

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

204141Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 204141

SUPPL # N/A

HFD # 540

Trade Name Topicort

Generic Name desoximetasone

Applicant Name Taro Pharmaceuticals USA, Inc.

Approval Date, If Known 04/2013

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# 017856 Topicort (desoximetasone) Cream, 0.25%
NDA# 018309 Topicort LP (desoximetasone) Cream, 0.05%
NDA# 018586 Topicort (desoximetasone) Gel, 0.05%
NDA# 018594 Topicort (desoximetasone) Ointment, 0.05%
NDA# 018763 Topicort (desoximetasone) Ointment, 0.25%

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:

Investigation #1: DSXS 0808- 28-day, double-blind, vehicle-controlled (1:1), randomized, parallel groups

Investigation #2: DSXS 0914- 28-day, double-blind, vehicle-controlled (1:1), randomized, parallel groups

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"):

Investigation #1: DSXS 0808- 28-day, double-blind, vehicle-controlled (1:1), randomized, parallel groups
Investigation #2: DSXS 0914- 28-day, double-blind, vehicle-controlled (1:1), randomized, parallel groups

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 # 101789 YES ! NO
! Explain:

Investigation #2 !
IND # 101789 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:

Name of person completing form: J. Paul Phillips

Title: Regulatory Project Manager

Date: 2/6/2013

Name of Office/Division Director signing form: Tatiana Oussova
Title: Deputy Director for Safety

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

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

/s/

J P PHILLIPS
04/11/2013

GORDANA DIGLISIC
04/11/2013

TATIANA OUSSOVA
04/11/2013



Taro Pharmaceuticals U.S.A., Inc.

DEBARMENT CERTIFICATION

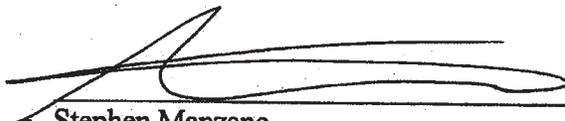
Taro Pharmaceuticals U.S.A., Inc (Taro), hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this New Drug Application.

Kavita Srivastava

Kavita Srivastava
Executive Director, Regulatory Affairs
Taro Pharmaceuticals U.S.A., Inc.

May 2, 2012

Date



Stephen Manzano
Vice President, Associate General Counsel
Taro Pharmaceuticals U.S.A., Inc.

May 7, 2012

Date

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 204141	NDA Supplement # 000	If NDA, Efficacy Supplement Type: n/a
Proprietary Name: Topicort Established/Proper Name: desoximetasone Dosage Form: Spray		Applicant: Taro Pharmaceuticals USA, Inc. Agent for Applicant (if applicable): n/a
RPM: J. Paul Phillips		Division: Dermatology and Dental Products
<p><u>NDA and NDA Efficacy Supplements:</u></p> <p>NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) 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 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></p> <p>Listed drug(s) relied upon for approval (include NDA #(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"/> This application does not rely upon a listed drug. <input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> This application relies on (explain)</p> <p><u>For ALL (b)(2) applications, two months prior to EVERY action, review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input type="checkbox"/> No changes <input type="checkbox"/> Updated 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>
❖ Actions		
<ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>04/12/2013</u> 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> • Previous actions (<i>specify type and date for each action taken</i>) 		<input checked="" type="checkbox"/> None

¹ 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.

² For resubmissions, (b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

<p>❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____</p>	<input type="checkbox"/> Received
<p>❖ Application Characteristics³</p>	
<p>Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only):</p> <p><input type="checkbox"/> Fast Track <input type="checkbox"/> Rx-to-OTC full switch <input type="checkbox"/> Rolling Review <input type="checkbox"/> Rx-to-OTC partial switch <input type="checkbox"/> Orphan drug designation <input type="checkbox"/> Direct-to-OTC</p> <p>NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies</p> <p><input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request</p> <p>BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies</p> <p>REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Communication Plan <input type="checkbox"/> ETASU <input type="checkbox"/> MedGuide w/o REMS <input checked="" type="checkbox"/> REMS not required</p> <p>Comments:</p>	
<p>❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)</p>	<input type="checkbox"/> Yes, dates
<p>❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)</p>	<input type="checkbox"/> Yes <input type="checkbox"/> No
<p>❖ Public communications (<i>approvals only</i>)</p>	
<ul style="list-style-type: none"> Office of Executive Programs (OEP) liaison has been notified of action 	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> Press Office notified of action (by OEP) 	<input type="checkbox"/> Yes <input type="checkbox"/> No
<ul style="list-style-type: none"> Indicate what types (if any) of information dissemination are anticipated 	<input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

³ Answer all questions in all sections in relation 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"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <i>Refer to 21 CFR 316.3(b)(13) for the definition of “same drug” for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification.</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i> 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date exclusivity expires:
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <i>(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.)</i> 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # and date 10-year limitation expires:
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [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). 	<input type="checkbox"/> No paragraph III certification Date patent will expire
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). <i>(If the application does not include any paragraph IV certifications, mark “N/A” and skip to the next section below (Summary Reviews)).</i> 	<input type="checkbox"/> N/A (no paragraph IV certification) <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

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

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

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

Yes No

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

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

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

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

Yes No

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

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

<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>	<input type="checkbox"/> Yes <input type="checkbox"/> No
---	--

CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ⁴	<input checked="" type="checkbox"/> Included
Officer/Employee List	
❖ 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>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Approval- 04/11/2013
Labeling	
❖ Package Insert (<i>write submission/communication date at upper right of first page of PI</i>)	
<ul style="list-style-type: none"> • Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	04/10/2013
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	06/11/2012
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	n/a

⁴ Fill in blanks with dates of reviews, letters, etc.

<ul style="list-style-type: none"> ❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling (<i>write submission/communication date at upper right of first page of each piece</i>) 	<input type="checkbox"/> Medication Guide <input checked="" type="checkbox"/> Patient Package Insert <input checked="" type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> • Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format. 	02/11/2013 (PPI, IFU)
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	06/11/2012 (PPI); 12/19/2012 (IFU)
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	n/a
<ul style="list-style-type: none"> ❖ Labels (full color carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>) 	
<ul style="list-style-type: none"> • Most-recent draft labeling 	02/22/2013
<ul style="list-style-type: none"> ❖ Proprietary Name <ul style="list-style-type: none"> • Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>) • Review(s) (<i>indicate date(s)</i>) • Ensure that both the proprietary name(s), if any, and the generic name(s) are listed in the Application Product Names section of DARRTS, and that the proprietary/trade name is checked as the 'preferred' name. 	02/05/2013 (Acceptable letter) 02/04/2013 (Review)
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input checked="" type="checkbox"/> RPM 07/18/2012 <input checked="" type="checkbox"/> DMPP/PLT 01/11/2013 <input checked="" type="checkbox"/> ODPD 01/15/2013 <input checked="" type="checkbox"/> DMEPA 01/25/2013 <input checked="" type="checkbox"/> SEALD 03/20/2013 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
<ul style="list-style-type: none"> ❖ Administrative Reviews (<i>e.g., RPM Filing Review⁵/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) 	<input checked="" type="checkbox"/> 07/23/2012 (RPM filing)
<ul style="list-style-type: none"> ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>) 	<input checked="" type="checkbox"/> Not a (b)(2) <input checked="" type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm 	
<ul style="list-style-type: none"> • Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> • This application is on the AIP <ul style="list-style-type: none"> ○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>) ○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> ❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> • Date reviewed by PeRC <u>1/9/2013</u> If PeRC review not necessary, explain: _____ • Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>) 	<input checked="" type="checkbox"/> Verified, statement is acceptable

⁵ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.

❖ Outgoing communications (<i>letters, including response to FD RR (do not include previous action letters in this tab), emails, faxes, telecons</i>)	N=26
❖ Internal memoranda, telecons, etc.	N/A
❖ Minutes of Meetings	
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> 07/20/2011
• EOP2 meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)	n/a
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	n/a
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	n/a
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> 04/10/2013
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> 02/12/2013
PMR/PMC Development Templates (<i>indicate total number</i>)	<input checked="" type="checkbox"/> n= 2
Clinical Information⁶	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	02/12/2013 (see CDTL)
• Clinical review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> 07/23/2012 (filing); 01/30/2013
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	Pg. 17 of Clinical review (01/30/2013)
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> 12/03/2012 (PMHS) <input checked="" type="checkbox"/> 12/05/2012 (DMEP)
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> Not applicable
❖ Risk Management	
• REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>)	
• REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)	<input checked="" type="checkbox"/> None
• Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)	
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input checked="" type="checkbox"/> 12/26/2012

⁶ Filing reviews should be filed with the discipline reviews.

Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None
Clinical Microbiology Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Statistical Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> 07/23/2012 (filing); 01/16/2013 02/12/2013 (addendum)
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> 07/25/2012 (filing); 01/18/2013
❖ DSI Clinical Pharmacology Inspection Review Summary <i>(include copies of DSI letters)</i>	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Supervisory Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> 07/23/2012 (filing); 01/07/2013
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None
❖ DSI Nonclinical Inspection Review Summary <i>(include copies of DSI letters)</i>	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> 07/20/2012 (filing); 01/23/2013 03/21/2013 (addendum)
❖ Microbiology Reviews <input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) <i>(indicate date of each review)</i> <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> Not needed
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None

❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	Pg. 84 of CMC review (01/23/2013)
<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ Facilities Review/Inspection	
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁷</i>)	Date completed: 03/20/2013 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) (<i>original and supplemental BLAs</i>)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>)	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

⁷ I.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

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

/s/

J P PHILLIPS
04/12/2013

From: Phillips, J. Paul
Sent: Wednesday, April 10, 2013 11:00 AM
To: 'Kavita Srivastava'
Cc: Gould, Barbara
Subject: NDA 204141 (Topicort)

Ms. Srivastava,

Attached is draft labeling for NDA 204141 (Topicort Spray). We have made one additional edit in section 5.1 for clarification and consistency with section 12.2.



NDA
1_desoximetasone_

Please respond by tomorrow (4/11/2013).

Thank you.

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
Fax: (301) 796-9895
e-mail: Paul.Phillips@fda.hhs.gov

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

/s/

J P PHILLIPS
04/10/2013

From: Phillips, J. Paul
Sent: Thursday, April 04, 2013 7:52 AM
To: 'Kavita Srivastava'
Cc: Gould, Barbara
Subject: NDA 204141 Topicort (desoximetasone) Spray, 0.25%

Ms. Srivastava,

Please see the attached draft labeling for NDA 204141 (Topicort) with a small edit to the Highlights under Warnings and Precautions.



NDA
1_desoximetasone_

Please respond **by COB Friday, April 5, 2013.**

Regards,

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
Fax: (301) 796-9895
e-mail: Paul.Phillips@fda.hhs.gov

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

/s/

J P PHILLIPS
04/04/2013

PMR/PMC Development Template

This template should be completed by the PMR/PMC Development Coordinator and included for *each* PMR/PMC in the Action Package.

NDA/BLA # 204141
Product Name: Topicort (desoximetasone) Topical Spray, 0.25%

PMR/PMC Description: A two year dermal rat carcinogenicity study

PMR/PMC Schedule Milestones:	Final Protocol Submission:	<u>04/30/2015</u>
	Study/Trial Completion:	<u>05/31/2017</u>
	Final Report Submission:	<u>05/31/2018</u>
	Other:	<u>N/A</u>

1. During application review, explain why this issue is appropriate for a PMR/PMC instead of a pre-approval requirement. Check type below and describe.

- Unmet need
- Life-threatening condition
- Long-term data needed
- Only feasible to conduct post-approval
- Prior clinical experience indicates safety
- Small subpopulation affected
- Theoretical concern
- Other

It is acceptable for long-term carcinogenicity data to be submitted to NDA 204141 as a PMR in view of: 1) the historical use of desoximetasone cream 0.25%, gel 0.25% and ointment 0.25% has provided no known signals suggestive of carcinogenic potential and 2) desoximetasone was negative in a standard battery of genetic toxicology studies.

2. Describe the particular review issue and the goal of the study/clinical trial. If the study/clinical trial is a FDAAA PMR, describe the risk. If the FDAAA PMR is created post-approval, describe the “new safety information.”

Data that describe the carcinogenicity of the drug substance are appropriate in support of labeling products that are intended for chronic use (see the ICH S1A document “The Need for Long-term Rodent Carcinogenicity Studies of Pharmaceuticals”). By agreement with the Division, these data may be submitted post-approval, and will be incorporated into the label at that time.

The goal of the study is to assess the potential of desoximetasone spray product to induce carcinogenesis.

3. If the study/clinical trial is a **PMR**, check the applicable regulation.

If not a PMR, skip to 4.

