  | 17 yr. __ mo. | <input checked="" type="checkbox"/> | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/> |                              |
| <input type="checkbox"/> Other  | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/>            | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/> |                              |
| <input type="checkbox"/> Other  | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/>            | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/> |                              |
| <input type="checkbox"/> All Pediatric Populations  | 0 yr. 0 mo.   | 16 yr. 11 mo. | <input type="checkbox"/>            | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/> |                              |
| Date studies are due (mm/dd/yy):<br>A. PK/PD children 12 to 17: Study start June 2006; Report March 2010<br>B. PK in children ages 2 to 12: Study start July 2009; Report March 2012<br>C. Efficacy/Safety: Study start July 2009; Report July 2011<br>D. Long term safety: Study start October 2009; Report 2012 |               |               |                                     |   |   |                          |                              |

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

\* Other Reason: \_\_\_\_\_

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

**Section D: Completed Studies (for some or all pediatric subpopulations).**

Pediatric subpopulation(s) in which studies have been completed (check below):

| Population  | minimum       | maximum       | PeRC Pediatric Assessment form attached?. |                             |
|---|---------------|---------------|---|-----------------------------|
| <input type="checkbox"/> Neonate                      | __ wk. __ mo. | __ wk. __ mo. | Yes <input type="checkbox"/>              | No <input type="checkbox"/> |
| <input type="checkbox"/> Other                        | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/>              | No <input type="checkbox"/> |
| <input type="checkbox"/> Other                        | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/>              | No <input type="checkbox"/> |
| <input type="checkbox"/> Other                        | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/>              | No <input type="checkbox"/> |
| <input type="checkbox"/> Other                        | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/>              | No <input type="checkbox"/> |
| <input type="checkbox"/> All Pediatric Subpopulations | 0 yr. 0 mo.   | 16 yr. 11 mo. | Yes <input type="checkbox"/>              | No <input type="checkbox"/> |

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

*Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):**

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:

| Population  | minimum       | maximum       |
|---|---------------|---------------|
| <input type="checkbox"/> Neonate                      | __ wk. __ mo. | __ wk. __ mo. |
| <input type="checkbox"/> Other                        | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> Other                        | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> Other                        | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> Other                        | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/> All Pediatric Subpopulations | 0 yr. 0 mo.   | 16 yr. 11 mo. |

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

*If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)**

*Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as*

IF THERE ARE QUESTIONS, PLEASE CONTACT THE CDER PMHS VIA EMAIL ([cderrpmhs@fda.hhs.gov](mailto:cderrpmhs@fda.hhs.gov)) OR AT 301-796-6700.

pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

| Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations: |               |               |                                     |                          |
|---|---------------|---------------|-------------------------------------|--------------------------|
| Population  | minimum       | maximum       | Extrapolated from:                  |                          |
|   |               |               | Adult Studies?                      | Other Pediatric Studies? |
| <input type="checkbox"/> Neonate  | __ wk. __ mo. | __ wk. __ mo. | <input type="checkbox"/>            | <input type="checkbox"/> |
| <input checked="" type="checkbox"/> Other   | 2 yr. 0 mo.   | 17 yr. 0 mo.  | <input checked="" type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/> Other  | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/>            | <input type="checkbox"/> |
| <input type="checkbox"/> Other  | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/>            | <input type="checkbox"/> |
| <input type="checkbox"/> Other  | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/>            | <input type="checkbox"/> |
| <input type="checkbox"/> All Pediatric Subpopulations   | 0 yr. 0 mo.   | 16 yr. 11 mo. | <input type="checkbox"/>            | <input type="checkbox"/> |

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

If there are additional indications, please complete the attachment for each one of those indications. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

(Revised: 6/2008)

NOTE: If you have no other indications for this application, you may delete the attachments from this document.

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**Attachment A**

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: \_\_\_\_\_

**Q1: Does this indication have orphan designation?**

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

**Q2: Is there a full waiver for all pediatric age groups for this indication (check one)?**

- Yes: (Complete Section A.)
  - No: Please check all that apply:
    - Partial Waiver for selected pediatric subpopulations (Complete Sections B)
    - Deferred for some or all pediatric subpopulations (Complete Sections C)
    - Completed for some or all pediatric subpopulations (Complete Sections D)
    - Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
    - Extrapolation in One or More Pediatric Age Groups (Complete Section F)
- (Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

**Section A: Fully Waived Studies (for all pediatric age groups)**

**Reason(s) for full waiver: (check, and attach a brief justification for the reason(s) selected)**

- Necessary studies would be impossible or highly impracticable because:
  - Disease/condition does not exist in children
  - Too few children with disease/condition to study
  - Other (e.g., patients geographically dispersed): \_\_\_\_\_
- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are fully waived on this ground, this information must be included in the labeling.)
- Justification attached.

*If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.*

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**Section B: Partially Waived Studies (for selected pediatric subpopulations)**

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

|                          |         | Reason (see below for further detail): |               |                           |   |                                    |                                 |
|--------------------------|---------|--|---------------|---------------------------|---|------------------------------------|---------------------------------|
|                          |         | minimum                                | maximum       | Not feasible <sup>#</sup> | Not meaningful therapeutic benefit <sup>*</sup> | Ineffective or unsafe <sup>†</sup> | Formulation failed <sup>Δ</sup> |
| <input type="checkbox"/> | Neonate | __ wk. __ mo.                          | __ wk. __ mo. | <input type="checkbox"/>  | <input type="checkbox"/>                        | <input type="checkbox"/>           | <input type="checkbox"/>        |
| <input type="checkbox"/> | Other   | __ yr. __ mo.                          | __ yr. __ mo. | <input type="checkbox"/>  | <input type="checkbox"/>                        | <input type="checkbox"/>           | <input type="checkbox"/>        |
| <input type="checkbox"/> | Other   | __ yr. __ mo.                          | __ yr. __ mo. | <input type="checkbox"/>  | <input type="checkbox"/>                        | <input type="checkbox"/>           | <input type="checkbox"/>        |
| <input type="checkbox"/> | Other   | __ yr. __ mo.                          | __ yr. __ mo. | <input type="checkbox"/>  | <input type="checkbox"/>                        | <input type="checkbox"/>           | <input type="checkbox"/>        |
| <input type="checkbox"/> | Other   | __ yr. __ mo.                          | __ yr. __ mo. | <input type="checkbox"/>  | <input type="checkbox"/>                        | <input type="checkbox"/>           | <input type="checkbox"/>        |

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

Reason(s) for partial waiver (check reason corresponding to the category checked above, and attach a brief justification):

# Not feasible:

- Necessary studies would be impossible or highly impracticable because:
  - Disease/condition does not exist in children
  - Too few children with disease/condition to study
  - Other (e.g., patients geographically dispersed): \_\_\_\_\_

\* Not meaningful therapeutic benefit:

- Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

- Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)
- Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (Note: if studies are partially waived on this ground, this information must be included in the labeling.)

Δ Formulation failed:

- Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)

Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Section C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so,

proceed to Section F).. Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

**Section C: Deferred Studies (for some or all pediatric subpopulations).**

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

| Deferrals (for each or all age groups):            |               |               | Reason for Deferral          |   |   | Applicant Certification † |
|--|---------------|---------------|------------------------------|---|---|---------------------------|
| Population   | minimum       | maximum       | Ready for Approval in Adults | Need Additional Adult Safety or Efficacy Data | Other Appropriate Reason (specify below)* | Received                  |
| <input type="checkbox"/> Neonate                   | __ wk. __ mo. | __ wk. __ mo. | <input type="checkbox"/>     | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/>  |
| <input type="checkbox"/> Other                     | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/>     | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/>  |
| <input type="checkbox"/> Other                     | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/>     | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/>  |
| <input type="checkbox"/> Other                     | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/>     | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/>  |
| <input type="checkbox"/> Other                     | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/>     | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/>  |
| <input type="checkbox"/> All Pediatric Populations | 0 yr. 0 mo.   | 16 yr. 11 mo. | <input type="checkbox"/>     | <input type="checkbox"/>                      | <input type="checkbox"/>                  | <input type="checkbox"/>  |
| Date studies are due (mm/dd/yy): _____             |               |               |                              |   |   |                           |

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

\* Other Reason: \_\_\_\_\_

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

**Section D: Completed Studies (for some or all pediatric subpopulations).**

| Pediatric subpopulation(s) in which studies have been completed (check below): |                              |               |               |  |                             |
|--|------------------------------|---------------|---------------|--|-----------------------------|
| Population   |                              | minimum       | maximum       | PeRC Pediatric Assessment form attached? |                             |
| <input type="checkbox"/>   | Neonate                      | __ wk. __ mo. | __ wk. __ mo. | Yes <input type="checkbox"/>             | No <input type="checkbox"/> |
| <input type="checkbox"/>   | Other                        | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/>             | No <input type="checkbox"/> |
| <input type="checkbox"/>   | Other                        | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/>             | No <input type="checkbox"/> |
| <input type="checkbox"/>   | Other                        | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/>             | No <input type="checkbox"/> |
| <input type="checkbox"/>   | Other                        | __ yr. __ mo. | __ yr. __ mo. | Yes <input type="checkbox"/>             | No <input type="checkbox"/> |
| <input type="checkbox"/>   | All Pediatric Subpopulations | 0 yr. 0 mo.   | 16 yr. 11 mo. | Yes <input type="checkbox"/>             | No <input type="checkbox"/> |

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

*Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):**

| Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed: |                              |               |               |
|--|------------------------------|---------------|---------------|
| Population   |                              | minimum       | maximum       |
| <input type="checkbox"/>   | Neonate                      | __ wk. __ mo. | __ wk. __ mo. |
| <input type="checkbox"/>   | Other                        | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/>   | Other                        | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/>   | Other                        | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/>   | Other                        | __ yr. __ mo. | __ yr. __ mo. |
| <input type="checkbox"/>   | All Pediatric Subpopulations | 0 yr. 0 mo.   | 16 yr. 11 mo. |

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

*If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.*

**Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)**

*Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.*

| Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations: |                              |               |               |                          |                          |
|---|------------------------------|---------------|---------------|--------------------------|--------------------------|
| Population  |                              | minimum       | maximum       | Extrapolated from:       |                          |
|   |                              |               |               | Adult Studies?           | Other Pediatric Studies? |
| <input type="checkbox"/>  | Neonate                      | __ wk. __ mo. | __ wk. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/>  | Other                        | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/>  | Other                        | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/>  | Other                        | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/>  | Other                        | __ yr. __ mo. | __ yr. __ mo. | <input type="checkbox"/> | <input type="checkbox"/> |
| <input type="checkbox"/>  | All Pediatric Subpopulations | 0 yr. 0 mo.   | 16 yr. 11 mo. | <input type="checkbox"/> | <input type="checkbox"/> |

Are the indicated age ranges (above) based on weight (kg)?  No;  Yes.

Are the indicated age ranges (above) based on Tanner Stage?  No;  Yes.

*Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.*

*If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS or DARRTS as appropriate after clearance by PeRC.*

This page was completed by:

*(See appended electronic signature page)*

\_\_\_\_\_  
Regulatory Project Manager

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

(Revised: 6/2008)

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

/s/

-----  
Susan Walker  
1/23/2009 05:45:31 PM

Appears This Way  
On Original

### 1.3.3 DEBARMENT CERTIFICATION

In accordance with the requirements of the Federal Food, Drug and Cosmetic Act section 306(k)(1), the Applicant makes the following statement in connection with this New Drug Application for Silkis (calcitriol) Ointment, 3 µg/g.<sup>1</sup>

Galderma Laboratories, L.P. hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.