- **Which regulation?**

- Accelerated Approval (subpart H/E)
- Animal Efficacy Rule
- Pediatric Research Equity Act
- FDAAA required safety study/clinical trial

- **If the PMR is a FDAAA safety study/clinical trial, does it: (check all that apply)**

- Assess a known serious risk related to the use of the drug?
- Assess signals of serious risk related to the use of the drug?
- Identify an unexpected serious risk when available data indicate the potential for a serious risk?

- **If the PMR is a FDAAA safety study/clinical trial, will it be conducted as:**

- Analysis of spontaneous postmarketing adverse events?
Do not select the above study/clinical trial type if: such an analysis will not be sufficient to assess or identify a serious risk
- Analysis using pharmacovigilance system?
Do not select the above study/clinical trial type if: the new pharmacovigilance system that the FDA is required to establish under section 505(k)(3) has not yet been established and is thus not sufficient to assess this known serious risk, or has been established but is nevertheless not sufficient to assess or identify a serious risk
- Study: all other investigations, such as investigations in humans that are not clinical trials as defined below (e.g., observational epidemiologic studies), animal studies, and laboratory experiments?
Do not select the above study type if: a study will not be sufficient to identify or assess a serious risk
- Clinical trial: any prospective investigation in which the sponsor or investigator determines the method of assigning investigational product or other interventions to one or more human subjects?

4. What type of study or clinical trial is required or agreed upon (describe and check type below)? If the study or trial will be performed in a subpopulation, list here.

The sponsor agreed to conduct a 2 year dermal rat carcinogenicity study post-approval.
--

Required

- Observational pharmacoepidemiologic study
- Registry studies
- Primary safety study or clinical trial
- Pharmacogenetic or pharmacogenomic study or clinical trial if required to further assess safety
- Thorough Q-T clinical trial
- Nonclinical (animal) safety study (e.g., carcinogenicity, reproductive toxicology)

Continuation of Question 4

- Nonclinical study (laboratory resistance, receptor affinity, quality study related to safety)
 - Pharmacokinetic studies or clinical trials
 - Drug interaction or bioavailability studies or clinical trials
 - Dosing trials
 - Additional data or analysis required for a previously submitted or expected study/clinical trial (provide explanation)
-
- Meta-analysis or pooled analysis of previous studies/clinical trials
 - Immunogenicity as a marker of safety
 - Other (provide explanation)
-

Agreed upon:

- Quality study without a safety endpoint (e.g., manufacturing, stability)
 - Pharmacoepidemiologic study not related to safe drug use (e.g., natural history of disease, background rates of adverse events)
 - Clinical trials primarily designed to further define efficacy (e.g., in another condition, different disease severity, or subgroup) that are NOT required under Subpart H/E
 - Dose-response study or clinical trial performed for effectiveness
 - Nonclinical study, not safety-related (specify)
-
- Other
-

5. Is the PMR/PMC clear, feasible, and appropriate?

- Does the study/clinical trial meet criteria for PMRs or PMCs?
- Are the objectives clear from the description of the PMR/PMC?
- Has the applicant adequately justified the choice of schedule milestone dates?
- Has the applicant had sufficient time to review the PMRs/PMCs, ask questions, determine feasibility, and contribute to the development process?

PMR/PMC Development Coordinator:

- This PMR/PMC has been reviewed for clarity and consistency, and is necessary to further refine the safety, efficacy, or optimal use of a drug, or to ensure consistency and reliability of drug quality.*

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

/s/

J P PHILLIPS
03/28/2013

GORDANA DIGLISIC
03/28/2013

TATIANA OUSSOVA
03/28/2013

PMR/PMC Development Template

This template should be completed by the PMR/PMC Development Coordinator and included for *each* PMR/PMC in the Action Package.

NDA/BLA # 204141
Product Name: Topicort (desoximetasone) Topical Spray, 0.25%

PMR/PMC Description: Conduct a trial in 100 evaluable pediatric patients with plaque psoriasis ages 2 to 16 years and 11 months. Evaluate the safety and effect of Topicort (desoximetasone) Topical Spray, 0.25% on the hypothalamic-pituitary-adrenal axis and pharmacokinetics of desoximetasone under maximal use conditions after 4 weeks of treatment. Conduct the trial in sequential cohorts, for example:

Cohort 1: age 12 years to 16 years 11 months
Cohort 2: age 6 years -11 years and 11 month
Cohort 3: age 2 years to 5 years and 11 months

PMR/PMC Schedule Milestones: Final Protocol Submission: 04/30/2014
Study/Trial Completion: 04/30/2016
Final Report Submission: 04/30/2017
Other: n/a

1. During application review, explain why this issue is appropriate for a PMR/PMC instead of a pre-approval requirement. Check type below and describe.

- Unmet need
- Life-threatening condition
- Long-term data needed
- Only feasible to conduct post-approval
- Prior clinical experience indicates safety
- Small subpopulation affected
- Theoretical concern
- Other

We are deferring submission of the pediatric trial described above for ages 2 to 16 years and 11 months for this application because this product is ready for approval for use in adults and the pediatric trial has not been completed.

2. Describe the particular review issue and the goal of the study/clinical trial. If the study/clinical trial is a FDAAA PMR, describe the risk. If the FDAAA PMR is created post-approval, describe the “new safety information.”

Under section 2 of the Pediatric Research Equity Act (PREA) the applicant is required to submit adequate safety and efficacy data for pediatric subjects. There is no clinical pharmacology and safety data for subjects with plaque psoriasis of the body age less than 18 years to support labeling.

3. If the study/clinical trial is a **PMR**, check the applicable regulation.

If not a PMR, skip to 4.

- **Which regulation?**

- Accelerated Approval (subpart H/E)
 Animal Efficacy Rule
 Pediatric Research Equity Act
 FDAAA required safety study/clinical trial

- **If the PMR is a FDAAA safety study/clinical trial, does it: (check all that apply)**

- Assess a known serious risk related to the use of the drug?
 Assess signals of serious risk related to the use of the drug?
 Identify an unexpected serious risk when available data indicate the potential for a serious risk?

- **If the PMR is a FDAAA safety study/clinical trial, will it be conducted as:**

- Analysis of spontaneous postmarketing adverse events?
Do not select the above study/clinical trial type if: such an analysis will not be sufficient to assess or identify a serious risk
- Analysis using pharmacovigilance system?
Do not select the above study/clinical trial type if: the new pharmacovigilance system that the FDA is required to establish under section 505(k)(3) has not yet been established and is thus not sufficient to assess this known serious risk, or has been established but is nevertheless not sufficient to assess or identify a serious risk
- Study: all other investigations, such as investigations in humans that are not clinical trials as defined below (e.g., observational epidemiologic studies), animal studies, and laboratory experiments?
Do not select the above study type if: a study will not be sufficient to identify or assess a serious risk
- Clinical trial: any prospective investigation in which the sponsor or investigator determines the method of assigning investigational product or other interventions to one or more human subjects?

4. What type of study or clinical trial is required or agreed upon (describe and check type below)? If the study or trial will be performed in a subpopulation, list here.

Conduct a trial in 100 evaluable pediatric patients with plaque psoriasis ages 2 to 16 years and 11 months. Evaluate the safety and effect of Topicort (desoximetasone) Topical Spray, 0.25% on the hypothalamic-pituitary axis and pharmacokinetics of desoximetasone under maximal use conditions after 4 weeks of treatment. Conduct the trial in sequential cohorts

Cohort 1: age 12 years to 16 years 11 months
Cohort 2: age 6 years -11 years and 11 month
Cohort 3: age 2 years to 5 years and 11 months

Required

- Observational pharmacoepidemiologic study
- Registry studies
- Primary safety study or clinical trial
- Pharmacogenetic or pharmacogenomic study or clinical trial if required to further assess safety
- Thorough Q-T clinical trial
- Nonclinical (animal) safety study (e.g., carcinogenicity, reproductive toxicology)

Continuation of Question 4

- Nonclinical study (laboratory resistance, receptor affinity, quality study related to safety)
 - Pharmacokinetic studies or clinical trials
 - Drug interaction or bioavailability studies or clinical trials
 - Dosing trials
 - Additional data or analysis required for a previously submitted or expected study/clinical trial (provide explanation)
-
- Meta-analysis or pooled analysis of previous studies/clinical trials
 - Immunogenicity as a marker of safety
 - Other (provide explanation)

Agreed upon:

- Quality study without a safety endpoint (e.g., manufacturing, stability)
 - Pharmacoepidemiologic study not related to safe drug use (e.g., natural history of disease, background rates of adverse events)
 - Clinical trials primarily designed to further define efficacy (e.g., in another condition, different disease severity, or subgroup) that are NOT required under Subpart H/E
 - Dose-response study or clinical trial performed for effectiveness
 - Nonclinical study, not safety-related (specify)
-
- Other

5. Is the PMR/PMC clear, feasible, and appropriate?

- Does the study/clinical trial meet criteria for PMRs or PMCs? - Yes
- Are the objectives clear from the description of the PMR/PMC? - Yes
- Has the applicant adequately justified the choice of schedule milestone dates? - Yes

- Has the applicant had sufficient time to review the PMRs/PMCs, ask questions, determine feasibility, and contribute to the development process? - Yes
-

PMR/PMC Development Coordinator:

- This PMR/PMC has been reviewed for clarity and consistency, and is necessary to further refine the safety, efficacy, or optimal use of a drug, or to ensure consistency and reliability of drug quality.*

(signature line for BLAs)

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

/s/

J P PHILLIPS
03/28/2013

GORDANA DIGLISIC
03/28/2013

TATIANA OUSSOVA
03/28/2013

From: Phillips, J. Paul
Sent: Thursday, March 21, 2013 12:34 PM
To: 'Kavita Srivastava'
Cc: Gould, Barbara
Subject: NDA 204141 Topicort (desoximetasone) Spray

Ms. Srivastava,

I have attached some corrections and an additional edit to the Topicort Spray (NDA 204141) labeling, reflected in track changes.



NDA
I_desoximetasone_I

We ask that you respond tomorrow (3/22/2013) by the close of business.

Regards,

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
Fax: (301) 796-9895
e-mail: Paul.Phillips@fda.hhs.gov

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

/s/

J P PHILLIPS
03/21/2013

From: Phillips, J. Paul
Sent: Thursday, March 14, 2013 3:05 PM
To: 'Kavita Srivastava'
Cc: Gould, Barbara
Subject: NDA 204141 Topicort (desoximetasone) Spray, 0.25%

Ms. Srivastava,

Regarding NDA 204141 Topicort (desoximetasone) Spray, 0.25%, attached are some additional draft labeling edits and edits to the PREA PMR language in track changes. Please respond by Monday, **March 18, 2013**.

Draft Labeling



NDA
11_desoximetasone

PREA PMR

Conduct a trial in 100 evaluable pediatric patients with plaque psoriasis (b) (4) ages 2 to 16 years and 11 months. Evaluate the safety and effect of Topicort (desoximetasone) Topical Spray, 0.25% on the hypothalamic-pituitary-adrenal axis and pharmacokinetics of desoximetasone under maximal use conditions after 4 weeks of treatment. Conduct the trial in sequential cohorts, **for example**:

- Cohort 1: age 12 years to 16 years 11 months
- Cohort 2: age 6 years -11 years and 11 month
- Cohort 3: age 2 years to 5 years and 11 months

Final Protocol Submission:	<u>04/30/2014</u>
Study/Trial Completion:	<u>04/30/2016</u>
Final Report Submission:	<u>04/30/2017</u>

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
Fax: (301) 796-9895
e-mail: Paul.Phillips@fda.hhs.gov

Phillips, J. Paul

From: Phillips, J. Paul
Sent: Monday, March 18, 2013 9:54 AM
To: 'Kavita Srivastava'
Cc: Gould, Barbara; Senajda Celaj; Czarina Ochoa; Nancy Westcott; Marina Fatakhova; Pamela Sheppard; Lul Ogba-Ghebriel; Mary Anne Menhenitt; Avi Avramoff; Natalie Yantovskiy; Sara Ketsela
Subject: RE: NDA 204141 Topicort (desoximetasone) Spray, 0.25%

Ms. Srivastava,

Looking at your cover letter it looks like you inserted "of the body" into the PREA PMR language. I apologize if the track changes language was not clear. The intention was to delete the phrase "of the body". Please correct before submitting if you would.

Thank you.