10 Dec 07

(Date)

Paul Clark

(Signature)

Paul M. Clark  
Director, Regulatory Affairs  
Galderma Laboratories, L.P.

Appears This Way  
On Original

<sup>1</sup> Guidance for Industry: Submitting Debarment Certification Statements *Drift Guidance* – September 1998

## ACTION PACKAGE CHECKLIST

| APPLICATION INFORMATION <sup>1</sup>  |                               |   |
|---|-------------------------------|---|
| NDA # 22-087<br>BLA #   | NDA Supplement #<br>BLA STN # | If NDA, Efficacy Supplement Type:   |
| Proprietary Name: Vectical<br>Established/Proper Name: calcitriol,<br>Dosage Form: Ointment, 3 mcg/g  |                               | Applicant: Galderma Laboratories, L.P.<br>Agent for Applicant (if applicable):  |
| RPM: Emetia Annum   |                               | Division: Dermatology and Dental Products   |
| <p><b>NDA:</b><br/>                     NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1)    <input type="checkbox"/> 505(b)(2)<br/>                     Efficacy Supplement:    <input type="checkbox"/> 505(b)(1)    <input type="checkbox"/> 505(b)(2)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the NDA Regulatory Filing Review for this application or Appendix A to this Action Package Checklist.)</p> |                               | <p><b>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</b><br/>                     Listed drug(s) referred to in 505(b)(2) application (include NDA/ANDA #(s) and drug name(s)):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p><input type="checkbox"/> If no listed drug, check here and explain:</p> <p>Prior to approval, review and confirm the information previously provided in Appendix B to the Regulatory Filing Review by re-checking the Orange Book for any new patents and pediatric exclusivity. If there are any changes in patents or exclusivity, notify the OND ADRA immediately and complete a new Appendix B of the Regulatory Filing Review.</p> <p style="text-align: center;"><input type="checkbox"/> No changes                      <input type="checkbox"/> Updated<br/>Date of check:</p> <p>If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</p> <p>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</p> |
| <p>◆ User Fee Goal Date<br/>Action Goal Date (if different)</p>   |                               | January 27, 2009  |
| <p>◆ Actions</p> <p>• Proposed action</p>   |                               | <p><input checked="" type="checkbox"/> AP    <input type="checkbox"/> TA    <input type="checkbox"/> AE<br/> <input type="checkbox"/> NA    <input type="checkbox"/> CR</p>   |
| <p>• Previous actions (specify type and date for each action taken)</p>   |                               | <p>Refuse to File 22 Nov 2006<br/>User Fee Goal Date 10-27-2008</p>   |
| <p>◆ Promotional Materials (accelerated approvals only)<br/>                     Note: If accelerated approval (21 CFR 314.510/601.41), promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see guidance <a href="http://www.fda.gov/cder/guidance/2197dft.pdf">www.fda.gov/cder/guidance/2197dft.pdf</a>). If not submitted, explain _____</p>   |                               | <p><input type="checkbox"/> Received <b>N/A</b></p>   |

<sup>1</sup> The Application Information section is (only) a checklist. The Contents of Action Package section (beginning on page 5) lists the documents to be included in the Action Package.

|  |   |
|--|---|
| ♦ Application <sup>2</sup> Characteristics   |   |
| Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority<br>Chemical classification (new NDAs only): 3 (New Dosage Form)  |   |
| <input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch<br><input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch<br><input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC |   |
| NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510)<br><input type="checkbox"/> Restricted distribution (21 CFR 314.520)<br>Subpart I <input type="checkbox"/> Approval based on animal studies   |   |
| BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41)<br><input type="checkbox"/> Restricted distribution (21 CFR 601.42)<br>Subpart H <input type="checkbox"/> Approval based on animal studies   |   |
| <input type="checkbox"/> Submitted in response to a PMR<br><input type="checkbox"/> Submitted in response to a PMC   |   |
| Comments: _____  |   |
| ♦ Date reviewed by PeRC (required for approvals only)<br>If PeRC review not necessary, explain: _____  | 1/9/09, 10/22/08  |
| ♦ BLAs only: RMS-BLA Product Information Sheet for TBP has been completed and forwarded to OBPS/DRM (approvals only)   | <input type="checkbox"/> Yes, date <u>N/A</u>   |
| ♦ BLAs only: is the product subject to official FDA lot release per 21 CFR 610.2 (approvals only)  | <input type="checkbox"/> Yes <input type="checkbox"/> No <u>N/A</u>   |
| ♦ Public communications (approvals only)   |   |
| <ul style="list-style-type: none"> <li>Office of Executive Programs (OEP) liaison has been notified of action</li> </ul>   | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |
| <ul style="list-style-type: none"> <li>Press Office notified of action (by OEP)</li> </ul>   | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No   |
| <ul style="list-style-type: none"> <li>Indicate what types (if any) of information dissemination are anticipated</li> </ul>  | <input checked="" type="checkbox"/> None<br><input type="checkbox"/> HHS Press Release<br><input type="checkbox"/> FDA Talk Paper<br><input type="checkbox"/> CDER Q&As<br><input type="checkbox"/> Other |

<sup>2</sup> All questions in all sections pertain to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new RMS-BLA Product Information Sheet for TBP must be completed.

|  |   |
|--|---|
| ◆ Exclusivity  |   |
| <ul style="list-style-type: none"> <li>Is approval of this application blocked by any type of exclusivity?</li> </ul>  | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes   |
| <ul style="list-style-type: none"> <li>NDA and 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.</li> </ul>   | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes<br>If, yes, NDA/BLA # _____ and date exclusivity expires: _____   |
| <ul style="list-style-type: none"> <li>(b)(2) NDAs only: 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.)</li> </ul>   | <input type="checkbox"/> No <input type="checkbox"/> Yes<br>If yes, NDA # _____ and date exclusivity expires: _____   |
| <ul style="list-style-type: none"> <li>(b)(2) NDAs only: 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.)</li> </ul>   | <input type="checkbox"/> No <input type="checkbox"/> Yes<br>If yes, NDA # _____ and date exclusivity expires: _____   |
| <ul style="list-style-type: none"> <li>(b)(2) NDAs only: 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.)</li> </ul>  | <input type="checkbox"/> No <input type="checkbox"/> Yes<br>If yes, NDA # _____ and date exclusivity expires: _____   |
| <ul style="list-style-type: none"> <li>NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? (Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.)</li> </ul>   | <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes<br>If yes, NDA # _____ and date 10-year limitation expires: _____   |
| ◆ Patent Information (NDAs only)   |   |
| <ul style="list-style-type: none"> <li>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.</li> </ul>  | <input checked="" type="checkbox"/> Verified<br>Not applicable because drug is an old antibiotic.   |
| <ul style="list-style-type: none"> <li>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.</li> </ul>   | 21 CFR 314.50(i)(1)(i)(A)<br><input type="checkbox"/> Verified <u>N/A</u><br><br>21 CFR 314.50(i)(1)<br><input type="checkbox"/> (ii) <input type="checkbox"/> (iii) <u>N/A</u> |
| <ul style="list-style-type: none"> <li>[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).</li> </ul>  | <input type="checkbox"/> No paragraph III certification<br>Date patent will expire <u>N/A</u>   |
| <ul style="list-style-type: none"> <li>[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)).</li> </ul> | <input checked="" type="checkbox"/> N/A (no paragraph IV certification)<br><input type="checkbox"/> 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 notice of certification?

Yes     No  
**N/A**

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

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

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

Yes     No  
**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 the rest of the patent questions.

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

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

Yes     No  
**N/A**

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

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

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

Yes     No  
**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).

|   |  |
|---|--|
| <p>(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?</p> <p>(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 within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p> | <p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p> <p><b>N/A</b></p>   |
| <b>CONTENTS OF ACTION PACKAGE</b>   |  |
| <p>◆ Copy of this Action Package Checklist<sup>3</sup></p>  | X  |
| <b>Officer/Employee List</b>  |  |
| <p>◆ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)</p>  | <input checked="" type="checkbox"/> Included   |
| <p>Documentation of consent/non-consent by officers/employees</p>   | <input checked="" type="checkbox"/> Included   |
| <b>Action Letters</b>   |  |
| <p>◆ Copies of all action letters (<i>including approval letter with final labeling</i>)</p>  | Action(s) and date(s) Approval<br>1/23/09  |
| <b>Labeling</b>   |  |
| <p>◆ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)</p>   |  |
| <ul style="list-style-type: none"> <li>• Most recent division-proposed labeling (only if generated after latest applicant submission of labeling)</li> </ul>  | 1-16-2009  |
| <ul style="list-style-type: none"> <li>• Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version)</li> </ul>  | 1-14-2009  |
| <ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>  | 12-21-2007   |
| <ul style="list-style-type: none"> <li>• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable</li> </ul>   | Calcijex Injection 7-01-2007<br>Rocaltrol Capsules and Solution 6-09-2004,<br>Rocaltrol oral Solution and Capsules 2-01-2002 |
| <p>◆ Medication Guide/Patient Package Insert/Instructions for Use (<i>write submission/communication date at upper right of first page of each piece</i>)</p>   | <input type="checkbox"/> Medication Guide<br><input type="checkbox"/> Patient Package Insert                                 |

<sup>3</sup> Fill in blanks with dates of reviews, letters, etc.  
Version: 9/5/08