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
Fax: (301) 796-9895
e-mail: Paul.Phillips@fda.hhs.gov

From: Kavita Srivastava [mailto:Kavita.Srivastava@taro.com]
Sent: Friday, March 15, 2013 6:43 PM
To: Phillips, J. Paul
Cc: Gould, Barbara; Senajda Celaj; Czarina Ochoa; Nancy Westcott; Marina Fatakhova; Pamela Sheppard; Lul Ogba-Ghebriel; Mary Anne Menhenitt; Avi Avramoff; Natalie Yantovskiy; Sara Ketsela
Subject: Re: NDA 204141 Topicort (desoximetasone) Spray, 0.25%

Dear Mr. Phillips:

Taro Pharmaceuticals U.S.A., Inc. (Taro) today submitted an Amendment to application- Response to draft labeling and PREA PMR comments for the above referenced NDA Desoximetasone Spray, 0.25% via ESG. The following are attached:

1. Cover letter dated March 15, 2013

2. Acknowledgement for core id:ci1363370370800.396731@lhap12_te

Please do not hesitate to call me if there are questions.

Sincerely,

Kavita Srivastava
Executive Director, Regulatory Affairs
Taro Pharmaceuticals U.S.A., Inc.
(914) 345-9001 x6160
(914) 703-7397 Cell
(914) 593-0078 fax

From: "Phillips, J. Paul" <Paul.Phillips@fda.hhs.gov>
To: Kavita Srivastava <Kavita.Srivastava@taro.com>
Cc: "Gould, Barbara" <Barbara.Gould@fda.hhs.gov>
Date: 03/14/2013 03:07 PM
Subject: NDA 204141 Topicort (desoximetasone) Spray, 0.25%

Ms. Srivastava,

Regarding NDA 204141 Topicort (desoximetasone) Spray, 0.25%, attached are some additional draft labeling edits and edits to the PREA PMR language in track changes. Please respond by Monday, **March 18, 2013**.

Draft Labeling

PREA PMR

Conduct a trial in 100 evaluable pediatric patients with plaque psoriasis of the body ages 2 to 16 years and 11 months. Evaluate the safety and effect of Topicort (desoximetasone) Topical Spray, 0.25% on the hypothalamic-pituitary-adrenal axis and pharmacokinetics of desoximetasone under maximal use conditions after 4 weeks of treatment. Conduct the trial in sequential cohorts, for example:

- Cohort 1: age 12 years to 16 years 11 months
- Cohort 2: age 6 years -11 years and 11 month
- Cohort 3: age 2 years to 5 years and 11 months

Final Protocol Submission: 04/30/2014
Study/Trial Completion: 04/30/2016
Final Report Submission: 04/30/2017

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
Fax: (301) 796-9895
e-mail: Paul.Phillips@fda.hhs.gov

From: Phillips, J. Paul
Sent: Thursday, March 21, 2013 12:34 PM
To: 'Kavita Srivastava'
Cc: Gould, Barbara
Subject: NDA 204141 Topicort (desoximetasone) Spray

Ms. Srivastava,

I have attached some corrections and an additional edit to the Topicort Spray (NDA 204141) labeling, reflected in track changes.



NDA
1_desoximetasone_1

We ask that you respond tomorrow (3/22/2013) by the close of business.

Regards,

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
Fax: (301) 796-9895
e-mail: Paul.Phillips@fda.hhs.gov

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

/s/

J P PHILLIPS
03/21/2013

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

/s/

J P PHILLIPS
03/14/2013

From: Phillips, J. Paul
Sent: Tuesday, February 19, 2013 4:04 PM
To: 'Kavita Srivastava'
Cc: Gould, Barbara
Subject: NDA 204141 Topicort (desoximetasone) Spray, 0.25%

Ms. Srivastava,

We refer to your February 11, 2013 submission to NDA 204141 Topicort (desoximetasone) Spray, 0.25%. Below are some additional comments regarding your proposed carton/container labels:

A. Container labels and Carton labeling (all package sizes)

1. Revise the statement "For Topical Use Only" to use a larger font.
2. Revise the statement "Not for Oral, Ophthalmic, or Intravaginal Use" to be presented on a single line.
3. Relocate the statement "Use no longer than 4 weeks" to follow immediately after the statement "Rub in gently"

B. Container labels (all package sizes)

1. Delete the background spiral graphic. As currently presented it is distracting and interferes with readability.

C. Container label (30 mL bottles)

1. Delete the ingredient list statement and provide white space between the usual dosage and storage statements. As currently presented this small label is crowded and difficult to read.

(b) (4)

Please respond by February 22, 2013.

Regards,

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
Fax: (301) 796-9895
e-mail: Paul.Phillips@fda.hhs.gov

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

/s/

J P PHILLIPS
02/19/2013



NDA 204141

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Taro Pharmaceuticals U.S.A., Inc.
3 Skyline Drive
Hawthorne, NY 10532

ATTENTION: Kavita Srivastava
Executive Director, Regulatory Affairs

Dear Ms. Srivastava:

Please refer to your New Drug Application (NDA) dated June 11, 2012, received June 12, 2012, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Desoximetasone Spray, 0.25%.

We also refer to your November 7, 2012, correspondence, received November 8, 2012, requesting review/reconsideration of your proposed proprietary name, Topicort. We have completed our review of the proposed proprietary name and have concluded that it is acceptable.

The proposed proprietary name, Topicort, will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

If **any** of the proposed product characteristics as stated in your November 7, 2012 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact, Janet Anderson, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0675. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Paul Phillips at (301) 796-3935.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh

Director

Division of Medication Error Prevention and Analysis

Office of Medication Error Prevention and Risk Management

Office of Surveillance and Epidemiology

Center for Drug Evaluation and Research

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

/s/

CAROL A HOLQUIST
02/05/2013

From: Phillips, J. Paul
Sent: Tuesday, January 29, 2013 4:37 PM
To: 'Kavita Srivastava'
Cc: Gould, Barbara
Subject: NDA 204141 (desoximetasone)

Ms. Srivastava,

Attached are the draft Package Insert (PI), Patient Package Insert (PPI) and Instructions for Use (IFU) with FDA edits.



NDA



desoximetasone



desoximetasone

!1_desoximetasone (TOPICORT Topic...(TOPICORT Topic...

Below are comments regarding the proposed carton/container labeling.

General Comments for carton/container labels (applicable to all sizes):

1. Change the displayed name to the following:
Topicort (desoximetasone) Topical Spray, 0.25%
2. Revise the presentation of the established name to ensure that it is at least ½ the size of the proprietary name taking into account all pertinent factors, including typography, layout, contrast, and other printing features per CFR 201.10(g)(2).
3. Under **Each Gram Contains**: change the descriptor of the product from (b) (4) to "clear, colorless liquid."
4. Add the statement "Discard the product 30 days after dispensing by pharmacist."
5. Add the statement "This medication is flammable; avoid heat, flame, or smoking when applying this product."
6. Add the statement "Keep this and all medications out of the reach of children."
7. Add the statement "Use no longer than 4 weeks."
8. As currently presented the Topicort topical spray and cream formulations share the similar (b) (4) scheme. It is important to provide adequate color differentiation to minimize selection errors, because both formulations also share the same strength. Select another color scheme for the spray formulation that is not currently utilized for another product in any of the Topicort product line
9. Revise the presentation of the route of administration statements to appear in title case and increase the prominence of the correct route of administration statement, "For Topical Use Only", by presenting the statement on a separate line above the negative route of administration statement "Not for Oral, Ophthalmic, or Intravaginal Use". Also consider bolding the correct route of administration statement "For Topical Use Only".

(b) (4)

Specific comments for immediate container labels (all sizes):

1. Delete the direction (b) (4)
2. Delete reference to (b) (4)
3. It is unclear from the container labels submitted in your Application if their placement on the bottle is in a vertical or horizontal orientation. Ensure the text on the container labels appear in a horizontal orientation, instead of a vertical orientation, in relation to the

orientation the product will normally be stored, held and used by healthcare providers and patients.

Below is the language and milestones for the postmarketing requirements.

1. A two year dermal rat carcinogenicity study.

Final Protocol Submission:	<u>04/30/2015</u>
Study/Trial Completion:	<u>05/31/2017</u>
Final Report Submission:	<u>05/31/2018</u>

2. Conduct a trial in 100 evaluable pediatric patients with plaque psoriasis of the body ages 2 to 16 years and 11 months. Evaluate the safety and effect of (desoximetasone) Topical Spray, 0.25% on the hypothalamic-pituitary-adrenal axis and pharmacokinetics of desoximetasone under maximal use conditions after 4 weeks of treatment. Conduct the trial in sequential cohorts.

Cohort 1: age 12 years to 16 years 11 months
Cohort 2: age 6 years -11 years and 11 month
Cohort 3: age 2 years to 5 years and 11 months

Final Protocol Submission:	<u>04/30/2013</u>
Study/Trial Completion:	<u>04/30/2016</u>
Final Report Submission:	<u>04/30/2017</u>

We ask that you respond **by February 12, 2013.**

Regards,

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
Fax: (301) 796-9895
e-mail: Paul.Phillips@fda.hhs.gov

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

/s/

J P PHILLIPS
01/29/2013



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Division of Dermatology and Dental Product
Office of Drug Evaluation III
Center for Drug Evaluation and Research
Food and Drug Administration
Silver Spring MD 20993

Tel: 301 796-2110
Fax: 301 796-9894

MEMORANDUM OF TCON

Date of Teleconference: 1/16/2013

Time: 12:00 p.m. (EST)

Application: NDA 204141

Product: (desoximetasone) Spray, (b) (4)

Applicant: Taro Pharmaceuticals, Inc.

FDA Participants:

Tatiana Oussova, MD, MPH, Deputy Director for Safety, DDDP
Gordana Diglisic, MD, Clinical Team Leader, DDDP
Melinda McCord, MD, Clinical Reviewer, DDDP
J. Paul Phillips, MS, Regulatory Health Project Manager, DDDP

Applicant Participants:

Kavita Srivastava, Executive Director, Regulatory Affairs, Taro Pharmaceuticals, and other participants from Taro whose names were not captured during the tcon.

Purpose:

To convey comments that resulted from internal discussion with the Pediatric Review Committee (PeRC) about the applicant's proposed pediatric plan to address PREA requirements.

Discussion Summary:

The applicant was notified that their proposed pediatric plan should include 100 evaluable subjects with plaque psoriasis of the body, ages 2 to 16 years 11 months. Safety evaluation would include an evaluation of HPA axis suppression and the pharmacokinetics of desoximetasone under maximal use conditions after 4 weeks of treatment. Safety assessments should also include: vital signs, physical examination, assessment for local and systemic adverse events.

Upon inquiry from the applicant, the FDA indicated that details related to the study protocol would be addressed following future submission of the proposed protocol to the IND after an action on the marketing application.

The conversation ended amicably.

P. Phillips/1-16-13
B. Gould/1-28-2013
M. McCord/1-17-13
G. Diglisic/1-17-13
T. Oussova/1-23-13

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

/s/

J P PHILLIPS
01/29/2013

Phillips, J. Paul

From: Phillips, J. Paul
At: Friday, January 11, 2013 3:56 PM
'Kavita Srivastava'
Cc: Gould, Barbara
Subject: NDA 204141 (desoximetasone)

Ms. Srivastava,

The sections of the FD&C Act to which you may refer for your PREA related submission to NDA 204141 (desoximetasone) are:

505B(a)(3)- Deferral
505B(a)(4)(B)- Partial Waiver

Regards,

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
(301) 796-9895
il: Paul.Phillips@fda.hhs.gov

Phillips, J. Paul

From: Phillips, J. Paul
Sent: Friday, December 21, 2012 9:42 AM
To: 'Kavita Srivastava'
Cc: Avi Avramoff; Sara Ketsela; kkook@; kwhite@salamandra.net; Wattanaporn Abramowitz; Marina Fatakhova; Senajda Celaj; Shen Gao; Lul Ogba-Ghebriel; Malini Kandasamy; Mary Anne Menhenitt; Toniann Thompson; Gould, Barbara
Subject: RE: NDA # 204141Desoximetasone Spray, 0.25%-Amendment to Application Sequence 0019

Ms. Srivastava,

Please provide a Microsoft WORD copy of the proposed PPI. This is necessary for our review and any additional edits that may be proposed by the FDA. You may simply provide this WORD copy of the labeling to me by email today.

Thank you.