|  |  |
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|  | <input type="checkbox"/> Instructions for Use<br><input checked="" type="checkbox"/> None  |
| <ul style="list-style-type: none"> <li>• Most-recent division-proposed labeling (only if generated after latest applicant submission of labeling)</li> </ul>   |  |
| <ul style="list-style-type: none"> <li>• Most recent submitted by applicant labeling (only if subsequent division labeling does not show applicant version)</li> </ul>   |  |
| <ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>   |  |
| <ul style="list-style-type: none"> <li>• Other relevant labeling (e.g., most recent 3 in class, class labeling), if applicable</li> </ul>  |  |
| <ul style="list-style-type: none"> <li>◆ Labels (full color carton and immediate-container labels) (write submission/communication date at upper right of first page of each submission)</li> </ul>  |  |
| <ul style="list-style-type: none"> <li>• Most-recent division proposal for (only if generated after latest applicant submission)</li> </ul>  | 1-16-2009  |
| <ul style="list-style-type: none"> <li>• Most recent applicant-proposed labeling</li> </ul>  | 1-14-2009  |
| <ul style="list-style-type: none"> <li>◆ Labeling reviews (indicate dates of reviews and meetings)</li> </ul>  | <input checked="" type="checkbox"/> RPM 3-19-2008<br><input checked="" type="checkbox"/> DMEPA 10-16-2008<br><input type="checkbox"/> DRISK<br><input checked="" type="checkbox"/> DDMAC 10-02-2008<br><input checked="" type="checkbox"/> CLINICAL 1-16-2009<br><input checked="" type="checkbox"/> CHEMISTRY 1-16-2009 |
| <ul style="list-style-type: none"> <li>◆ Proprietary Name           <ul style="list-style-type: none"> <li>• Review(s) (indicate date(s))</li> <li>• Acceptability/non-acceptability letter(s) (indicate date(s))</li> </ul> </li> </ul>   | <b>Acceptable</b><br>Vectical 10/16/08<br><b>Non-acceptability</b><br>(included in DMEPA Labeling Review 10-16-2008)<br>Silkis Review 4-04-2008<br>Silkis Letter 6-23-2008   |
| <b>Administrative / Regulatory Documents</b>   |  |
| <ul style="list-style-type: none"> <li>◆ Administrative Reviews (e.g., RPM Filing Review<sup>4</sup>/Memo of Filing Meeting) (indicate date of each review)</li> </ul>   | RPM Checklist Filing 1/23/09   |
| <ul style="list-style-type: none"> <li>◆ NDAs only: Exclusivity Summary (signed by Division Director)</li> </ul>   | <input checked="" type="checkbox"/> Included 1/23/09   |
| <ul style="list-style-type: none"> <li>◆ Application Integrity Policy (AIP) Status and Related Documents<br/> <a href="http://www.fda.gov/ors/compliance_rsf/aip_page.html">www.fda.gov/ors/compliance_rsf/aip_page.html</a> <ul style="list-style-type: none"> <li>• Applicant in on the AIP</li> </ul> </li> </ul> | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No  |
| <ul style="list-style-type: none"> <li>• This application is on the AIP           <ul style="list-style-type: none"> <li>○ If yes, Center Director's Exception for Review memo (indicate date)</li> <li>○ If yes, OC clearance for approval (indicate date of clearance communication)</li> </ul> </li> </ul>        | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No<br><br><input type="checkbox"/> Not an AP action   |
| <ul style="list-style-type: none"> <li>◆ Pediatric Page (approvals only, must be reviewed by PERC before finalized)</li> </ul>   | <input checked="" type="checkbox"/> Included   |
| <ul style="list-style-type: none"> <li>◆ 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)</li> </ul>   | <input checked="" type="checkbox"/> Verified, statement is acceptable 12/10/2007   |
| <ul style="list-style-type: none"> <li>◆ Postmarketing Requirement (PMR) Studies</li> </ul>  | <input type="checkbox"/> None  |
| <ul style="list-style-type: none"> <li>• Outgoing communications (if located elsewhere in package, state where located)</li> </ul>   | Included in Action Letter 01-23-2009   |

<sup>4</sup> Filing reviews for other disciplines should be filed behind the discipline tab.  
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|  |  |
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| • Incoming submissions/communications  | 01-07-2009   |
| ❖ Postmarketing Commitment (PMC) Studies   | <input checked="" type="checkbox"/> None   |
| • Outgoing Agency request for postmarketing commitments (if located elsewhere in package, state where located)   |  |
| • Incoming submission documenting commitment   |  |
| ❖ Outgoing communications (letters (except previous action letters), emails, faxes, telecons)  | 1/22/09 (2), 1/16/09, 1/14/09 (5), 12/15/08, 11/4/08, 10/27/08, 10/23/08, 10/20/08, 10/15/08, 6/25/08, 6/23/08, 3/10/08, 2/8/08, 1/22/07, 11/22/06, 10/24/06, 10/23/06, 10/14/06 |
| ❖ Internal memoranda, telecons, etc.   | 12/1/06, 11/29/06, 11/22/06, 10/23/06  |
| ❖ Minutes of Meetings  |  |
| • PeRC (indicate date; approvals only)   | <input type="checkbox"/> Not applicable PENDING  |
| • Pre-Approval Safety Conference (indicate date; approvals only)   | <input checked="" type="checkbox"/> Not applicable   |
| • Regulatory Briefing (indicate date)  | <input checked="" type="checkbox"/> No mtg   |
| • Pre-NDA/BLA meeting (indicate date)  | <input type="checkbox"/> No mtg 6/14/06  |
| • EOP2 meeting (indicate date)   | <input type="checkbox"/> No mtg 11/15/99   |
| • Other (e.g., EOP2a, CMC pilot programs)  | <input checked="" type="checkbox"/> No mtg   |
| ❖ Advisory Committee Meeting(s)  | <input checked="" type="checkbox"/> No AC meeting  |
| • Date(s) of Meeting(s)  |  |
| • 48-hour alert or minutes, if available   |  |
| <b>Decisional and Summary Memos</b>  |  |
| ❖ Office Director Decisional Memo (indicate date for each review)  | <input checked="" type="checkbox"/> None   |
| Division Director Summary Review (indicate date for each review)   | <input type="checkbox"/> None 1/23/09  |
| Cross-Discipline Team Leader Review (indicate date for each review)  | <input type="checkbox"/> None 1-12-2009  |
| <b>Clinical Information<sup>5</sup></b>  |  |
| ❖ Clinical Reviews   |  |
| • Clinical Team Leader Review(s) (indicate date for each review)   | See CDTL Review  |
| • Clinical review(s) (indicate date for each review)   | 1-16-2009, 9-22-2008, 3-7-2008, 11-22-2006   |
| • Social scientist review(s) (if OTC drug) (indicate date for each review)   | <input checked="" type="checkbox"/> None   |
| ❖ Safety update review(s) (indicate location/date if incorporated into another review)   | Included in 9-29-2008 Clinical Review Page 121   |
| ❖ Financial Disclosure reviews(s) or location/date if addressed in another review<br>OR<br>If no financial disclosure information was required, review/memo explaining why not | Included in 9-29-2008 Clinical Review Page 11  |
| ❖ Clinical reviews from other clinical areas/divisions/Centers (indicate date of each review)  | <input checked="" type="checkbox"/> None   |
| ❖ Controlled Substance Staff review(s) and Scheduling Recommendation (indicate date of each review)  | <input checked="" type="checkbox"/> Not needed   |

<sup>5</sup> Filing reviews should be filed with the discipline reviews.  
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|   |   |
|---|---|
| ♦ Risk Management <ul style="list-style-type: none"> <li>• Review(s) and recommendations (including those by OSE and CSS) (indicate date of each review and indicate location/date if incorporated into another review)</li> <li>• REMS Memo (indicate date)</li> <li>• REMS Document and Supporting Statement (indicate date(s) of submission(s))</li> </ul> | <input checked="" type="checkbox"/> None  |
| ♦ DSI Clinical Inspection Review Summary(ies) (include copies of DSI letters to investigators)  | <input type="checkbox"/> None<br>Review Summary 9-10-2008<br>DSI Letters<br>9-26-2008, 7-10-2008      |
| <b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None   |   |
| ♦ Clinical Microbiology Team Leader Review(s) (indicate date for each review)   | <input checked="" type="checkbox"/> None  |
| Clinical Microbiology Review(s) (indicate date for each review)   | <input checked="" type="checkbox"/> None  |
| <b>Biostatistics</b> <input type="checkbox"/> None  |   |
| ♦ Statistical Division Director Review(s) (indicate date for each review)   | <input checked="" type="checkbox"/> None  |
| Statistical Team Leader Review(s) (indicate date for each review)   | <input checked="" type="checkbox"/> None  |
| Statistical Review(s) (indicate date for each review)   | <input type="checkbox"/> None<br>9-19-2008, 11-14-2006  |
| <b>Clinical Pharmacology</b> <input type="checkbox"/> None  |   |
| ♦ Clinical Pharmacology Division Director Review(s) (indicate date for each review)   | <input checked="" type="checkbox"/> None  |
| Clinical Pharmacology Team Leader Review(s) (indicate date for each review)   | <input checked="" type="checkbox"/> None  |
| Clinical Pharmacology review(s) (indicate date for each review)   | <input type="checkbox"/> None<br>8-29-2008, 2-15-2008   |
| ♦ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)   | <input checked="" type="checkbox"/> None  |
| <b>Nonclinical</b> <input type="checkbox"/> None  |   |
| ♦ Pharmacology/Toxicology Discipline Reviews  |   |
| <ul style="list-style-type: none"> <li>• ADP/T Review(s) (indicate date for each review)</li> </ul>   | <input checked="" type="checkbox"/> None  |
| <ul style="list-style-type: none"> <li>• Supervisory Review(s) (indicate date for each review)</li> </ul>   | <input checked="" type="checkbox"/> None  |
| <ul style="list-style-type: none"> <li>• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)</li> </ul>   | <input type="checkbox"/> None<br>7-2-2008, 2-12-2008, 11-13-2006                                      |
| ♦ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)  | <input checked="" type="checkbox"/> None  |
| ♦ Statistical review(s) of carcinogenicity studies (indicate date for each review)  | <input type="checkbox"/> No care<br>5-20-2008   |
| ♦ ECAC/CAC report/memo of meeting   | <input type="checkbox"/> None<br>Included in P/T review, page 59<br>Memo of mtg: 5-29-2008, 4-11-2003 |
| ♦ DSI Nonclinical Inspection Review Summary (include copies of DSI letters)   | <input checked="" type="checkbox"/> None requested  |
| <b>CMC/Quality</b> <input type="checkbox"/> None  |   |
| ♦ CMC/Quality Discipline Reviews  |   |
| <ul style="list-style-type: none"> <li>• ONDQA/OBP Division Director Review(s) (indicate date for each review)</li> </ul>   | <input checked="" type="checkbox"/> None  |
| <ul style="list-style-type: none"> <li>• Branch Chief/Team Leader Review(s) (indicate date for each review)</li> </ul>  | <input checked="" type="checkbox"/> None  |
| <ul style="list-style-type: none"> <li>• CMC/product quality review(s) (indicate date for each review)</li> </ul>   | <input type="checkbox"/> None<br>10-09-2008, 1-28-2008, 11-21-  |

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|  | 2006   |
| <ul style="list-style-type: none"> <li>• BLAs only: Facility information review(s) (indicate dates)</li> </ul>   | <input type="checkbox"/> None <u>N/A</u>   |
| <ul style="list-style-type: none"> <li>◆ Microbiology Reviews             <ul style="list-style-type: none"> <li>• NDAs: Microbiology reviews (sterility &amp; pyrogenicity) (indicate date of each review)</li> <li>• BLAs: Sterility assurance, product quality microbiology (indicate date of each review)</li> </ul> </li> </ul> | <input checked="" type="checkbox"/> Not needed   |
| <ul style="list-style-type: none"> <li>◆ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)</li> </ul>  | <input checked="" type="checkbox"/> None   |
| <ul style="list-style-type: none"> <li>◆ Environmental Assessment (check one) (original and supplemental applications)</li> </ul>  |  |
| <input type="checkbox"/> Categorical Exclusion (indicate review date)(all original applications and all efficacy supplements that could increase the patient population)   | Included in 10-09-2008 CMC Review Page 96  |
| <input type="checkbox"/> Review & FONSI (indicate date of review)  | N/A  |
| <input type="checkbox"/> Review & Environmental Impact Statement (indicate date of each review)  | N/A  |
| <ul style="list-style-type: none"> <li>◆ NDAs: Methods Validation</li> </ul>   | <input type="checkbox"/> Completed<br><input type="checkbox"/> Requested<br><input type="checkbox"/> Not yet requested<br><input checked="" type="checkbox"/> Not needed   |
| <ul style="list-style-type: none"> <li>◆ Facilities Review/Inspection</li> </ul>   |  |
| <ul style="list-style-type: none"> <li>• NDAs: Facilities inspections (include EER printout) (date completed must be within 2 years of action date)</li> </ul>   | Date completed: 10-20-2008<br><input checked="" type="checkbox"/> Acceptable<br><input type="checkbox"/> Withhold recommendation   |
| <ul style="list-style-type: none"> <li>• BLAs:             <ul style="list-style-type: none"> <li>○ TBP-EER</li> <li>○ Compliance Status Check (approvals only, both original and all supplemental applications except CBEs) (date completed must be within 60 days prior to AP)</li> </ul> </li> </ul>                              | <u>N/A</u><br>Date completed:<br><input type="checkbox"/> Acceptable<br><input type="checkbox"/> Withhold recommendation<br>Date completed:<br><input type="checkbox"/> Requested<br><input type="checkbox"/> Accepted <input type="checkbox"/> Hold |