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
Fax: (301) 796-9895
e-mail: Paul.Phillips@fda.hhs.gov

From: Kavita Srivastava [mailto:Kavita.Srivastava@taro.com]
Sent: Wednesday, December 19, 2012 5:16 PM
To: Phillips, J. Paul
Cc: Avi Avramoff; Sara Ketsela; kkook@; kwhite@salamandra.net; Wattanaporn Abramowitz; Marina Fatakhova; Senajda Celaj; Shen Gao; Lul Ogba-Ghebriel; Malini Kandasamy; Mary Anne Menhenitt; Toniann Thompson; Kavita Srivastava
Subject: RE: NDA # 204141Desoximetasone Spray, 0.25%-Amendment to Application Sequence 0019

Dear Mr. Phillips

Taro Pharmaceuticals U.S.A., Inc. (Taro) today submitted an 'Amendment to Application', sequence 0019 for the above referenced NDA 204141 Desoximetasone Spray, 0.25% pursuant to meeting discussion with the Agency on December 3, 2012 via ESG Gateway. The following are attached:

1. Cover letter
2. Pediatric HPA axis study proposal

3. Instructions for Use of the pump

Please do not hesitate to call me if there are questions.
Sincerely,

Kavita Srivastava
Executive Director, Regulatory Affairs
Taro Pharmaceuticals U.S.A., Inc.
(914) 345-9001 x6160
(914) 703-7397 Cell
(914) 593-0078 fax

From: "Phillips, J. Paul" <Paul.Phillips@fda.hhs.gov>
To: Kavita Srivastava <Kavita.Srivastava@taro.com>
Date: 11/30/2012 07:59 AM
Subject: RE: NDA # 204141Desoximetasone Spray, 0.25%

Ms. Srivastava,

Thank you.

J. Paul Phillips, MS
Regulatory Health Project Manager

Division of Dermatology and Dental Products
Center for Drug Evaluation and Research
Food & Drug Administration
W.O. Bldg. 22, Room 5189
10903 New Hampshire Ave.
Silver Spring, MD 20993

Telephone: (301) 796-3935
Fax: (301) 796-9895
e-mail: Paul.Phillips@fda.hhs.gov

From: Kavita Srivastava [<mailto:Kavita.Srivastava@taro.com>]
Sent: Thursday, November 29, 2012 8:47 PM
To: Phillips, J. Paul
Cc: Gould, Barbara; Jerzy Zadykowicz; Sara Ketsela; Lul Ogba-Ghebriel; Malini Kandasamy; Avi Avramoff; Senajda Celaj; Marina Fatakhova; Marinela Dabija; Kavita Srivastava
Subject: NDA # 204141Desoximetasone Spray, 0.25%

Dear Mr. Phillips

Reference is made to your telephone message regarding scheduling a conference call on December 3 to

discuss 'Instructions for Use' and Pediatric study for the above referenced NDA. The telephone conference information is provided below.

US Toll-Free: 1-888-252-7931 or 1-888-447-2911

Canada: 1-888-456-4281

Israel: 1-80-921-2662

Guest Code: 98412

Please note Taro will have 3-4 participants in this meeting. Kindly confirm the receipt of this e-mail.

Sincerely,

Kavita Srivastava
Executive Director, Regulatory Affairs
Taro Pharmaceuticals U.S.A., Inc.
(914) 345-9001 x6160
(914) 703-7397 Cell
(914) 593-0078 fax



Division of Dermatology and Dental Product
Office of Drug Evaluation III
Center for Drug Evaluation and Research
Food and Drug Administration
Silver Spring MD 20993

Tel: 301 796-2110
Fax: 301 796-9894

MEMORANDUM OF TCON

Date of Teleconference: 12/3/2012

Time: 11:45 a.m. (EST)

Application: NDA 204141

Product: (desoximetasone) Spray, (b) (4)

Applicant: Taro Pharmaceuticals, Inc.

FDA Participants:

Tatiana Oussova, MD, MPH, Deputy Director for Safety, DDDP
Gordana Diglisic, MD, Clinical Team Leader, DDDP
Melinda McCord, MD, Clinical Reviewer, DDDP
J. Paul Phillips, MS, Regulatory Health Project Manager, DDDP

Applicant Participants:

Kavita Srivastava, Executive Director, Regulatory Affairs, Taro Pharmaceuticals, and other participants from Taro whose names were not captured during the tcon.

Purpose:

To request a submission of a revised pediatric plan and proposed Instructions for Use to support patient labeling.

Discussion Summary:

The applicant was notified that a pediatric study(s) would be required for subjects ages 2 years – 16 years 11 months. The applicant would likely receive a waiver for subjects less than 2 years of age. The applicant was encouraged to consider a staged cohort approach (based on subjects' age). The applicant agreed to revise their proposed pediatric plan and submit for review.

The FDA pointed out that the type of information needed for the Instructions for Use in the patient labeling should be consistent with the information provided to subjects during clinical trials. The FDA requested that the applicant submit the instructions that were provided to subjects during the clinical trials. The applicant agreed to submit a revised IFU and supporting information.

The conversation ended amicably.

P. Phillips/12-28-12
B. Gould/1-28-2013
M. McCord/12-30-12
G. Diglisic/1-17-13
T. Oussova/1-23-13

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

/s/

J P PHILLIPS
01/29/2013



NDA 204141

INFORMATION REQUEST

Taro Pharmaceuticals USA, Inc.
Attention: Kavita Srivastava
Executive Director, Regulatory Affairs
3 Skyline Drive
Hawthorne, NY 10532

Dear Ms. Srivastava:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (desoximetasone) Spray, 0.25%.

We are reviewing your application and ask that you provide the following information.

1. We acknowledge that you provided a response to the clinical pharmacology information request in the Information Request letter dated 10/12/2012. However, the information provided for the (b)(4) developed acid protein precipitation assay was incomplete. To permit our review of the validity of the HPA axis suppression study results from (b)(4), provide the following information:
For the (b)(4) developed acid protein precipitation assay conducted at (b)(4) Provide data from in-house validations and/or quality control results during the same time frame of study DSXS-0805.
2. Provide additional data regarding the vehicle spray arm in the pooled safety data set for the assessment of vital sign changes. Modify the following tables to include data from subjects who were exposed to vehicle spray applied twice per day and vehicle spray applied once per day:

Integrated Summary of Safety (10/17/2012)

 - o Table 14.10.3 Summary of Change in Vital Sign Measurements
 - o Table 24 Descriptive Statistics for Baseline Values and Changes from Baseline in Blood Pressure
 - o Table 26 Descriptive Statistics for Baseline Values and Changes from Baseline in Pulse
3. You provided a list of adverse events for all Topicort® formulations in the FDA's postmarketing database. Provide full reports of all cases of Cushing's Syndrome.

4. Per your protocol(s) for Phase 3 trials (Section 9.2.1), subjects were provided instructions on the dosing technique. Provide more detailed information regarding these instructions.
5. Develop instructions for use (IFU) of the pump as part of the labeling (PPI).

We ask that you provide the above information by November 27, 2012.

If you have any questions, call Paul Phillips, Regulatory Project Manager, at (301) 796-3935.

Sincerely,

{See appended electronic signature page}

Tatiana Oussova, MD, MPH
Deputy Director for Safety
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

TATIANA OUSSOVA
11/20/2012



NDA 204141

**PROPRIETARY NAME REQUEST
WITHDRAWN**

Taro Pharmaceuticals USA, Inc.
3 Skyline Drive
Hawthorne, NY 10532

ATTENTION: Kavita Srivastava
Executive Director, Regulatory Affairs

Dear Ms. Srivastava:

Please refer to your New Drug Application (NDA) dated June 11, 2012, received June 12, 2012, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Desoximetasone Spray, 0.25%.

We acknowledge receipt of your November 1, 2012 correspondence, on November 2, 2012, notifying us that you are withdrawing your request for a review of the proposed proprietary names [REDACTED] ^{(b) (4)}. This proposed proprietary name request is considered withdrawn as of November 2, 2012.

We note that you have proposed an alternate proprietary name in your submission dated November 7, 2012, received November 8, 2012.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, call Janet Anderson, Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0675. For any other information regarding this application, contact the Office of New Drugs (OND) Regulatory Project Manager, Paul Phillips at (301) 796-3935.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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

/s/

CAROL A HOLQUIST
11/21/2012



NDA 204141

INFORMATION REQUEST

Taro Pharmaceuticals USA, Inc.
Attention: Kavita Srivastava
Executive Director, Regulatory Affairs
3 Skyline Drive
Hawthorne, NY 10532

Dear Ms. Srivastava:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (desoximetasone) Spray, 0.25%.

We are reviewing your application and ask that you provide the following information.

1. For the commercial kit Cobas Elecsys Cortisol Assay by Roche conducted at (b) (4) Provide data from in-house (i.e., from the laboratory that conducted the sample analysis) validations and/or quality control results during the same time frame of study DSXS-0805.
2. For the commercial kit Vitros Cortisol Assay by (b) (4) conducted at (b) (4) Provide data from in-house validations and/or quality control results during the same time frame of study DSXS-0805.
3. For the (b) (4) developed acid protein precipitation assay conducted at (b) (4) Provide method validation report as well as data from in-house validations and/or quality control results during the same time frame of study DSXS-0805.

Please provide the above information by October 29, 2012.

If you have any questions, call Paul Phillips, Regulatory Project Manager, at (301) 796-3935.

Sincerely,

{See appended electronic signature page}

Gordana Diglisic, MD
Clinical Team Leader
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

GORDANA DIGLISIC
10/12/2012



NDA 204141

INFORMATION REQUEST

Taro Pharmaceuticals USA, Inc.
Attention: Kavita Srivastava
Executive Director, Regulatory Affairs
3 Skyline Drive
Hawthorne, NY 10532

Dear Ms. Srivastava:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (desoximetasone) Spray, 0.25%.

We are reviewing your application and ask that you provide the following information.

Reconcile the following discrepancies regarding data from subjects enrolled in both the Phase 2 and Phase 3 trials:

- 0808-05-150 and 0906-04-146 are identified as same subjects in Table 13 (Integrated Summary of Safety, pg 38) but differ in ethnicity, height (175 decreased to 173 kg) and weight (70 to 90 kg) at baseline.
- 0914-02-058 and 0906-03-056 are identified as same subject in Table 13 but differ in ethnicity and weight (106 decreased to 103) at baseline.
- The following pair of subjects may represent the same subject, which increase the total number of subjects enrolled in more than one trial to 36.
- 808-05-153 and 906-04-262 have the same birth date, medical history (e.g. tubal ligation) and weight but the height has increased from 130 to 160 cm and one subject is male and one subject is female. The initials are not written clearly on the CRF (MCV for 808-05-153 and M-C or M-V for 906-04-262).

Please respond to the above request by October 29, 2012.

If you have any questions, call Paul Phillips, Regulatory Project Manager, at (301) 796-3935.

Sincerely,

{See appended electronic signature page}

Gordana Diglisic, MD
Clinical Team Leader
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

GORDANA DIGLISIC
10/12/2012

REQUEST FOR CONSULTATION

TO (Office/Division): DMEP

FROM (Name, Office/Division, and Phone Number of Requestor): DDDP
J. Paul Phillips, x6-3935

DATE
10/9/2012

IND NO.

NDA NO.
204141

TYPE OF DOCUMENT

DATE OF DOCUMENT
06/11/2012

NAME OF DRUG
(desoximetasone) spray,
(b) (4)

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE
11/9/2012

NAME OF FIRM: Taro Pharmaceuticals

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

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

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS:

Background

On June 11, 2012 Taro submitted a New Drug application for Topicort (desoximetasone) spray, 0.25% for "the relief of (b) (4) plaque psoriasis in patients 18 years of age or older". In the NDA submission, the applicant included a request for a waiver of the requirement to complete a pediatric assessment for children with psoriasis who are (b) (4). The applicant states that the proposed product, desoximetasone spray, 0.25%, (b) (4)

The applicant conducted Trial DSXS-0805 to assess potential HPA axis suppression in adults following the application of desoximetasone spray. However, the criteria used to define normal HPA axis functioning were different than those recommended by the FDA.

Applicant criteria:

- basal serum cortisol concentration >5 µg/100 mL

- response to cosyntropin stimulation of 18 µg/dL or higher 30 minutes after stimulation (representing an increase of at least 7 µg/dL above the basal concentration).

FDA criteria:

- response to cosyntropin stimulation of 18 µg/dL or higher 30 minutes after stimulation

The results of the HPA suppression assessment differ based on the criteria applied.

- According to FDA criteria: 3/24 subjects (13%) had a serum cortisol concentration at Day 28 that met at least one of the criteria for adrenal suppression (1 in the group with baseline 10-15% BSA involvement and 2 in the group with baseline > 15% BSA involvement).
- According to applicant criteria: 5/24 subjects (21%) had a serum cortisol concentration at Day 28 that met at least one of the criteria for adrenal suppression (2 in the group with baseline 10-15% BSA involvement and 3 in the group with baseline > 15% BSA involvement).