### 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 ADRA.

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

/s/

-----  
Barbara Gould  
1/26/2009 05:31:17 PM

Appears This Way  
On Original

**NDA REGULATORY FILING REVIEW**  
(Including Memo of Filing Meeting)

NDA # 22-807 Supplement # n/a Efficacy Supplement Type SE- n/a

Proprietary Name: Silkis  
Established Name: calcitriol  
Strengths: 3 mcg/g

Applicant: Galderma Laboratories, L.P.  
Agent for Applicant (if applicable): n/a

Date of Application: December 21, 2008  
Date of Receipt: December 27, 2008  
Date clock started after UN: n/a  
Date of Filing Meeting: February 8, 2008  
Filing Date: February 25, 2008  
Action Goal Date (optional):

User Fee Goal Date: October 27, 2008

Indication(s) requested: plaque-type psoriasis

Type of Original NDA: (b)(1)  (b)(2)   
AND (if applicable)  
Type of Supplement: (b)(1)  (b)(2)

**NOTE:**

(1) If you have questions about whether the application is a 505(b)(1) or 505(b)(2) application, see Appendix A. A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). If the application or efficacy supplement is a (b)(2), complete Appendix B.

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

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

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

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

- Is there any 5-year or 3-year exclusivity on this active moiety in any approved (b)(1) or (b)(2) application? YES  NO   
If yes, explain:

Note: If the drug under review is a 505(b)(2), this issue will be addressed in detail in appendix B.

- Does another drug have orphan drug exclusivity for the same indication? YES  NO   
If yes, is the drug considered to be the same drug according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]? YES  NO

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

- Is the application affected by the Application Integrity Policy (AIP)? YES  NO   
If yes, explain:
- If yes, has OC/DMPQ been notified of the submission? YES  NO
- Does the submission contain an accurate comprehensive index? YES  NO   
If no, explain:
- Was form 356h included with an authorized signature? YES  NO   
If foreign applicant, both the applicant and the U.S. agent must sign.
- Submission complete as required under 21 CFR 314.50? YES  NO   
If no, explain:

- Answer 1, 2, or 3 below (do not include electronic content of labeling as an partial electronic submission).

1. This application is a paper NDA YES
2. This application is an eNDA or combined paper + eNDA YES   
This application is: All electronic  Combined paper + eNDA   
This application is in: NDA format  CTD format   
Combined NDA and CTD formats

Does the eNDA, follow the guidance?  
(<http://www.fda.gov/cder/guidance/2353fnl.pdf>) YES  NO

If an eNDA, all forms and certifications must be in paper and require a signature.

If combined paper + eNDA, which parts of the application were submitted in electronic format?

- Draft package insert
- Statistical data from the carcinogenicity studies
- Statistical data from the Phase 3 clinical studies

Additional comments: n/a

3. This application is an eCTD NDA. YES   
If an eCTD NDA, all forms and certifications must either be in paper and signed or be electronically signed.

Additional comments: All forms and certifications are paper and signed.

- Patent information submitted on form FDA 3542a? YES  NO
- Exclusivity requested? YES, 3 Years NO   
*NOTE: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*
- Correctly worded Debarment Certification included with authorized signature? YES  NO   
If foreign applicant, both the applicant and the U.S. Agent must sign the certification.

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

- Are the required pediatric assessment studies and/or deferral/partial waiver/full waiver of pediatric studies (or request for deferral/partial waiver/full waiver of pediatric studies) included? YES  NO
- If the submission contains a request for deferral, partial waiver, or full waiver of studies, does the application contain the certification required under FD&C Act sections 505B(a)(3)(B) and (4)(A) and (B)? YES  NO
- Is this submission a partial or complete response to a pediatric Written Request? YES  NO

If yes, contact PMHT in the OND-IO

- Financial Disclosure forms included with authorized signature? YES  NO   
(Forms 3454 and/or 3455 must be included and must be signed by the APPLICANT, not an agent.)  
*NOTE: Financial disclosure is required for bioequivalence studies that are the basis for approval.*
- Field Copy Certification (that it is a true copy of the CMC technical section) YES  NO
- PDUFA and Action Goal dates correct in tracking system? YES  NO   
If not, have the document room staff correct them immediately. These are the dates EES uses for calculating inspection dates.
- Drug name and applicant name correct in COMIS? If not, have the Document Room make the corrections. Ask the Doc Rm to add the established name to COMIS for the supporting IND if it is not already entered.
- List referenced IND numbers: 62,151
- Are the trade, established/proper, and applicant names correct in COMIS? YES  NO   
If no, have the Document Room make the corrections.
- End-of-Phase 2 Meeting(s)? Date(s) 11/15/1999 NO   
If yes, distribute minutes before filing meeting.
- Pre-NDA Meeting(s)? Date(s) 5/17/2006 NO

If yes, distribute minutes before filing meeting.

- Any SPA agreements? Date(s) \_\_\_\_\_ NO   
If yes, distribute letter and/or relevant minutes before filing meeting.

**Project Management**

- If Rx, was electronic Content of Labeling submitted in SPL format? YES  NO   
If no, request in 74-day letter.
- If Rx, for all new NDAs/efficacy supplements submitted on or after 6/30/06:  
Was the PI submitted in PLR format? YES  NO   
If no, explain. Was a waiver or deferral requested before the application was received or in the submission? If before, what is the status of the request:
- If Rx, all labeling (PI, PPI, MedGuide, carton and immediate container labels) has been consulted to DDMAC? YES  NO
- If Rx, trade name (and all labeling) consulted to OSE/DMETS? YES  NO
- If Rx, MedGuide and/or PPI (plus PI) consulted to ODE/DSRCS?  
N/A  YES  NO
- Risk Management Plan consulted to OSE/IO? N/A  YES  NO
- If a drug with abuse potential, was an Abuse Liability Assessment, including a proposal for scheduling submitted? NA  YES  NO

**If Rx-to-OTC Switch or OTC application:**

- Proprietary name, all OTC labeling/packaging, and current approved PI consulted to OSE/DMETS? YES  NO
- If the application was received by a clinical review division, has DNPCE been notified of the OTC switch application? Or, if received by DNPCE, has the clinical review division been notified? YES  NO

**Clinical**

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

**Chemistry**

- Did applicant request categorical exclusion for environmental assessment? YES  NO   
If no, did applicant submit a complete environmental assessment? YES  NO   
If EA submitted, consulted to EA officer, OPS? YES  NO
- Establishment Evaluation Request (EER) submitted to DMPQ? YES  NO

- If a parenteral product, consulted to Microbiology Team? YES  NO

ATTACHMENT

MEMO OF FILING MEETING

DATE: 2/3/08

NDA #: 22-087

DRUG NAMES: calcitriol ointment, 3 mcg/g

APPLICANT: Galderma Laboratories, L.P.

BACKGROUND: Calcitriol Ointment, 3 mcg/g is a 505(b)(1) NDA for the treatment of plaque-type psoriasis. This is a resubmission after refusal to file issued on 11/22/06.

ATTENDEES: Susan Walker, M.D., Jill Lindstrom, M.D., Patricia Brown, M.D., Paul Brown, Ph.D., Norman See, Ph.D., Shulin Ding, Ph.D., Jane Chang, Ph.D., Mat Soukup, Ph.D., Mohamed Alesh, Ph.D., Lydia Velazquez, Ph.D., Tapash Ghosh, Ph.D.

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

Discipline/Organization

Medical:

Secondary Medical:

Statistical:

Pharmacology:

Statistical Pharmacology:

Chemistry:

Environmental Assessment (if needed):

Biopharmaceutical:

Microbiology, sterility:

Microbiology, clinical (for antimicrobial products only):

DSI:

OPS:

Regulatory Project Management:

Other Consults:

Reviewer

Patricia Brown, M.D.

Jill Lindstrom, M.D.

Matthew Soukup, Ph.D.

Norman See, Ph.D.

Steven Thomson, Ph.D.

Jane Chang, Ph.D.

n/a

Tapash Ghosh, Ph.D.

n/a

n/a

Roy Blay, Ph.D.

Margo Owens

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

CLINICAL FILE  REFUSE TO FILE

- Clinical site audit(s) needed? YES  NO   
If no, explain:
- Advisory Committee Meeting needed? YES, date if known \_\_\_\_\_ NO
- If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?

|                       |   |                                     |                                     |                                     |                                     |                          |                                     |
|-----------------------|---|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|--------------------------|-------------------------------------|
|                       |   | N/A                                 | <input checked="" type="checkbox"/> | YES                                 | <input type="checkbox"/>            | NO                       | <input type="checkbox"/>            |
| CLINICAL MICROBIOLOGY | N/A   | <input checked="" type="checkbox"/> | FILE                                | <input type="checkbox"/>            | REFUSE TO FILE                      | <input type="checkbox"/> |                                     |
| STATISTICS            | N/A   | <input type="checkbox"/>            | FILE                                | <input checked="" type="checkbox"/> | REFUSE TO FILE                      | <input type="checkbox"/> |                                     |
| BIOPHARMACEUTICS      |   |                                     | FILE                                | <input checked="" type="checkbox"/> | REFUSE TO FILE                      | <input type="checkbox"/> |                                     |
|                       | • Biopharm. study site audits(s) needed?<br>YES                     |                                     |                                     |                                     | <input type="checkbox"/>            | NO                       | <input checked="" type="checkbox"/> |
| PHARMACOLOGY/TOX      | N/A   | <input type="checkbox"/>            | FILE                                | <input checked="" type="checkbox"/> | REFUSE TO FILE                      | <input type="checkbox"/> |                                     |
|                       | • GLP audit needed?   |                                     |                                     | YES                                 | <input type="checkbox"/>            | NO                       | <input checked="" type="checkbox"/> |
| CHEMISTRY             |   |                                     | FILE                                | <input checked="" type="checkbox"/> | REFUSE TO FILE                      | <input type="checkbox"/> |                                     |
|                       | • Establishment(s) ready for inspection?                            |                                     |                                     | YES                                 | <input checked="" type="checkbox"/> | NO                       | <input type="checkbox"/>            |
|                       | • Sterile product?  |                                     |                                     | YES                                 | <input type="checkbox"/>            | NO                       | <input checked="" type="checkbox"/> |
|                       | If yes, was microbiology consulted for validation of sterilization? |                                     |                                     | YES                                 | <input type="checkbox"/>            | NO                       | <input type="checkbox"/>            |

**ELECTRONIC SUBMISSION:**

Any comments:

**REGULATORY CONCLUSIONS/DEFICIENCIES:**

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

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

**ACTION ITEMS:**

1.  Ensure that the review and chemical classification codes, as well as any other pertinent classification codes (e.g., orphan, OTC) are correctly entered into COMIS.
2.  If RTE, notify everybody who already received a consult request of RTE action. Cancel the EER.
3.  If filed and the application is under the AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
4.  If filed, complete the Pediatric Page at this time. (If paper version, enter into DFS.)
5.  Convey document filing issues/no filing issues to applicant by Day 74.

Margo Owens  
Regulatory Project Manager

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/s/

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Margo Owens  
1/23/2009 11:33:42 AM  
CSO

Margo Owens  
1/23/2009 11:38:58 AM  
CSO

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## Annum, Emelia K

---

**From:** CLARK Paul [paul.clark@galderma.com]  
**Sent:** Tuesday, January 13, 2009 2:45 PM  
**To:** Annum, Emelia K  
**Subject:** RE: Teleconference for NDA 22-087

**Attachments:** emfinfo.txt



emfinfo.txt (582 B)

Hi Emelia:

Please call me at my office 817 961 5336 at 4 pm EST.

Thanks,

Paul

Paul Clark  
Director, Regulatory Affairs  
Galderma Laboratoris, L.P.  
817 961 5336

-----Original Message-----

**From:** Annum, Emelia K [mailto:Emelia.Annum@fda.hhs.gov]  
**Sent:** Tuesday, January 13, 2009 12:25 PM  
**To:** CLARK Paul  
**Subject:** Teleconference for NDA 22-087

Hi Paul,

I left a voice mail message indicating that we have scheduled a teleconference with you to discuss your NDA application at 4pm, eastern time. Please call if you will not be participate in the telecon. I apologize for the short notice. Thanks.

Emelia Annum, MSc.  
Division of Dermatology and Dental Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
Telephone # 301-796-2223

My Documents\NDAN22087\_CalcitriolForms\NDA 22-087 Vectical (calcitriol) Ointment Labeling .txt

From: Annum, Emelia K

Sent: Thursday, January 15, 2009 1:35 PM

To: 'CLARK Paul'

Cc: Lindstrom, Jill; Brown, Patricia C (ODEIII); Chang, Jane; Haffer, Andrew; Gould, Barbara

Subject: NDA 22-087 Vectical (calcitriol) Ointment Labeling

Attachments: NDA 22-087\_FDA 1\_14\_1\_3 DRAFT LABELING TEXT 15 Jan 2008.doc

Hi Paul,

We have reviewed the PI, and the carton and container labels and we have the following comments:

1

---

2. A hyphen should be used for "dl-?-tocopherol" in the package insert (Section 11 Description), container and carton labels. This is to be consistent with the nomenclature used in IUPAC (<http://www.chem.qmul.ac.uk/iupac/misc/toc.html>). The Greek symbols are always preferred when the font is available for use because otherwise the name would be too long.

Attached is a revised draft copy of the label. Please contact me if you have questions. Thanks.

Emelia Annum, MSc.  
Division of Dermatology and Dental Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
Telephone # 301-796-2223

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-----  
Emelia Annum

1/22/2009 03:06:10 PM

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CDataMy DocumentsNDAN22087\_CalcitriolFormsNDA 22-087 Draft Agency Proposed Labeling.txt  
From: Annum, Emelia K  
Sent: Tuesday, January 13, 2009 5:15 PM  
To: 'CLARK Paul'  
Cc: Lindstrom, Jill; Brown, Patricia C (ODEIII); Gould, Barbara  
Subject: NDA 22-087 Draft Agency Proposed Labeling

Attachments: NDA 22-087\_FDA 1\_14\_1\_3 DRAFT LABELING TEXT 1- 06 09  
Revised\_ JC PB JL.doc

Hi Paul,  
Attached is the draft proposed labeling. Please have the labeling back to us no  
later than COB 1/14/09. Thanks.

Emelia Annum, MSc.  
Division of Dermatology and Dental Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
Telephone # 301-796-2223

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Emelia Annum  
1/22/2009 02:58:39 PM  
CSO

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CDataMy DocumentsNDAN22087\_CalcitriolFormsCalcitriol Labeling.txt  
From: CLARK Paul [paul.clark@galderma.com]  
Sent: Friday, January 09, 2009 11:05 AM  
To: Annum, Emelia K  
Subject: RE: Calcitriol Labeling

Attachments: emfinfo.txt

Emelia-

Thanks so much. This will help us respond.

Thanks,

Paul

Paul Clark  
Director, Regulatory Affairs  
Galderma Laboratoris, L.P.  
817 961 5336

-----Original Message-----

From: Annum, Emelia K [mailto:Emelia.Annum@fda.hhs.gov]  
Sent: Friday, January 09, 2009 9:25 AM  
To: CLARK Paul  
Subject: Calcitriol Labeling

Hi Paul,  
Please see the attached document. Thanks.

Emelia Annum, MSc.  
Division of Dermatology and Dental Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
Telephone # 301-796-2223

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Emelia Annum  
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NDA 22-087

**INFORMATION REQUEST LETTER**

Galderma Laboratories, LP  
Attention: Paul Clark  
Director, Regulatory Affairs  
14501 N. Freeway  
Fort Worth, TX 761177

Dear Mr. Clark

Please refer to your September 25, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for calcitrol ointment, 3 mcg/g.

On October 27, 2008 the Agency communicated to you that the PDUFA goal date for your NDA had been extended to January 17, 2009. Upon further review, we have determined that the PDUFA date provided is incorrect. The correct PDUFA goal date is January 27, 2009.

If you have any questions, call Emelia Annum, Project Manager, at 301-796-2223.

Sincerely,

*{See appended electronic signature page}*

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

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/s/

-----  
Emelia Annum  
1/16/2009 03:50:14 PM  
CSO

Stanka Kukich  
1/16/2009 03:53:38 PM  
MEDICAL OFFICER  
Signing for Dr. Susan Walker, Division Director

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CDatamy DocumentsNDAN22087\_CalcitriolPediatric Plan 22-087 (calcitriol) Ointment.txt  
From: Greeley, George  
Sent: Thursday, January 08, 2009 3:25 PM  
To: Annum, Emelia K  
Cc: Lindstrom, Jill; Brown, Patricia C (ODEIII)  
Subject: RE: Pediatric Plan 22-087 (calcitriol) Ointment

Great! That just about does it for this application. I will follow-up with you once the review is complete. Should be a few days or it could be tomorrow.

Thanks,  
George

-----Original Message-----

From: Annum, Emelia K  
Sent: Thursday, January 08, 2009 3:22 PM  
To: Greeley, George  
Cc: Lindstrom, Jill; Brown, Patricia C (ODEIII)  
Subject: RE: Pediatric Plan 22-087 (calcitriol) Ointment

Hi George,

We have modified the pediatric plan to incorporate the dates that the sponsor will submit the studies. Please see the attached document. Thanks.

Emelia Annum

-----Original Message-----

From: Greeley, George  
Sent: Thursday, January 08, 2009 12:20 PM  
To: Annum, Emelia K  
Cc: Lindstrom, Jill; Brown, Patricia C (ODEIII)  
Subject: RE: Pediatric Plan 22-087 (calcitriol) Ointment

Hi Emelia!

Thanks for the information. I note the study dates have been added to the deferral/plan template but the only date I do not see is the date the sponsor will submit the protocol. If this is included let me know as that is one the dates needed as well. Don't mean to be picky but I am fairly certain that the request will come back to me if I forward this on for review. Again, I may have missed it.

Thanks,  
George

-----Original Message-----

From: Annum, Emelia K  
Sent: Thursday, January 08, 2009 12:09 PM  
To: Greeley, George  
Cc: Lindstrom, Jill; Brown, Patricia C (ODEIII)  
Subject: Pediatric Plan 22-087 (calcitriol) Ointment

Hi George,

We are submitting the PREA waiver, PREA deferral and plan, and a Peds page for NDA 22-087 (calcitriol). It is our understanding during the PeRC meeting that occurred on 10/22/08, that the committee did not request another presentation in person, but requested the timelines for the proposed studies and reports. We recall that the committee said that they could review the above information via email. Let us know if you have questions with this submission. Thanks.

Emelia Annum, MSc.  
Division of Dermatology and Dental Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue

CDatamy DocumentsNDAN22087\_CalcitriolPediatric Plan 22-087 (calcitriol) Ointment.txt  
Silver Spring, MD 20993-0002  
Telephone # 301-796-2223

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Emelia Annum  
1/14/2009 10:34:35 AM  
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CDatamy DocumentsNDAN22087\_CalcitriolRequest for Pediatric Plan Timelines NDA 22-087.txt  
From: CLARK Paul [paul.clark@galderma.com]  
Sent: Thursday, January 08, 2009 10:07 AM  
To: Annum, Emelia K  
Cc: Lindstrom, Jill  
Subject: RE: Request for Pediatric Plan Timelines NDA 22-087

Attachments: emfinfo.txt

Hi Emelia:

I spoke with Jill yesterday and she needed another date: when the ongoing pk study would be completed.

PK in adloscents Report submission: March 2010

Let me know if you need anything else.

Paul

Paul Clark  
Director, Regulatory Affairs  
Galderma Laboratoris, L.P.  
817 961 5336

-----Original Message-----

From: Annum, Emelia K [mailto:Emelia.Annum@fda.hhs.gov]  
Sent: Tuesday, January 06, 2009 12:16 PM  
To: CLARK Paul  
Subject: Request for Pediatric Plan Timelines NDA 22-087

Hi Paul,

This is a follow up from a voice mail message in which I requested that you send us timelines on when you would be able to complete your Pk, safety efficacy and long term safety study of your pediatric plan. We need to provide Perc with this information for approval of the labeling. Please send us dates ASAP. Thanks.

Emelia Annum, MSc.  
Division of Dermatology and Dental Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
Telephone # 301-796-2223

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/s/

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Emelia Annum  
1/14/2009 10:50:52 AM  
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CDataMy DocumentsNDAN22087\_CalcitriolInformation Request for NDA 22-087.txt  
From: CLARK Paul [paul.clark@galderma.com]  
Sent: Wednesday, October 15, 2008 9:33 AM  
To: Annum, Emelia K  
Subject: RE: Information Request for NDA 22-087

Attachments: eminfo.txt

Dear Ms. Annum:

Thank you for emailing this request. An alternate fax number is 682 831 9124.

Best regards,

Paul

-----Original Message-----

From: Annum, Emelia K [mailto:Emelia.Annum@fda.hhs.gov]  
Sent: Wednesday, October 15, 2008 8:27 AM  
To: CLARK Paul  
Subject: Re: Information Request for NDA 22-087  
Importance: High

Hi Mr. Clark,

I have tried to fax you a request for information for NDA 22-087 Calcitriol ointment, but I have been unsuccessful. For NDA 22-087, the Agency requests that your Pediatric Deferral include subjects ages 0 to 17 years. Please submit your plan for a pediatric deferral for patients 0 to 17 years. We request that this information be submitted no later than 12 noon on Thursday, October 16, 2008. I will follow up with a fax request. Thanks.