Electronic Submission: [\\CDSESUB5\EVSPROD\NDA204141\204141.enx](#)

(SDN-1, eCTD #0000; receipt date 6/12/12)

Consult Questions

Please provide your recommendations regarding the conduct of the HPA axis evaluation in pediatric subjects for Topicort (desoximetasone) spray, 0.25%.

What is the youngest age for subjects to be enrolled in the HPA axis evaluation for Topicort (desoximetasone) spray, 0.25% (Class 1/Class 2 topical corticosteroid)?

Should we request that pediatric subjects be evaluated in sequential cohorts (e.g. 12-16 years, 6-11 years, 2-5 years etc.)?

If sequential cohorts are recommended, what criteria would allow assessment of the next youngest cohort (e.g. percent of subjects demonstrating HPA axis suppression etc.)?

Are there any special safety considerations in the youngest pediatric subjects?

What are your recommended safety assessments during the HPA Axis trial for Topicort (desoximetasone) spray, 0.25%?

SIGNATURE OF REQUESTOR J. Paul Phillips	METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DARRTS <input type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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

/s/

J P PHILLIPS
10/09/2012



MEMORANDUM OF TCON

Date of Teleconference: October 3, 2012

Time: 4:15 p.m. (EDT)

Application: NDA 204141

Product: (desoximetasone) Spray, (b) (4)

Sponsor/Applicant: Taro Pharmaceuticals

FDA Participants:

Tatiana Oussova, MD, MPH, Deputy Director for Safety, DDDP
Gordana Diglisic, MD, Clinical Team Leader, DDDP
Melinda McCord, MD, Clinical Reviewer, DDDP
Shulin Ding, PhD, Pharmaceutical Assessment Lead, ONDQA
Hamid Shafiei, PhD, Chemistry Reviewer, ONDQA
J. Paul Phillips, MS, Regulatory Health Project Manager, DDDP

Applicant Participants:

Kavita Srivastava, Executive Director, Regulatory Affairs, Taro Pharmaceuticals; and other participants from Taro who were not introduced by name due to time constraints

Purpose:

This tcon was to discuss the timing of the applicant's response to two CMC review issues listed in the 74-day letter dated August 15, 2012. In addition, the CMC reviewers wanted to provide clarification of the information requests related to these two review issues.

Discussion Summary:

1. Regarding Response Timeline for CMC Deficiencies on In-Use Stability and Extractables/leachables Studies

The applicant stated that they planned to submit the study results by Jan. 12, 2013 as indicated in their September 28, 2012 response to the 74 day letter. The Agency replied that it would be preferable if data could be received by early November of 2012. Based on GRMP, the CMC review is scheduled to be closed by mid January. It would be very difficult to include new study results in the review if the information comes in late.

2. In-Use Stability Study

The following three questions were asked by the applicant:

A. Can the 6 mL physician size be exempted from the in-use stability study?

The applicant explained that the pump used for the 6 mL size is identical to that used for the trade sizes (30, 50, 100 mL) except the length of the dip tube. The Agency responded that the total deliverable is fill size specific; therefore, it needs to be generated for each size including the 6 mL size. Additionally, the active ingredient is sensitive to oxygen; therefore, its degradation may be faster in the 6 mL size if the ratio of formulation to volume for the 6 mL size is not favorable. The same holds true for the weight loss. The Agency agreed that some tests might not need to be repeated in the physician sample size if the trade sizes represent the worst cases. The applicant was advised to provide a justification in the response if they choose to skip some tests.

The Agency stated that the concept of bracketing might be applicable to the in-use stability study if an acceptable justification based on the ratio of formulation to volume was provided in the response.

B. Sampling the discharged formulation

The applicant inquired about the usefulness of the results obtained from the discharged formulation since the sample weight may not be accurate due to the volatility of isopropyl alcohol (one of major formulation ingredients). The Agency suggested that the applicant might want to consider obtaining the accurate sample weight by weighing the discharged formulation in a cool room or using the difference of the bottle weights before and after actuation as the sample weight.

C. Weight Loss Monitoring in the In-Use Stability Study

The applicant questioned the necessity of generating weight loss data in the in-use stability study since weight loss data from one registration stability batch was provided in the original NDA. The Agency replied that the weight loss data from the registration batch was for a packaging configuration that did not include the pump head. Since the proposed product will be mounted with a pump head after dispensing, and an in-use period of one month is requested, the Agency needs to know how tight the pump configuration is in terms of potential loss of volatile ingredients. Some pump units have been reported to be leaky in the NDA. Leaky bottles can be detected by monitoring weight loss.

The applicant stated that the in-use stability study would be a 28 day study. The Agency advised the applicant to cover different sizes, and at least 10 units for each size for the in-use stability study.

3. Extractables/leachables

The applicant stated that the supplier(s) of the packaging components have agreed to provide formulation information for the plastics. The Agency reminded the applicant of the need for plastic information in the NDA for all pump components which may contact the formulation. The Agency suggested that a risk assessment be done on this topic. The applicant stated that they had replaced those pump components that were found blistering, bleaching, swelling, etc. with better ones, and the new ones do not have these issues. The Agency inquired whether Phase 3 and registration stability batches were manufactured using the new pump components. The applicant will provide this information in their response to the information request.

The conversation ended amicably.

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

/s/

J P PHILLIPS
10/12/2012



NDA 204141

INFORMATION REQUEST

Taro Pharmaceuticals USA, Inc.
Attention: Kavita Srivastava
Executive Director, Regulatory Affairs
3 Skyline Drive
Hawthorne, NY 10532

Dear Ms. Srivastava:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (desoximetasone) Spray, 0.25%.

We are reviewing your application and ask that you provide the following information.

1. You provided a single citation from your search of the worldwide medical literature from 2004 to 2011 to identify sources of clinical safety information for desoximetasone (conducted on May 4, 2011 and updated December 11, 2011).

Please provide a summary of the citations that you collected from your literature search of MEDLINE, Biosis Previews and Embase for clinical safety information for desoximetasone/Topicort for the publication years 2004 to 2011.

2. You provided a single report from your review of adverse events received since the last NDA annual reports for all Topicort formulations through December 31, 2011.

Please provide a summary of all adverse events reported during those time periods for all Topicort formulations.

Application Number	Product	Most Recent Annual Report Cut-off Date
NDA 18-594	Desoximetasone Ointment USP 0.05%	16 January 2011
NDA 18-763 ¹ ANDA 74-286	Desoximetasone Ointment USP 0.25%	6 June 2011
NDA 18-586 ¹ ANDA 74-904	Desoximetasone Gel USP 0.05%	13 July 2011
NDA 18-309 ² ANDA 73-210	Desoximetasone) Cream USP 0.05%	29 November 2011
NDA 17-856 ¹ ANDA 73-193	Desoximetasone Cream USP 0.25%	29 November 2011

¹ Product not currently marketed as Topicort[®]

3. Provide additional data (including duration of exposure, baseline characteristics, Summary of Disposition and Reasons for Discontinuation, TEAE Related to Treatment

Occurring in $\geq 1\%$ of subjects, -At Least one TEAE Occurring in $\geq 1\%$ of patients) for subjects who were exposed to vehicle spray twice per day and once per day. Modify the following tables to include data from subjects who were exposed to vehicle spray applied twice per day and vehicle spray applied once per day:

- Integrated Summary of Safety Table 18 pg. 42- Duration of Exposure
 - Integrated Summary of Safety Table 14 pg. 39- Baseline Characteristics
 - Clinical Summary pg. 18 Table 2.7.4:13 pg 18- Summary of Disposition and Reasons for Discontinuation
 - Integrated Summary of Safety, Table 23 pg 47- TEAE Related to Treatment Occurring in $\geq 1\%$ of subjects
 - Clinical Summary, Table 2.7.4:16 pg. 25 - At Least one TEAE Occurring in $\geq 1\%$ of patients
4. Provide your rationale for classifying (b)(4) as an adverse reaction and provide case report forms for each subject reporting this event.
5. Regarding the Information Request dated 9/12/2012, ensure that the tables you provide with the integrated data for item #1 and item #2 (below) include data from subjects who were exposed to vehicle spray applied twice per day and vehicle spray applied once per day.
- a. Tables of Adverse Reactions observed in greater than 1% of subjects by age (e.g. 18-65, >65 years), sex, race/ethnicity for DXSX 0914, DXSX 0906, DXSX 0808 separately and integrated.
 - b. Tables of "Amount of Daily Product Used" by treatment group (in grams) and Numbers of Applications and Total Product Used. Include median, mean, minimum, maximum for DXSX 0914, DXSX 0906, DXSX 0808 separately and integrated.

Please respond to the above information requests by October 17, 2012.

If you have any questions, call Paul Phillips, Regulatory Project Manager, at (301) 796-3935.

Sincerely,

{See appended electronic signature page}

Gordana Diglisic, MD
Clinical Team Leader
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

GORDANA DIGLISIC
10/02/2012



NDA 204141

INFORMATION REQUEST

Taro Pharmaceuticals USA, Inc.
Attention: Kavita Srivastava
Executive Director, Regulatory Affairs
3 Skyline Drive
Hawthorne, NY 10532

Dear Ms. Srivastava:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for (desoximetasone) Spray, 0.25%.

We are reviewing your application and ask that you provide the following information.

1. Tables of Adverse Reactions observed in greater than 1% of subjects by age (e.g. 18-65, >65 years), sex, race/ethnicity for DXSX 0914, DXSX 0906, DXSX 0808 separately and integrated.
2. Tables of "Amount of Daily Product Used" by treatment group (in grams) and Numbers of Applications and Total Product Used. Include median, mean, minimum, maximum for DXSX 0914, DXSX 0906, DXSX 0808 separately and integrated.
3. A subgroup analysis of efficacy data by age (e.g. 18-65, >65 years), sex, race/ ethnicity for DXSX 0914, DXSX 0906, DXSX 0808 separately.

If you have any questions, call Paul Phillips, Regulatory Project Manager, at (301) 796-3935.

Sincerely,

{See appended electronic signature page}

Gordana Diglisic, MD
Clinical Team Leader
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

GORDANA DIGLISIC
09/12/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION			Pediatric and Maternal Health Staff Request for Consultation	
TO: CDER Pediatric and Maternal Health Staff <i>(please check)</i>			FROM <i>(Name, Office/Division, and Phone Number of Requestor):</i> DDDP c/o J. Paul Phillips/RPM, x6-3935	
Pediatrics <input checked="" type="checkbox"/> Maternal Health <input type="checkbox"/> Both <input type="checkbox"/>				
DATE 9/11/2012	IND NO.	NDA/BLA NO. 204141	TYPE OF DOCUMENT New NDA/ PREA waiver request	DATE OF DOCUMENT 6/11/2012
NAME OF DRUG (desoximetasone) Spray, 0.25%		NAME OF FIRM Taro Pharmaceuticals	CLASSIFICATION OF DRUG corticosteroid	PDUFA Goal Date 04/12/2013
Requested Consult Completion Date: 10/12/2012		<input type="checkbox"/> Urgent* (< 14 days)	<input checked="" type="checkbox"/> Priority (14-29 days)	<input type="checkbox"/> Routine \geq 30 days
*Note: Any consult requests with a desired completion date of < 14 days from receipt must receive prior approval from PMHS team leaders. Also, please check one of the three boxes above and also put in a due date.				
REASON FOR REQUEST				
Pediatrics: <input type="checkbox"/> Labeling Review <input type="checkbox"/> Written Request/PPSR <input checked="" type="checkbox"/> PREA PMR/General Regulatory Question <input type="checkbox"/> SPA <input type="checkbox"/> Action Letter Review <input type="checkbox"/> 30-day IND Review <input type="checkbox"/> Other Protocol Review <input type="checkbox"/> Meeting Attendance <input type="checkbox"/> PeRC Preparation Assistance <input type="checkbox"/> Other (please explain):			Maternal Health Team: <input type="checkbox"/> Labeling Review <input type="checkbox"/> Pregnancy Exposure Registry (protocol or report) <input type="checkbox"/> Clinical Lactation Study (protocol or report) <input type="checkbox"/> Pregnancy PK (protocol or report) <input type="checkbox"/> 30-day IND Review <input type="checkbox"/> Risk Management – Pregnancy Prevention and Planning <input type="checkbox"/> Evaluation of possible safety signal <input type="checkbox"/> Guidance development <input type="checkbox"/> Other (please explain):	
Link to electronic submission (if available): \\CDSESUB5\EVSPROD\NDA204141\204141.enx			Materials to be reviewed:	
<p>1. Please briefly describe the submission including drug's indication(s): On June 11, 2012 Taro submitted a New Drug application for Topicort (desoximetasone) spray, 0.25% for the relief of moderate to severe plaque psoriasis in patients 18 years of age or older. In the NDA submission, the applicant included a request for a waiver of the requirement to complete a pediatric assessment for children with psoriasis who are under 18 years of age.</p> <p>2. Describe in detail the reason for your consult. Include specific questions: The applicant states that the proposed product, desoximetasone spray, 0.25%, is (b) (4)</p> <p>(b) (4)</p> <p>The applicant conducted Trial DSXS-0805 to assess potential HPA axis suppression in adults following the application of desoximetasone spray. However, the criteria used to define normal HPA axis functioning were different than those recommended by the FDA.</p> <p>Applicant criteria:</p> <ul style="list-style-type: none"> (b) (4) response to cosyntropin stimulation of 18 µg/dL or higher 30 minutes (b) (4) <p>FDA criteria:</p> <ul style="list-style-type: none"> response to cosyntropin stimulation of 18 µg/dL or higher 30 minutes after stimulation <p>The results of the HPA suppression assessment differ based on the criteria applied.</p>				

- According to FDA criteria: 3/24 subjects (13%) had a serum cortisol concentration at Day 28 that met at least one of the criteria for adrenal suppression (1 in the group with baseline 10-15% BSA involvement and 2 in the group with baseline > 15% BSA involvement).