Emelia Annum, MSc.  
Division of Dermatology and Dental Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
Telephone # 301-796-2223

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Emelia Annum  
1/14/2009 01:41:12 PM  
CSO

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Cdata\My Documents\NDAN22087\_Calcitriol\Information Request for NDA 22-087\_1.txt  
From: CLARK Paul [paul.clark@galderma.com]  
Sent: Wednesday, October 15, 2008 2:52 PM  
To: Annum, Emelia K  
Subject: RE: Information Request for NDA 22-087

Attachments: 22087 Pediatric Amendment 8 Feb 2008.pdf; emfinfo.txt

Dear Ms. Annum:

I don't fully understand this request. Galderma submitted pediatric waiver waiver/deferral information in the initial application and also in a clarification amendment dated February 8, 2008 (pdf attached). We requested

\_\_\_\_\_ We asked for \_\_\_\_\_  
\_\_\_\_\_

Is this request a denial of our request \_\_\_\_\_  
\_\_\_\_\_ Thanks for any clarification that can be provided.

b(4)

Sincerely,

Paul

-----Original Message-----

From: Annum, Emelia K [mailto:Emelia.Annum@fda.hhs.gov]  
Sent: Wednesday, October 15, 2008 8:27 AM  
To: CLARK Paul  
Subject: Re: Information Request for NDA 22-087  
Importance: High

Hi Mr. Clark,

I have tried to fax you a request for information for NDA 22-087 Calcitriol ointment, but I have been unsuccessful. For NDA 22-087, the Agency requests that your Pediatric Deferral include subjects ages 0 to 17 years. Please submit your plan for a pediatric deferral for patients 0 to 17 years. We request that this information be submitted no later than 12 noon on Thursday, October 16, 2008. I will follow up with a fax request. Thanks.

Emelia Annum, MSc.  
Division of Dermatology and Dental Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
Telephone # 301-796-2223

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/s/

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Emelia Annum  
1/14/2009 01:47:55 PM  
CSO

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804804.txt

From: CLARK Paul [paul.clark@galderma.com]  
Sent: Friday, October 17, 2008 11:17 AM  
To: Annum, Emilia K  
Subject: RE: Information Request for NDA 22-087

Attachments: emfinfo.txt

Dear Ms Annum:

FDA has recognized IMS NDTI as an estimation of prevalence. In fact, in the December 2, 1998 Final rule 63 FR 66632, the agency specifically mentions the use of IMS NDTI data as a method of establishing "a rough approximation" of the number of patients with the disease.

Please forward this to the appropriate personnel for their consideration.

Best regards,

Paul

<http://www.fda.gov/ohrms/dockets/98fr/120298c.pdf>

FDA has also revised the proposed definition of "a substantial number of pediatric patients." Many comments argued that the number chosen by FDA in the proposal (100,000 prescriptions per year or 100,000 pediatric patients with the disease) was arbitrary. Physician mention data from the IMS National Disease and Therapeutic Index (Ref. 38), which tracks the use of drugs by measuring the number of times physicians mention drugs during outpatient visits, shows that pediatric use of drugs is generally grouped in two distinct ranges. Physician mentions of drugs for pediatric use generally fall either below 15,000 per year or above 100,000 per year. Few drugs fall within the two ranges. Thus, selecting a cut-off

[[Page 66636]]

for "substantial number of pediatric patients" in the middle of the two ranges will provide a reasonable discrimination between products that are widely used and those that are less commonly used, and the specific number chosen will not arbitrarily include or exclude a significant number of drugs. FDA has therefore chosen 50,000 as the cut-off for a substantial number of pediatric patients. Because the number of pediatric patients with the disease or condition is easier to determine than the number of prescriptions per year, a substantial number of pediatric patients will be defined as 50,000 pediatric patients with the disease or condition for which the drug or biological product is indicated. Although physician mentions per year does not correspond exactly to the number of patients with the disease or condition, they provide a rough approximation and the IMS data show that the number of products included or excluded is relatively insensitive to changes in the cut-off chosen. As proposed, a partial waiver for a particular pediatric age group would be available under this method if 15,000 patients in that age group were affected by the disease or condition. This definition of "a substantial number of pediatric patients" has not been codified, however, and FDA may modify it, after consulting with a panel of pediatric experts. Any modification will be issued in a guidance document with an opportunity for comment.

804804.txt

<http://www.fda.gov/ohrms/dockets/98fr/120298c.pdf>

Best regards,

Paul

-----Original Message-----

From: Annum, Emelia K [mailto:Emelia.Annum@fda.hhs.gov]  
Sent: Thursday, October 16, 2008 4:43 PM  
To: CLARK Paul  
Subject: RE: Information Request for NDA 22-087

Hi Mr. Clark,  
The projected data on patient visits to office based physicians does not reflect disease prevalence.

Emelia Annum

-----Original Message-----

From: CLARK Paul [mailto:paul.clark@galderma.com]  
Sent: Wednesday, October 15, 2008 6:33 PM  
To: Annum, Emelia K  
Subject: RE: Information Request for NDA 22-087

Dear Ms. Annum:

I am again seeking clarification regarding this request. During our telephone conversation I understood that the reviewer did not receive adequate information relative to disease prevalence to evaluate the waiver.

On February 8, 2008 I received a telephone request from Margo Owens seeking "clarification of our pediatric waiver deferral request." A response was prepared and submitted on February 12.

In our waiver/deferral request of February 12, we cited two national surveys (IMS NDTI and Verispan PDDA)-of physician-reported activities. The data submitted covered a period of 5 years. These surveys collect patient demographics, diagnosis and treatment information from patient visits to office-based physicians nationwide. Data from both surveys showed that the prevalence of psoriasis in the pediatric population 0-12 is below \_\_\_\_\_ nationwide. Though this number has not been codified, it is the cut-off chosen by FDA for "a substantial number of pediatric patients" (See 63 FR 66632).

b(4)

These surveys are nationally recognized instruments that are used by industry and government entities to estimate prevalence data.

Could you share with me the additional information the reviewer would need to evaluate this waiver request? We will respond as quickly as possible.

Best regards,

Paul

-----Original Message-----

From: Annum, Emelia K [mailto:Emelia.Annum@fda.hhs.gov]  
Sent: Wednesday, October 15, 2008 3:25 PM  
To: CLARK Paul  
Subject: RE: Information Request for NDA 22-087

Page 2

804804.txt

Hi Paul,  
The team reached the conclusion that the waiver rational (i.e. supporting data per prevalence) was inadequate.

Emelia Annum  
Regulatory Project Manager

-----Original Message-----

From: CLARK Paul [mailto:paul.clark@galderma.com]  
Sent: Wednesday, October 15, 2008 2:52 PM  
To: Annum, Emelia K  
Subject: RE: Information Request for NDA 22-087

Dear Ms. Annum:

I don't fully understand this request. Galderma submitted pediatric waiver waiver/deferral information in the initial application and also in a clarification amendment dated February 8, 2008 (pdf attached). We requested

\_\_\_\_\_ We asked for \_\_\_\_\_  
\_\_\_\_\_

b(4)

Is this request a denial of our request \_\_\_\_\_  
\_\_\_\_\_ Thanks for any clarification that can be provided.

b(4)

Sincerely,

Paul

-----Original Message-----

From: Annum, Emelia K [mailto:Emelia.Annum@fda.hhs.gov]  
Sent: Wednesday, October 15, 2008 8:27 AM  
To: CLARK Paul  
Subject: Re: Information Request for NDA 22-087  
Importance: High

Hi Mr. Clark,  
I have tried to fax you a request for information for NDA 22-087 Calcitriol ointment, but I have been unsuccessful.  
For NDA 22-087, the Agency requests that your Pediatric Deferral include subjects ages 0 to 17 years. Please submit your plan for a pediatric deferral for patients 0 to 17 years. We request that this information be submitted no later than 12 noon on Thursday, October 16, 2008. I will follow up with a fax request. Thanks.

Emelia Annum, MSc.  
Division of Dermatology and Dental Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
Telephone # 301-796-2223

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/s/

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Emelia Annun  
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From: CLARK Paul [paul.clark@galderma.com]  
Sent: Thursday, January 08, 2009 10:07 AM  
To: Annum, Emelia K  
Cc: Lindstrom, Jill  
Subject: RE: Request for Pediatric Plan Timelines NDA 22-087

Attachments: emfinfo.txt

Hi Emelia:

I spoke with Jill yesterday and she needed another date: \_\_\_\_\_

b(4)

\_\_\_\_\_ report submission: March 2010

Let me know if you need anything else.

Paul

Paul Clark  
Director, Regulatory Affairs  
Galderma Laboratoris, L.P.  
817 961 5336

-----Original Message-----

From: Annum, Emelia K [mailto:Emelia.Annum@fda.hhs.gov]  
Sent: Tuesday, January 06, 2009 12:16 PM  
To: CLARK Paul  
Subject: Request for Pediatric Plan Timelines NDA 22-087

Hi Paul,

This is a follow up from a voice mail message in which I requested that you send us timelines on when you would be able to complete \_\_\_\_\_ safety efficacy and long term safety study of your pediatric plan. We need to provide Perc with this information for approval of the labeling. Please send us dates ASAP. Thanks.

b(4)

Emelia Annum, MSc.  
Division of Dermatology and Dental Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
Telephone # 301-796-2223

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/s/

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Emelia Annun  
1/14/2009 10:50:52 AM  
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**Annum, Emelia K**

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**From:** CLARK Paul [paul.clark@galderma.com]  
**Sent:** Thursday, January 08, 2009 12:47 PM  
**To:** Annum, Emelia K  
**Subject:** 22087 CALCITRIOL OINTMENT - PROTOCOL SUBMISSION DATES  
**Attachments:** emfinfo.txt

Hi Emelia:

We can submit the protocols for all three studies by April 1, 2009. If study start is dependent on FDA review of the protocols, we would like to have an agreement that they would be reviewed under the Special Protocol Assessment Guidance.

Thanks,

Paul

Paul Clark  
Director, Regulatory Affairs  
Galderma Laboratoris, L.P.  
817 961 5336

Appears This Way  
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1/26/2009

**Annum, Emelia K**

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**From:** CLARK Paul [paul.clark@galderma.com]  
**Sent:** Thursday, January 08, 2009 10:07 AM  
**To:** Annum, Emelia K  
**Cc:** Lindstrom, Jill  
**Subject:** RE: Request for Pediatric Plan Timelines NDA 22-087

**Attachments:** emfinfo.txt



emfinfo.txt (582 B)

Hi Emelia:

I spoke with Jill yesterday and she needed another date: when the \_\_\_\_\_ study would be completed.

b(4)

\_\_\_\_\_ Report submission: March 2010

Let me know if you need anything else.

Paul

Paul Clark  
Director, Regulatory Affairs  
Galderma Laboratoris, L.P.  
817 961 5336

-----Original Message-----

From: Annum, Emelia K [mailto:Emelia.Anum@fda.hhs.gov]  
Sent: Tuesday, January 06, 2009 12:16 PM  
To: CLARK Paul  
Subject: Request for Pediatric Plan Timelines NDA 22-087

Hi Paul,

This is a follow up from a voice mail message in which I requested that you send us timelines on when you would be able to complete \_\_\_\_\_ safety efficacy and long term safety study of your pediatric plan. We need to provide Perc with this information for approval of the labeling. Please send us dates ASAP. Thanks.

b(4)

Emelia Annum, MSc.  
Division of Dermatology and Dental Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
Telephone # 301-796-2223



NDA 22-087

INFORMATION REQUEST LETTER

Galerma Laboratories, L.P.  
Attention: Paul Clark  
Director, Regulatory Affairs  
14501 North Freeway  
Fort Worth TX 76177

Dear Mr. Clark:

Please refer to your September 27, 2006 New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for calcitriol ointment, 3 mcg/g.