According to applicant criteria

(b) (4)

Consult Question:

Please provide your recommendation regarding the evaluation of Pediatric subjects for this Class 1/Class 2 topical corticosteroid under PREA.

3. Meeting dates:

Mid-Cycle Mtg.: Nov. 2, 2012
 PeRC scheduled for Nov. 7, 2012
 Wrap-up Mtg.: 1/14/2013

4. DARRTS Reference ID # for Prior Peds or Maternal Health consults for this product (within the last 3 years):

N/A

Review team:

Project Manager: J. Paul Phillips
 Clinical reviewer & Team Leader: Melinda McCord/ Gordana Diglisic
 Pharmacology/Toxicology reviewer & Team Leader: Renqin Duan/ Barbara Hill
 Clinical Pharmacology reviewer & Team Leader: An-Chi "Angela" Liu/ Doanh "Donny" Tran

Other:

PRINTED NAME or SIGNATURE OF REQUESTOR:

J. Paul Phillips

METHOD OF DELIVERY (Please check)

DARRTS EMAIL HAND OTHER

Version: DARRTS 06/01/2011

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

/s/

J P PHILLIPS
09/11/2012

GORDANA DIGLISIC
09/11/2012



NDA 204141

FILING COMMUNICATION

Taro Pharmaceuticals USA, Inc.
Attention: Kavita Srivastava
Executive Director, Regulatory Affairs
3 Skyline Drive
Hawthorne, NY 10532

Dear Ms. Srivastava:

Please refer to your New Drug Application (NDA) dated June 11, 2012, received June 12, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for (desoximetasone) Spray, 0.25%.

We also refer to your amendments dated June 21, July 13, 20, and August 3, 2012.

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 April 12, 2013.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, midcycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by March 15, 2013.

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

1. The in-use stability studies provided in the initial submission appear highly inadequate.
2. The extractables/leachables studies provided in the initial submission appear highly inadequate.

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. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application.

We request that you submit the following information:

Chemistry, Manufacturing and Controls

1. Submit representative drug product samples for each proposed configuration for confirmation of dosage form and packaging design.
2. Provide annual production forecast for 5 years, and the calculation of the estimated concentration of the substance at the point of entry into the aquatic environment.
3. The letter of authorization provided in the initial submission for DMF (b) (4) does not contain language that authorizes FDA to access the DMF in connection with the review of NDAs submitted by Taro Pharmaceuticals. Re-submit the letter of authorization issued by the DMF holder with appropriate language for DMF (b) (4).
4. The in-use stability studies provided in the initial submission appear highly inadequate. Provide in-use stability data for all proposed configurations (including the (b) (4)). The data should be generated from the discharged (i.e. pumped out) formulation and cover multiple time points over the proposed "in-use expiration dating period." The discharged formulation should be tested minimally for the following parameters: assay of desoximetasone, related substances, assay of isopropyl alcohol, and leachables. Additionally, you should evaluate weight loss, package integrity (both interior and exterior for all formulation-contacting parts), and pump performance at multiple time points over the course of in-use stability studies.
5. The extractables/leachables studies provided in the initial submission appear highly inadequate. Because the extracts were analyzed using only an HPLC method (b) (4) it is very possible that extractables/leachables (b) (4) were missed. We recommend that (b) (4) and extracts be analyzed using GC/mass and/or LC/mass. Identify potential leachables from the extractables found in the extracts, and then check these potential leachables in the registration stability and in-use stability study samples. Any leachables once confirmed to be present in the stability samples at a level above ICH Q3B reporting/identification/qualification threshold, you should report/identity/qualify them accordingly.
6. Provide bulk stability data to support the proposed bulk hold time.

7. Provide the section on filling operation for Master Batch Record and Executed Batch Records. The section should include the proposed in-process control over fill volume (or fill weight).

Pharmacology/Toxicology

8. Provide the timeline for conduct of your carcinogenicity study as a postmarketing requirement and specify the date you will submit the final study protocol, complete the study and submit the final study report.

Clinical Pharmacology

9. In trial DSXS-0805, serum cortisol concentrations were analyzed at local laboratories using 3 different commercial kits. Submit the manufacturer's assay procedures and validation results for each kit. In addition, provide data from in-house validations performed at each local laboratory confirming that the kits were performing as expected at the local laboratories used in trial DSXS-0805.

Biostatistics

10. According to the submission, the randomization (b) (4) was performed using a computer-generated randomization scheme. It is not clear from the submission whether randomization was stratified by center, and consequently, whether stratification of the statistical analysis by center would be meaningful. Submit details of the randomization scheme and whether any stratification factors were considered for the randomization.

Clinical

11. You assigned the following functions to formulation excipients:
 - Glycerol oleate (b) (4)
 - Isopropyl myristate (b) (4)
 - L-Menthol (b) (4)
 - Mineral oil (b) (4)

These are clinical claims that cannot be substantiated using the physicochemical properties of the excipients alone and require supporting data. Clarify the physicochemical function of the excipients, provide these data or delete from Module 3.

12. Identify the MeDRA Version used to categorize Adverse Events in Trial **DSXS 0914**, **DSXS 0808**, **DSXS 0906**. If a different version was used in each trial, please explain how it was reconciled when you pooled the adverse event data.
13. Submit a "coding dictionary" listing all of the investigator verbatim terms and the preferred terms to which they were mapped.

Labeling

During our preliminary review of your submitted labeling, we have identified the following labeling format issues with the MS Word version of your labeling:

1. Highlights (HL) must be in two-column format, with ½ inch margins on all sides and in a minimum of 8-point font.

Comment: The Highlights and Table of Contents (TOC) in the applicant proposed MS Word labeling is in 12-point font, standard margins, and not in a two column format. The Highlights and TOC need to be changed to the format, size and margins described above.

2. The length of HL must be less than or equal to one-half page (the HL Boxed Warning does not count against the one-half page requirement) unless a waiver has been granted in a previous submission (i.e., the application being reviewed is an efficacy supplement).

Comment: See comment #1 above. Once formatting is corrected, the content will be reassessed to determine if it meets one-half page requirement.

3. White space must be present before each major heading in HL.

Comment: Some of the section headers are not preceded by white space. A hard return (i.e. blank space) should be added before each of the section headers in Highlights.

4. Each summarized statement in HL must reference the section(s) or subsection(s) of the Full Prescribing Information (FPI) that contains more detailed information. The preferred format is the numerical identifier in parenthesis [e.g., (1.1)] at the end of each information summary (e.g. end of each bullet).

Comment: The reference needs to be added at the end of the Adverse Reactions section in Highlights.

5. At the beginning of HL, the following heading must be bolded and appear in all UPPER CASE letters: “HIGHLIGHTS OF PRESCRIBING INFORMATION”.

Comment: The product title currently appears before the Highlights heading and should be deleted.

6. The bolded HL Limitation Statement must be on the line immediately beneath the HL heading and must state: “These highlights do not include all the information needed to use (insert name of drug product in UPPER CASE) safely and effectively. See full prescribing information for (insert name of drug product in UPPER CASE).”

Comment: The limitation statement contains the full product title rather than just the proprietary name. Only the proprietary name, in all caps, should appear in the Highlights limitation statement.

7. Initial U.S. Approval in HL must be placed immediately beneath the product title, bolded, and include the verbatim statement “Initial U.S. Approval:” followed by the 4-digit year.

Comment: Remove the empty line (extra return) between the route of administration line and the Initial US Approval line.

8. For drug products other than vaccines, the verbatim bolded statement must be present: “To report SUSPECTED ADVERSE REACTIONS, contact (insert name of manufacturer) at (insert manufacturer’s U.S. phone number) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch”.

Comment: The following words should be deleted from the Adverse Reactions reporting statement [REDACTED] (b) (4) so that it reads verbatim as outlined above and required under 21 CFR 201.57(a)(11)(ii).

9. Bolded revision date (i.e., “Revised: MM/YYYY or Month Year”) must be at the end of HL.

Comment: Replace [REDACTED] (b) (4) with “Revised” in front of the date at the end of Highlights as required under 21 CFR 201.57(a)(15).

10. If no Contraindications are known, this section must state “None”.

Comment: PLR format discourages use of theoretical contraindications. Unless documented hypersensitivity has occurred, this section should list “None” in both Highlights and in the FPI.

11. Patient Counseling Information must reference any FDA-approved patient labeling, including the type of patient labeling.

Comment: Applicant will need to add the appropriate reference “See FDA-approved patient labeling (Patient Information)” on the line immediately following the section 17 header in the FPI.

We request that you resubmit labeling that addresses these issues by September 14, 2012. The resubmitted labeling will be used for further labeling discussions.

Please respond only to the above requests for 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.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI), and patient package insert (PPI). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), and patient package insert (PPI), and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required.

If you have any questions, call Paul Phillips, Regulatory Project Manager, at (301) 796-3935.

Sincerely,

{See appended electronic signature page}

Susan J. Walker, MD, FAAD
Director
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

TATIANA OUSSOVA

08/15/2012

Signing on behalf of Division Director Dr. Susan Walker

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements [except SE8 (labeling change with clinical data) and SE9 (manufacturing change with clinical data)]

Application Information		
NDA # 204141	NDA Supplement #: n/a	Efficacy Supplement Type SE- n/a
Proprietary Name: (undetermined) Established/Proper Name: desoximetasone Dosage Form: Spray Strengths: 0.25%		
Applicant: Taro Pharmaceuticals USA, Inc. Agent for Applicant (if applicable): n/a		
Date of Application: 06/11/2012 Date of Receipt: 06/12/2012 Date clock started after UN: n/a		
PDUFA Goal Date: 04/12/2013	Action Goal Date (if different): 03/18/2013	
Filing Date: 08/10/2012	Date of Filing Meeting: 07/20/2012	
Chemical Classification: (1,2,3 etc.) (original NDAs only) Type 3 (New Dosage Form)		
Proposed indication(s)/Proposed change(s): Relief of moderate to severe plaque psoriasis in patients 18 yrs of age or older.		
Type of Original NDA: AND (if applicable) Type of NDA Supplement:	<input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)	
<i>If 505(b)(2): Draft the "505(b)(2) Assessment" review found at: http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499 and refer to Appendix A for further information.</i>		
Review Classification: <i>If the application includes a complete response to pediatric WR, review classification is Priority.</i> <i>If a tropical disease priority review voucher was submitted, review classification is Priority.</i>	<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority <input type="checkbox"/> Tropical Disease Priority Review Voucher submitted	
Resubmission after withdrawal? <input type="checkbox"/>	Resubmission after refuse to file? <input type="checkbox"/>	
Part 3 Combination Product? <input type="checkbox"/> <i>If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults</i>	<input type="checkbox"/> Convenience kit/Co-package <input type="checkbox"/> Pre-filled drug delivery device/system (syringe, patch, etc.) <input type="checkbox"/> Pre-filled biologic delivery device/system (syringe, patch, etc.) <input type="checkbox"/> Device coated/impregnated/combined with drug <input type="checkbox"/> Device coated/impregnated/combined with biologic <input type="checkbox"/> Separate products requiring cross-labeling <input type="checkbox"/> Drug/Biologic <input type="checkbox"/> Possible combination based on cross-labeling of separate products <input type="checkbox"/> Other (drug/device/biological product)	