We also refer to your submission dated August 26, 2008 containing two proposed proprietary names \_\_\_\_\_, and Vectical.

b(4)

**Proprietary Name**

The Proprietary Name Risk Assessment findings indicate that the proposed name, Vectical, is acceptable.

**Retail Container Labels and Carton Labeling**

The statement 'For external use only' should be more prominently displayed and relocated to the principle display panel.

Please note that the Federal Food Drug and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made, whether through a trade name or otherwise; this includes suggestions that a drug is better, more effective, useful in a broader range of conditions or patients, safer, has fewer, or lower incidence of, or less serious side effects or contraindications than has been demonstrated by substantial evidence or substantial clinical experience. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n); 21 CFR 202.1(e)(5)(i);(e)(6)(i)].

If you have any questions, call Emelia Annum, Project Manager, at 301-796-2223.

Sincerely,

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

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/s/

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Susan Walker  
12/15/2008 05:08:17 PM

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**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 22-087

**INFORMATION REQUEST LETTER**

Galderma Laboratories, LP  
Attention: Paul Clark  
Director, Regulatory Affairs  
14501 N. Freeway  
Fort Worth, TX 76177

Dear Mr. Clark

Please refer to your September 25, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for TRADENAME (calcitriol) Ointment, 3 mcg/g.

We are reviewing the Clinical section of your submission and have the following comments and information requests.

1. Provide the calcium-phosphate product for all subjects in studies for which it can be provided, or identify the location of this information in the NDA.
2. Identify a threshold for concern, justification for the threshold, line listings and shift tables. Identify the date by which the information will be provided.
3. Identify all studies in which calcitriol was assessed, or provide your rationale for not obtaining this information if it was not assessed (or identify the location in the NDA).

We request a prompt written response in order to continue our evaluation of your NDA.

If you have any questions, call Emelia Annum, Project Manager, at 301-796-2223.

Sincerely,

Emelia Annum  
Regulatory Project Manager  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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Emelia Annum

11/4/2008 04:49:01 PM

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**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 22-087

Galderma Laboratories, L.P.  
Attention: Paul Clark  
Director, Regulatory Affairs  
14501 North Freeway  
Fort Worth, TX 76177

Dear Mr. Clark:

Please refer to your December 27, 2006 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for TRADENAME (calcitriol) Ointment, 3 mcg/g for the treatment of plaque type psoriasis.

On October 20, 2008, we received your October 17, 2008 major amendment to this application. The receipt date is within 3 months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is January 17, 2009.

If you have any questions, call Emelia Annum, Project Manager, at 301-796-2223.

Sincerely,

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

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Susan Walker

10/27/2008 04:47:03 PM

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

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE: 10/23/08**

|  |  |
|--|--|
| <b>To: Mr. Paul Clark, Director, Regulatory Affairs</b>                  | <b>From: Emeilia Annum<br/>Project Manager</b>     |
| <b>Company: Galderma Laboratories, L.P.</b>                              | <b>Division of Dermatology and Dental Products</b> |
| <b>Fax number: (817) 961-0200</b>  | <b>Fax number: (301) 796-9894</b>                  |
| <b>Phone number: (817) 961-5336</b>                                      | <b>Phone number: (301) 796-2223</b>                |
| <b>Subject: FDA Proposed labeling for NDA 22-087 Calcitriol Ointment</b> |  |

---

**Total no. of pages including cover: 11**

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**Comments: Attached is the FDA proposed labeling for your NDA 22-087, TRADENAME (Calcitriol Ointment). Please review and provide your agreement with this proposal or your revisions/comments by COB October 24, 2008.**

**Thank you.**

---

**Document to be mailed:                      YES                       NO**

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20 Page(s) Withheld

       Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

       Draft Labeling (b5)

       Deliberative Process (b5)

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/s/

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Emelia Annun  
10/23/2008 02:34:20 PM  
CSO

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

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE: October 17, 2008**

|  |  |
|--|--|
| <b>To:</b> Mr. Paul Clark                | <b>From:</b> Emelia Ansum<br>Project Manager |
| <b>Company:</b> Galderma Laboratories LP | Division of Dermatology and Dental Products  |
| <b>Fax number:</b> (817) 961-0020        | <b>Fax number:</b> (301) 796-9894            |
| <b>Phone number:</b> (817) 961-5000      | <b>Phone number:</b> 301-796-2223            |

**Subject:** Information Request NDA 22-087

**Total no. of pages including cover:** 2

**Comments:**

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**Document to be mailed:**                       **YES**                       **NO**

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**For NDA 22-087, the Agency would like to revise our request for Pediatric Plan to cover ages 2 to 17 years.**

**We request that this information be submitted no later than 12 noon on Monday, October 20, 2008.**

**Thank you.**

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/s/

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Emelia Annun  
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Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation ODEIII

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE: 10/15/2008**

|  |  |
|--|--|
| <b>To: Mr. Paul Clark, Directory, Regulatory Affairs</b> | <b>From: Emelia Annum</b>                          |
| <b>Company: Galderma Laboratories, L.P.</b>              | <b>Regulatory Project manager</b>                  |
| <b>Fax number: (817) 961-0200</b>                        | <b>Division of Dermatology and Dental Products</b> |
| <b>Phone number: (817) 961-5336</b>                      | <b>Fax number: (301) 796-9894</b>                  |
|  | <b>Phone number: (301) 796-2330</b>                |
| <b>Subject: Information Request for NDA 22-087</b>       |  |

**Total no. of pages including cover: 2**

**Comments: Please send the response to the information request no later than 12 noon  
October 16, 2008.**

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**Document to be mailed:**       YES       NO

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**For NDA 22-087, the Agency requests that your Pediatric Deferral include subject's ages 0 to 17 years. Please submit your plan for a pediatric deferral for patients 0 to 17 years. We request that this information be submitted no later than 12 noon on Thursday, October 16, 2008.**

**Thank you.**

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/s/

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Emelia Annum  
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**MEMORANDUM**

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

---

**CLINICAL INSPECTION SUMMARY**

**DATE:** September 9, 2008

**TO:** Bronwyn Collier, Regulatory Project Manager  
Patricia Brown, M.D., Medical Officer  
Division of Dermatologic and Dental Drug Products

**FROM:** Roy Blay, Ph.D.  
Good Clinical Practice Branch 1  
Division of Scientific Investigations

**THROUGH:** Constance Lewin, M.D., M.P.H.  
Branch Chief  
Good Clinical Practice Branch 1  
Division of Scientific Investigations

**SUBJECT:** Evaluation of Clinical Inspections.

**NDA:** 22-087

**APPLICANT:** Galderma Laboratories, Inc.

**DRUG:** Silkis (calcitriol) Ointment, 3µg/g

**NME:** No

**THERAPEUTIC CLASSIFICATION:** Standard Review

**INDICATION:** Treatment of chronic psoriasis

**CONSULTATION REQUEST DATE:** April 17, 2008

**DIVISION ACTION GOAL DATE:** September 27, 2008

**PDUFA DATE:** October 19, 2008

**I. BACKGROUND:**

The conduct of protocol RD.06.SRE.18053, entitled "Evaluation of the Efficacy and Safety of Twice Daily Application of Calcitriol 3µg/g Ointment and its Vehicle, in the Treatment of Chronic Psoriasis" was inspected at two clinical sites. Subjects with chronic psoriasis were treated with the test article and evaluated for the severity of their psoriasis for eight weeks. Success in treatment was defined as a Global Severity Score of 0 (clear) or 1 (minimal) at the Week 8 Endpoint.

Dr. Arthur's site (#2123) was selected for inspection because of its relatively large sample size and high treatment effect (zero response for the vehicle and nearly 50% response for the active). Dr. Breneman's site (#1170) was selected for inspection because it enrolled 20 subjects of which 0/10 of subjects treated with active responded, whereas 3/10 treated with vehicle responded resulting in a treatment effect favoring vehicle.

**II. RESULTS (by Site):**

| Name of CI, CRO or Sponsor<br>Location   | Protocol #:<br># of Subjects | Inspection Dates | Final Classification                               |
|--|------------------------------|------------------|--|
| Debra Breneman, M.D.<br>University Dermatology Consultants, Inc.<br>222 Piedmont, Suite 5300<br>Cincinnati, OH 45219 | RD.06.SRE.18053:<br>20       | 5-7 May, 2008    | Pending<br>(Preliminary classification<br>is NAI.) |
| Elizabeth A. Arthur, M.D.<br>Dermatology and Cosmetic Center, LLP<br>1338 East Ridge Road<br>Rochester, NY 14621     | RD.06.SRE.18053:<br>15       | 29-30 May, 2008  | NAI  |

**Key to Classifications**

NAI = No deviation from regulations.

VAI = Deviation(s) from regulations.

OAI = Significant deviations from regulations. Data unreliable.

Pending = Preliminary classification based on information in 483 or preliminary communication with the field;  
EIR has not been received from the field and complete review of EIR is pending.

**1. Debra Breneman, M.D.**

University Dermatology Consultants, Inc.  
222 Piedmont, Suite 5300  
Cincinnati, OH 45219

**a. What was inspected:** The records for all 20 enrolled subjects were reviewed including, but not limited to, source documents, CRFs, informed consent forms, and reports of protocol deviations and adverse events.

**b. General observations/commentary:** Review of the records noted above revealed no significant discrepancies/regulatory violations.

- c. **Assessment of data integrity:** Data appear acceptable in support of the respective application.

Observations noted above are based on communications with the FDA field investigator. An inspection summary addendum will be generated if conclusions change upon receipt and review of the EIR.

- 2. Elizabeth A. Arthur, M.D.  
Dermatology and Cosmetic Center, LLP  
1338 East Ridge Road  
Rochester, NY 14621

- a. **What was inspected:** Records reviewed for all 17 randomized subjects included, but were not limited to, consent forms, adverse event reports, test article accountability forms, and a comparison of CRFs to source documents.
- b. **General observations/commentary:** Review of the records noted above revealed no significant discrepancies/regulatory violations.
- c. **Assessment of data integrity:** Data appear acceptable in support of the respective application.

### III. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Review of the establishment inspection report (EIR) for Dr. Breneman is pending. An addendum to this clinical inspection summary will be forwarded to the review division should there be a change in the final classification or additional observations of clinical and regulatory significance are discovered after reviewing the EIR. Otherwise, the data generated by the clinical sites of Drs. Breneman and Arthur appear acceptable in support of the respective application.