<input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> Orphan Designation <input type="checkbox"/> Rx-to-OTC switch, Full <input type="checkbox"/> Rx-to-OTC switch, Partial <input type="checkbox"/> Direct-to-OTC Other:	<input type="checkbox"/> PMC response <input type="checkbox"/> PMR response: <input type="checkbox"/> FDAAA [505(o)] <input type="checkbox"/> PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)] <input type="checkbox"/> Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) <input type="checkbox"/> Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)			
Collaborative Review Division (<i>if OTC product</i>):				
List referenced IND Number(s): 101789				
Goal Dates/Product Names/Classification Properties	YES	NO	NA	Comment
PDUFA and Action Goal dates correct in tracking system? <i>If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.</i>	X			
Are the proprietary, established/proper, and applicant names correct in tracking system? <i>If no, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into tracking system.</i>	X			Proprietary name not yet determined. Established name is in the system.
Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, 505(b)(2), orphan drug)? <i>For NDAs/NDA supplements, check the New Application and New Supplement Notification Checklists for a list of all classifications/properties at: http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm</i> <i>If no, ask the document room staff to make the appropriate entries.</i>	X			
Application Integrity Policy	YES	NO	NA	Comment
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at: http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</i>		X		
If yes, explain in comment column.				
If affected by AIP, has OC/OMPQ been notified of the submission? If yes, date notified:			X	
User Fees	YES	NO	NA	Comment
Is Form 3397 (User Fee Cover Sheet) included with authorized signature?	X			1.1.3

<p><u>User Fee Status</u></p> <p><i>If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period. Review stops. Send Unacceptable for Filing (UN) letter and contact user fee staff.</i></p>	<p>Payment for this application:</p> <p><input checked="" type="checkbox"/> Paid <input type="checkbox"/> Exempt (orphan, government) <input type="checkbox"/> Waived (e.g., small business, public health) <input type="checkbox"/> Not required</p>																			
<p><i>If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Send UN letter and contact the user fee staff.</i></p>	<p>Payment of other user fees:</p> <p><input checked="" type="checkbox"/> Not in arrears <input type="checkbox"/> In arrears</p>																			
<p>505(b)(2) (NDAs/NDA Efficacy Supplements only)</p>	<p>YES</p>	<p>NO</p>	<p>NA</p>	<p>Comment</p>																
<p>Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?</p>		<p>X</p>																		
<p>Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug (RLD)? [see 21 CFR 314.54(b)(1)].</p>		<p>X</p>																		
<p>Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug [see 21 CFR 314.54(b)(2)]?</p> <p><i>If you answered yes to any of the above questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the (b)(2) review staff in the Immediate Office of New Drugs</i></p>		<p>X</p>																		
<p>Is there unexpired exclusivity on the active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? Check the <i>Electronic Orange Book</i> at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm</p> <p>If yes, please list below:</p> <table border="1" data-bbox="203 1451 1349 1587"> <thead> <tr> <th>Application No.</th> <th>Drug Name</th> <th>Exclusivity Code</th> <th>Exclusivity Expiration</th> </tr> </thead> <tbody> <tr> <td> </td> <td> </td> <td> </td> <td> </td> </tr> <tr> <td> </td> <td> </td> <td> </td> <td> </td> </tr> <tr> <td> </td> <td> </td> <td> </td> <td> </td> </tr> </tbody> </table>	Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration														<p>X</p>		
Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration																	
<p><i>If there is unexpired, 5-year exclusivity remaining on the active moiety for the proposed drug product, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 314.108(b)(2). Unexpired, 3-year exclusivity will only block the approval, not the submission of a 505(b)(2) application.</i></p>																				
<p>Exclusivity</p>	<p>YES</p>	<p>NO</p>	<p>NA</p>	<p>Comment</p>																
<p>Does another product (same active moiety) have orphan exclusivity for the same indication? <i>Check the Orphan Drug Designations and Approvals list at:</i> http://www.accessdata.fda.gov/scripts/opdlisting/opd/index.cfm</p>		<p>X</p>																		

If another product has orphan exclusivity , is the product considered to be the same product according to the orphan drug definition of sameness [see 21 CFR 316.3(b)(13)]? <i>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy</i>			X	
Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? (<i>NDAs/NDA efficacy supplements only</i>) If yes, # years requested: 3 years <i>Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i>	X			1.3.5.3
Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use (<i>NDAs only</i>)?		X		
If yes , did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)? <i>If yes, contact Mary Ann Holovac, Director of Drug Information, OGD/DLPS/LRB.</i>			X	

Format and Content				
<i>Do not check mixed submission if the only electronic component is the content of labeling (COL).</i>	<input type="checkbox"/> All paper (except for COL) <input type="checkbox"/> All electronic <input checked="" type="checkbox"/> Mixed (paper/electronic) <input checked="" type="checkbox"/> CTD <input type="checkbox"/> Non-CTD <input type="checkbox"/> Mixed (CTD/non-CTD)			
If mixed (paper/electronic) submission , which parts of the application are submitted in electronic format?	Thus far the sponsor appears to be submitting everything in both paper and duplicate in electronic.			
Overall Format/Content	YES	NO	NA	Comment
If electronic submission , does it follow the eCTD guidance? ¹ If not , explain (e.g., waiver granted).	X			
Index : Does the submission contain an accurate comprehensive index?	X			
Is the submission complete as required under 21 CFR 314.50 (<i>NDAs/NDA efficacy supplements</i>) or under 21 CFR 601.2	X			

1

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072349.pdf>

(BLAs/BLA efficacy supplements) including: <input checked="" type="checkbox"/> legible <input checked="" type="checkbox"/> English (or translated into English) <input checked="" type="checkbox"/> pagination <input checked="" type="checkbox"/> navigable hyperlinks (electronic submissions only) If no, explain.				
BLAs only: Companion application received if a shared or divided manufacturing arrangement? If yes, BLA #			X	
Forms and Certifications				
<i>Electronic forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise, paper forms and certifications with hand-written signatures must be included. Forms include: user fee cover sheet (3397), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.</i>				
Application Form	YES	NO	NA	Comment
Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)? <i>If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].</i>	X			1.1.2
Are all establishments and their registration numbers listed on the form/attached to the form?	X			1.1.2
Patent Information (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	X			Submitted as amendment 6/22/12. Applicant indicated there are no current patents.
Financial Disclosure	YES	NO	NA	Comment
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)? <i>Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].</i> <i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i>	X			1.3.4
Clinical Trials Database	YES	NO	NA	Comment
Is form FDA 3674 included with authorized signature? <i>If yes, ensure that the application is also coded with the supporting document category, "Form 3674."</i> <i>If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant</i>	X			1.1

Debarment Certification	YES	NO	NA	Comment
<p>Is a correctly worded Debarment Certification included with authorized signature?</p> <p><i>Certification is not required for supplements if submitted in the original application; If foreign applicant, both the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].</i></p> <p><i>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...”</i></p>	X			<p>1.3.3</p> <p>Taro (sponsor) certificate is correct in wording; however, other certificates from contract manufacturers vary in their wording.</p> <p>ADRA indicated that we only consider sponsor certificate.</p>
Field Copy Certification (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
<p>For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included?</p> <p><i>Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)</i></p> <p><i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i></p>			X	eCTD; however Field Copy Certification was included anyway in 1.3.2
Controlled Substance/Product with Abuse Potential	YES	NO	NA	Comment
<p><u>For NMEs:</u> Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)?</p> <p><i>If yes, date consult sent to the Controlled Substance Staff:</i></p> <p><u>For non-NMEs:</u> <i>Date of consult sent to Controlled Substance Staff:</i></p>			X	
Pediatrics	YES	NO	NA	Comment
<p><u>PREA</u></p> <p>Does the application trigger PREA?</p> <p><i>If yes, notify PeRC RPM (PeRC meeting is required)²</i></p> <p><i>Note: NDAs/BLAs/efficacy supplements for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.</i></p>	X			New dosage form

² <http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/PediatricandMaternalHealthStaff/ucm027829.htm>

If the application triggers PREA , are the required pediatric assessment studies or a full waiver of pediatric studies included?		X		
If studies or full waiver not included , is a request for full waiver of pediatric studies OR a request for partial waiver and/or deferral with a pediatric plan included? <i>If no, request in 74-day letter</i>	X			Request for ^(b) ₍₄₎ pediatric waiver 1.9.1
If a request for full waiver/partial waiver/deferral is included , does the application contain the certification(s) required by FDCA Section 505B(a)(3) and (4)? <i>If no, request in 74-day letter</i>	X			1.9.1
BPCA (NDAs/NDA efficacy supplements only): Is this submission a complete response to a pediatric Written Request? <i>If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required)³</i>		X		
Proprietary Name	YES	NO	NA	Comment
Is a proposed proprietary name submitted? <i>If yes, ensure that the application is also coded with the supporting document category, "Proprietary Name/Request for Review."</i>		X		Sponsor using "Topicort" which was previously approved for other dosage forms. Sponsor was contacted and asked to submit a proprietary name request for review.
REMS	YES	NO	NA	Comment
Is a REMS submitted? <i>If yes, send consult to OSE/DRISK and notify OC/OSI/DSC/PMSB via the CDER OSI RMP mailbox</i>		X		
Prescription Labeling	<input type="checkbox"/> Not applicable			
Check all types of labeling submitted.	<input checked="" type="checkbox"/> Package Insert (PI) <input checked="" type="checkbox"/> Patient Package Insert (PPI) <input type="checkbox"/> Instructions for Use (IFU) <input type="checkbox"/> Medication Guide (MedGuide) <input checked="" type="checkbox"/> Carton labels <input checked="" type="checkbox"/> Immediate container labels <input type="checkbox"/> Diluent <input type="checkbox"/> Other (specify)			
	YES	NO	NA	Comment
Is Electronic Content of Labeling (COL) submitted in SPL format?	X			

³ <http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/PediatricandMaternalHealthStaff/ucm027837.htm>

<i>If no, request applicant to submit SPL before the filing date.</i>				
Is the PI submitted in PLR format? ⁴	X			MS Word copy— Highlights is not formatted in two columns w/8 pt font.

If PI not submitted in PLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.</i>			X	
All labeling (PI, PPI, MedGuide, IFU, carton and immediate container labels) consulted to OPDP?	X			Consult sent 7/16/12
MedGuide, PPI, IFU (plus PI) consulted to OSE/DRISK? (send WORD version if available)	X			Consult sent 7/16/12 to DMPP (PLT) for PPI
Carton and immediate container labels, PI, PPI sent to OSE/DMEPA and appropriate CMC review office (OBP or ONDQA)?	X			Consult sent 7/16/12
OTC Labeling	<input checked="" type="checkbox"/> Not Applicable			
Check all types of labeling submitted.	<input type="checkbox"/> Outer carton label <input type="checkbox"/> Immediate container label <input type="checkbox"/> Blister card <input type="checkbox"/> Blister backing label <input type="checkbox"/> Consumer Information Leaflet (CIL) <input type="checkbox"/> Physician sample <input type="checkbox"/> Consumer sample <input type="checkbox"/> Other (specify)			
	YES	NO	NA	Comment
Is electronic content of labeling (COL) submitted? <i>If no, request in 74-day letter.</i>				
Are annotated specifications submitted for all stock keeping units (SKUs)? <i>If no, request in 74-day letter.</i>				
If representative labeling is submitted, are all represented SKUs defined? <i>If no, request in 74-day letter.</i>				
All labeling/packaging, and current approved Rx PI (if switch) sent to OSE/DMEPA?				
Other Consults	YES	NO	NA	Comment

4

<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/StudyEndpointsandLabelingDevelopmentTeam/ucm025576.htm>

Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team) <i>If yes, specify consult(s) and date(s) sent:</i> (see comment)	X			OSI consult sent 7/19/12 for two domestic clinical sites.
Meeting Minutes/SPAs	YES	NO	NA	Comment
End-of Phase 2 meeting(s)? Date(s): <i>If yes, distribute minutes before filing meeting</i>		X		
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? Date(s): 7/20/11 <i>If yes, distribute minutes before filing meeting</i>	X			1.6.3
Any Special Protocol Assessments (SPAs)? Date(s): <i>If yes, distribute letter and/or relevant minutes before filing meeting</i>		X		

ATTACHMENT

MEMO OF FILING MEETING

DATE: 07/20/2012

NDA: 204141

PROPRIETARY NAME: (undetermined)

ESTABLISHED/PROPER NAME: desoximetasone

DOSAGE FORM/STRENGTH: Spray, 0.25%

APPLICANT: Taro Pharmaceuticals USA, Inc.