*{See appended electronic signature page}*

Roy Blay, Ph.D.  
Good Clinical Practice Branch I  
Division of Scientific Investigations

CONCURRENCE:

*{See appended electronic signature page}*

Constance Lewin, M.D., M.P.H.  
Branch Chief  
Good Clinical Practice Branch I  
Division of Scientific Investigations

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/s/

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Roy Blay  
9/10/2008 02:00:25 PM  
CSO

Constance Lewin  
9/10/2008 02:09:49 PM  
MEDICAL OFFICER

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# **REGULATORY PROJECT MANAGER LABELING REVIEW (PHYSICIAN LABELING RULE)**

## **Division of Dermatology and Dental Products**

**Application Number:** 22-087

**Name of Drug:** Silkis (calcitriol) Ointment, 3mcg/g

**Applicant:** Galderma Laboratories, LLC

### **Material Reviewed:**

**Submission Date:** December 21, 2007

**Receipt Date:** December 27, 2007

**Submission Date of Structure Product Labeling (SPL):** December 21, 2007

**Type of Labeling Reviewed:** WORD

### **Background and Summary**

New Drug Application 22-087 Silkis (calcitriol) Ointment, 3mcg/g for the treatment of Plaque-Type Psoriasis was originally submitted September 25, 2006. The Agency issued a Refusal-to-File letter on November 22, 2006 due to Chemistry, Manufacturing and Controls deficiencies. The current application, submitted on December 21, 2007, is the resubmission after refusal to file.

### **Review**

The applicant's proposed PLR formatted labeling was reviewed for formatting issues/deficiencies. The deficiencies identified are listed below.

#### **Highlights of Prescribing Information:**

1. The Highlights must be limited in length to one-half page, in 8 point type, two-column format. [See 21 CFR 201-57(d)(8)].
2. 21 CFR 201.57(a)(6) requires that if a product is a member of an established pharmacologic class, the following statement must appear under the Indications and Usage heading in the Highlights:

“(Drug/Biologic Product) is a (name of class) indicated for (indication(s)).”

The sponsor should propose an established pharmacologic class that is scientifically valid AND clinically meaningful to practitioners or rationale why pharmacologic class should be omitted from the Highlights.

3. A Horizontal line must separate the Highlights, Contents, and FPI [See 21 CFR 201.57(d)(2)].

**Full Prescribing Information: Contents - Table of Contents:**

4. The Agency recommends use of a two-column format for the Table of Contents, and if possible, that it be limited in length to one-half page.
5. The section and subsection headings and numbering used in the Table of Contents must match the section and subsection headings and numbering used in the FPI. [See 21 CFR 201.57(b).
6. The Table of Contents section headings must be in bold type. The Contents subsection headings must be indented and not bolded. [See 21 CFR 201.57(d)(10)].

**Full Prescribing Information:**

7. The preferred presentation of cross-references in the FPI is the section (not subsection) followed by the numerical identifier. For example, [*See Use in Specific Populations (8.4)*].

**Recommendations**

The identified deficiencies/issues will be conveyed to the applicant in the 74 day letter. The applicant will be asked to re-submit labeling addressing the identified deficiencies by April 30, 2008. This updated version of labeling will be used for further labeling discussions.

---

Margo Owens  
Lead Regulatory Health Project Manager

Supervisory Comment/Concurrence:

---

Maria Walsh  
Project Management Officer  
Office of Drug Evaluation III

**Drafted: mlo/3/6/08**

**Revised/Initialed:**

**Finalized:**

**Filename: CSO Labeling Review Template (updated 1-16-07).doc**

**CSO LABELING REVIEW OF PLR FORMAT**

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Margo Owens  
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Maria Walsh  
3/19/2008 08:12:30 AM  
CSO

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

**FILING COMMUNICATION**

NDA 22-087

Galderma Laboratories, LLC  
Attention: Paul Clark  
Director, Regulatory Affairs  
14501 N. Freeway  
Fort Worth, TX 76177

Dear Mr. Clark:

Please refer to your new drug application (NDA) dated December 21, 2007, received December 27, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Silkis (calcitriol) Ointment, 3 mcg/g.

We also refer to your submissions dated February 12 and 14, 2008.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is Standard. Therefore, the user fee goal date is October 27, 2008.

During our filing review of your application, we identified the following potential review issues:

The effect of the product on cardiac repolarization has not been adequately addressed. Data from a thorough QT/QT<sub>c</sub> study or a rationale for why such a study is not needed is not included your application.

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:

- A. Information to address the potential of the product to affect cardiac repolarization.
- B. A rationale for assuming the applicability of foreign data in the submission to the U.S. population (or its location in the submission).

- C. A rationale for pediatric waiver wherein the prevalence of psoriasis in the pediatric population is not based on projected data (e.g., from pharmacy sales).
- D. Details of disclosable financial arrangements and interests for 5 investigators;  
\_\_\_\_\_ or location in the submission).
- E. A statement of Good Clinical Practice for all of the clinical studies.
- F. An English translation for foreign labeling 1.14.5.3 (Columbia) and 1.14.5.4 (China).

b(6)

Please respond 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.

We are also reviewing the draft labeling, submitted in Physician's Labeling Rule (PLR) format, and have identified the following formatting issues:

**Highlights of Prescribing Information:**

1. The Highlights must be limited in length to one-half page, in 8 point type, two-column format. [See 21 CFR 201-57(d)(8)].
2. 21 CFR 201.57(a)(6) requires that if a product is a member of an established pharmacologic class, the following statement must appear under the Indications and Usage heading in the Highlights:

"(Drug/Biologic Product) is a (name of class) indicated for (indication(s))."

The sponsor should propose an established pharmacologic class that is scientifically valid AND clinically meaningful to practitioners or rationale why pharmacologic class should be omitted from the Highlights.

3. A Horizontal line must separate the Highlights, Contents, and FPI [See 21 CFR 201.57(d)(2)].

**Full Prescribing Information: Contents - Table of Contents:**

4. The Agency recommends use of a two-column format for the Table of Contents, and if possible, that it be limited in length to one-half page.
5. The section and subsection headings and numbering used in the Table of Contents must match the section and subsection headings and numbering used in the FPI. [See

21 CFR 201.57(b).

6. The Table of Contents section headings must be in bold type. The Contents subsection headings must be indented and not bolded. [See 21 CFR 201.57(d)(10)].

**Full Prescribing Information:**

7. The preferred presentation of cross-references in the FPI is the section (not subsection) followed by the numerical identifier. For example, [*See Use in Specific Populations (8.4)*].

Submit revised draft labeling addressing the above issues no later than April 30, 2008.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable. We note that you have not fulfilled the requirements. We acknowledge receipt of your request for a partial waiver of pediatric studies for this application for the age group of 0 to less than 12 and your request for a partial deferral of pediatric studies for the age group of 12 to 17 for this application. Once review of your waiver and deferral requests is complete, we will notify you whether the requested waiver and deferral have been granted.

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

Sincerely,

*{See appended electronic signature page}*

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

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/s/

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Susan Walker

3/10/2008 12:50:56 PM

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**From:** Owens, Margo  
**Sent:** Friday, February 08, 2008 10:41 AM  
**To:** 'CLARK Paul'  
**Cc:** Owens, Margo  
**Subject:** Information Request for NDA 22-087 calcitriol ointment, 3mcg/g

Paul,

The following is an information request from the Pharmacology/Toxicology Reviewer for your NDA 22-087 Calcitriol Ointment, 3mcg/g.

The current data sets lack concise tumor names. When printing our report we only print the first 30 characters for both tumor names and organ names, so concise labels are very useful. Also, they provide different tumor codes (variable: TUMORCOD) for definitely incidental, probably incidental, probably fatal, definitely fatal tumors, etc. for each specific tumor. But these are all the same type of tumor and should all have the same TUMORCOD value, but should differ on the cause of death variable (DEATHCAU). Further, there is at least one case in the rat data set where the tumor name (TUMORNAM) indicates that the tumor is probably fatal but the cause of death indicates it is incidental. This is a case of adenoma of pars distalis in the pituitary.

**Please submit this information officially to your NDA by February 22, 2008.**

**Margo Owens  
Regulatory Project Manager  
Division of Dermatology and Dental Products  
Office of Drug Evaluation III  
Office of New Drugs**

**Margo.Owens@fda.hhs.gov  
Phone: 301-796-2110 Room 5165  
Fax: 301-796-9894  
Mail: FDA CDER  
Division of Dermatology and Dental Products  
5901-B Amundale Rd  
Beltsville, MD 20705-1266**

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/s/

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Marge Owens  
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**NDA 22-087**

**Galderma Laboratories, L.P.  
Attention: Paul Clark  
Director, Regulatory Affairs  
14501 North Freeway  
Forth Worth, TX 76177**

**Dear Mr. Clark:**

We received your December 14, 2006 correspondence, requesting a meeting to discuss Calcitriol Ointment. We are granting this meeting to provide guidance on a pathway forward should you choose to pursue a future NDA submission. We will not be discussing a reconsideration of our decision not to file NDA 22-087.

Based on our guidance for industry titled *Formal Meetings with Sponsors and Applicants for PDUFA Products* (February, 2000), we consider this a Type A meeting. The meeting is scheduled for:

**Meeting Date: Friday, February 23, 2007  
Time: 10:00-11:00 AM, EST  
Location: 10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002**

Provide the background information for this meeting at least two weeks prior to the meeting. Submit the original copy to your IND, and 15 bound copies, each marked "DESK COPY", directly to Tisha Washington at the above address, Room 5164. If we do not receive it by February 9, 2007, we may need to reschedule the meeting.

If you have any questions, call Tisha Washington, Technical Information Specialist, at 301-796-2110.

Sincerely,

*{See appended electronic signature page}*

**Margaret Kober, R.Ph., M.P.A.  
Acting Supervisor, Project Management Staff  
Division of Dermatology & Dental Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 22-087

Galderma Laboratories, L.P.  
ATTENTION: Paul Clark  
Director, Regulatory Affairs  
14501 North Freeway  
Fort Worth, Texas 76177

Dear Mr. Clark:

Please refer to your New Drug Application (NDA 22-087) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for calcitriol ointment. To permit ongoing review of the clinical and statistical information in the application, please respond to the following requests:

**Statistics:**

The electronic lab data set (LAB2663.XPT) for study 2663 did not contain any numerical values for the variable RESULT. Please resubmit the data set LAB2663 making sure that numerical values for RESULT are included.

**Clinical:**

Please provide population data (N, Mean, SD) and reference range for 24 hour urine calcium at screening and at Week 8/final for both pivotal studies (SRE.18053 and SRE.18054), similar to the information provided for total calcium, adjusted calcium, phosphorous, PTH, and calcitriol. Please see Text Table 26, section 5.3.5.1.1.01, p. 92 in Study Report RD.SRE.18053 and section 5.3.5.1.1.02, p. 93 in Study Report RD.SRE.18054. If this information is located in the NDA submission, please provide the location.

**Combined Clinical & Statistics - Vehicle effect:**

Pivotal study 18053 has notably higher vehicle effect than study 18054. Please provide the following information to aid in assessing this effect.

1. It is unclear from the electronic database whether multiple batches of drug were used in the studies. If multiple batches were used, provide the following information in the electronic data set using the current naming convention.

FATNO - subject number  
BATCH - batch number  
TREAT - treatment arm

2. Provide the following information for each placebo ointment batch used in the pivotal Phase 3 clinical studies:
- a. Batch number and clinical study number
  - b. Formulation composition
  - c. Manufacturing process if it is different from that for the calcitriol ointment (other than absence of calcitriol)
  - d. Manufacturing site
  - e. Any significant differences in raw materials such as quality or supplier when compared with other placebo or active batches

If you have any questions, contact Bronwyn Collier, Acting Chief, Project Management Staff, at (301) 796-2110.

Sincerely,

*{See appended electronic signature page}*

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

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/s/

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Bronwyn Collier  
6/25/2008 04:35:27 PM  
Signed for Susan J. Walker, M.D., F.A.A.D.

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