PROPOSED INDICATION(S)/PROPOSED CHANGE(S): New dosage form (spray) proposed for the relief of moderate to severe plaque psoriasis in patients 18 yrs of age or older.

BACKGROUND: The active ingredient, desoximetasone, is currently marketed by Taro Pharmaceuticals U.S.A., Inc. in the United States in various topical dosage forms (cream 0.05% & 0.25%, ointment 0.05% & 0.25%, and gel 0.05%). The original product was approved as a cream in 1977. The currently marketed dosage forms are approved for the *topical treatment of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.*

The sponsor is seeking approval for a new dosage form (spray 0.25%) for the *topical treatment of plaque psoriasis in patients 18 years of age or older.*

There was not an End-of-Phase 2 meeting or an SPA for this product. There was a Pre-NDA meeting on 7/20/11.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Paul Phillips	Y
	CPMS/TL:	Barbara Gould	N
Cross-Discipline Team Leader (CDTL)	Gordana Diglisic		Y
Clinical	Reviewer:	Melinda McCord	Y
	TL:	Gordana Diglisic	Y
Social Scientist Review (<i>for OTC products</i>)	Reviewer:		
	TL:		
OTC Labeling Review (<i>for OTC</i>)	Reviewer:		

<i>products)</i>			
	TL:		
Clinical Microbiology (<i>for antimicrobial products)</i>	Reviewer:		
	TL:		

Clinical Pharmacology	Reviewer:	Angela Lu	Y
	TL:	Doanh Tran	Y
Biostatistics	Reviewer:	Carin Kim	Y
	TL:	Mohamed Alesh	Y
Nonclinical (Pharmacology/Toxicology)	Reviewer:	Renqin Duan	Y
	TL:	Barbara Hill	Y
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Immunogenicity (assay/assay validation) (<i>for BLAs/BLA efficacy supplements</i>)	Reviewer:		
	TL:		
Product Quality (CMC)	Reviewer:	Hamid Shafiei	Y
	TL:	Shulin Ding	Y
Quality Microbiology (<i>for sterile products</i>)	Reviewer:		
	TL:		
CMC Labeling Review	Reviewer:		
	TL:		
Facility Review/Inspection	Reviewer:	Shawn Gould	Y
	TL:		
OSE/DMEPA (proprietary name)	Reviewer:	Carlos Mena-Grillasca	Y
	TL:	Lubna Merchant	N
OSE/DRISK (REMS)	Reviewer:		

	TL:		
OC/OSI/DGCPC/GCPAB	Reviewer:	Roy Blay	Y
	TL:	Susan Thompson	N
Bioresearch Monitoring (OSI)	Reviewer:		
	TL:		
Controlled Substance Staff (CSS)	Reviewer:		
	TL:		
Other reviewers	Karen Dowdy (DMPP)		Y
Other attendees	Tatiana Oussova (DDDP) Jessica Weintraub (OSE/DPVT)		

FILING MEETING DISCUSSION:

GENERAL	
<ul style="list-style-type: none"> 505(b)(2) filing issues? <p>If yes, list issues:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> Per reviewers, are all parts in English or English translation? <p>If no, explain:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> Electronic Submission comments <p>List comments: None</p>	<input type="checkbox"/> Not Applicable
CLINICAL	
<p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input checked="" type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> Clinical study site(s) inspections(s) needed? <p>If no, explain:</p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> Advisory Committee Meeting needed? 	<input type="checkbox"/> YES Date if known:

<p>Comments: New dosage form only. Product marketed since 1977.</p> <p><i>If no, for an original NME or BLA application, include the reason. For example:</i></p> <ul style="list-style-type: none"> ○ <i>this drug/biologic is not the first in its class</i> ○ <i>the clinical study design was acceptable</i> ○ <i>the application did not raise significant safety or efficacy issues</i> ○ <i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i> 	<input checked="" type="checkbox"/> NO <input type="checkbox"/> To be determined Reason:
<ul style="list-style-type: none"> • Abuse Liability/Potential <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> • 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? <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<p>CLINICAL MICROBIOLOGY</p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>CLINICAL PHARMACOLOGY</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input checked="" type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> • Clinical pharmacology study site(s) inspections(s) needed? 	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<p>BIOSTATISTICS</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input checked="" type="checkbox"/> Review issues for 74-day letter
<p>NONCLINICAL</p>	<input type="checkbox"/> Not Applicable

<p>(PHARMACOLOGY/TOXICOLOGY)</p> <p>Comments:</p>	<input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input checked="" type="checkbox"/> Review issues for 74-day letter
<p>IMMUNOGENICITY (BLAs/BLA efficacy supplements only)</p> <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p>PRODUCT QUALITY (CMC)</p> <p>Comments: Sponsor's extractable/leachable assay has problems and in-use stability data did not look at interaction with the pump. These are not filing issues but may be potential review issues per CMC.</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input checked="" type="checkbox"/> Review issues for 74-day letter
<p><u>Environmental Assessment</u></p> <ul style="list-style-type: none"> • Categorical exclusion for environmental assessment (EA) requested? <p>If no, was a complete EA submitted?</p> <p>If EA submitted, consulted to EA officer (OPS)?</p> <p>Comments:</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> YES <input type="checkbox"/> NO
<p><u>Quality Microbiology (for sterile products)</u></p> <ul style="list-style-type: none"> • Was the Microbiology Team consulted for validation of sterilization? (NDAs/NDA supplements only) <p>Comments:</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO

<p><u>Facility Inspection</u></p> <ul style="list-style-type: none"> • Establishment(s) ready for inspection? ▪ Establishment Evaluation Request (EER/TBP-EER) submitted to OMPQ? <p>Comments:</p>	<p><input type="checkbox"/> Not Applicable</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p><u>Facility/Microbiology Review (BLAs only)</u></p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>
<p><u>CMC Labeling Review</u></p> <p>Comments:</p>	<p><input type="checkbox"/> Review issues for 74-day letter</p>
REGULATORY PROJECT MANAGEMENT	
<p>Signatory Authority: Susan J. Walker, MD (Division Director)</p> <p>21st Century Review Milestones (listing review milestones in this document is <u>optional</u>):</p> <p>Comments:</p>	
REGULATORY CONCLUSIONS/DEFICIENCIES	
<input type="checkbox"/>	The application is unsuitable for filing. Explain why:
<input checked="" type="checkbox"/>	<p>The application, on its face, appears to be suitable for filing.</p> <p><u>Review Issues:</u></p> <p><input type="checkbox"/> No review issues have been identified for the 74-day letter.</p> <p><input checked="" type="checkbox"/> Review issues have been identified for the 74-day letter.</p> <p><u>Review Classification:</u></p> <p><input checked="" type="checkbox"/> Standard Review</p> <p><input type="checkbox"/> Priority Review</p>
ACTIONS ITEMS	

<input checked="" type="checkbox"/>	Ensure that any updates to the review priority (S or P) and classifications/properties are entered into tracking system (e.g., chemical classification, combination product classification, 505(b)(2), orphan drug).
<input type="checkbox"/>	If RTF, notify everybody who already received a consult request, OSE PM, and Product Quality PM (to cancel EER/TBP-EER).
<input type="checkbox"/>	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
<input type="checkbox"/>	BLA/BLA supplements: If filed, send 60-day filing letter
<input type="checkbox"/>	If priority review: <ul style="list-style-type: none"> • notify sponsor in writing by day 60 (For BLAs/BLA supplements: include in 60-day filing letter; For NDAs/NDA supplements: see CST for choices) • notify OMPQ (so facility inspections can be scheduled earlier)
<input type="checkbox"/>	Send review issues/no review issues by day 74
<input checked="" type="checkbox"/>	Conduct a PLR format labeling review and include labeling issues in the 74-day letter
<input type="checkbox"/>	BLA/BLA supplements: Send the Product Information Sheet to the product reviewer and the Facility Information Sheet to the facility reviewer for completion. Ensure that the completed forms are forwarded to the CDER RMS-BLA Superuser for data entry into RMS-BLA one month prior to taking an action [These sheets may be found in the CST eRoom at: http://eroom.fda.gov/eRoom/CDER2/CDERStandardLettersCommittee/0_1685f]
<input type="checkbox"/>	Other

Appendix A (NDA and NDA Supplements only)

NOTE: The term "original application" or "original NDA" as used in this appendix denotes the NDA submitted. It does not refer to the reference drug product or "reference listed drug."

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

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) 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, and.
- (3) 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) 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, or
- (3) 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 OND ADRA or OND IO.

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

/s/

J P PHILLIPS
07/23/2012

BARBARA J GOULD
07/23/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR CONSULTATION		
TO (Division/Office): Mail: OSE/DMEPA		FROM: DDDP J. Paul Phillips/x6-3935		
DATE 07/16/2012	IND NO.	NDA NO. 204141	TYPE OF DOCUMENT New NDA—Labeling	DATE OF DOCUMENT 06/11/2012
NAME OF DRUG (desoximetasone) Spray, 0.25%		PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE 01/04/2013
NAME OF FIRM: Taro Pharmaceuticals USA, Inc.				
REASON FOR REQUEST				
I. GENERAL				
<input type="checkbox"/> NEW PROTOCOL <input type="checkbox"/> PROGRESS REPORT <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> MEETING PLANNED BY <input type="checkbox"/> PRE--NDA MEETING <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> PAPER NDA <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> FORMULATIVE REVIEW <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH		STATISTICAL APPLICATION BRANCH		
<input type="checkbox"/> TYPE A OR B NDA REVIEW <input type="checkbox"/> END OF PHASE II MEETING <input type="checkbox"/> CONTROLLED STUDIES <input type="checkbox"/> PROTOCOL REVIEW <input type="checkbox"/> OTHER (SPECIFY BELOW):		<input type="checkbox"/> CHEMISTRY REVIEW <input type="checkbox"/> PHARMACOLOGY <input type="checkbox"/> BIOPHARMACEUTICS <input type="checkbox"/> OTHER (SPECIFY BELOW):		
III. BIOPHARMACEUTICS				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> BIOAVAILABILITY STUDIES <input type="checkbox"/> PHASE IV STUDIES		<input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> PROTOCOL-BIOPHARMACEUTICS <input type="checkbox"/> IN-VIVO WAIVER REQUEST		
IV. DRUG EXPERIENCE				
<input type="checkbox"/> PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL <input type="checkbox"/> DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP		<input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE <input type="checkbox"/> POISON RISK ANALYSIS		
V. SCIENTIFIC INVESTIGATIONS				
<input type="checkbox"/> CLINICAL		<input type="checkbox"/> PRECLINICAL		
COMMENTS/SPECIAL INSTRUCTIONS: Background The active moiety (desoximetasone) was originally approved in 1977 as Topicort (desoximetasone) Cream, 0.25%. Since that time, there have been subsequent approvals for additional dosage forms for Gel (0.05%) and Ointment (0.05%, 0.25%). In the current NDA (204141) the sponsor (Taro) has submitted information for the newest dosage form, Spray (0.25%). Application is electronic. EDR: \\CDSESUB5\EVSPROD\NDA204141\204141.enx Consult Request Please review the proposed carton/container labels and provide any comments. Mid-Cycle Meeting: 11/2/12 Labeling Meetings: 11/5/12; 11/26/12; 12/3/12; 12/10/12 Wrap-Up Meeting: 1/14/13				
SIGNATURE OF REQUESTER J. Paul Phillips		METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input checked="" type="checkbox"/> DARRTS <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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

/s/

J P PHILLIPS
07/16/2012

**REQUEST FOR OPDP (previously DDMAC) LABELING REVIEW
CONSULTATION**

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

****Please send immediately following the Filing/Planning meeting****

TO:
CDER-DDMAC-RPM

FROM: (Name/Title, Office/Division/Phone number of requestor)
J. Paul Phillips/RPM, DDDP/06-3935

REQUEST DATE
07/16/2012

IND NO.
101789

NDA/BLA NO.
204141

TYPE OF DOCUMENTS
(PLEASE CHECK OFF BELOW)

NAME OF DRUG
(desoximetasone) Spray, 0.25%

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG
Corticosteroid

DESIRED COMPLETION DATE
(Generally 1 week before the wrap-up meeting)

1/4/2013

NAME OF FIRM:
Taro Pharmaceuticals USA Inc.

PDUFA Date:
4/12/2013

TYPE OF LABEL TO REVIEW

TYPE OF LABELING:

(Check all that apply)

- PACKAGE INSERT (PI)
- PATIENT PACKAGE INSERT (PPI)
- CARTON/CONTAINER LABELING
- MEDICATION GUIDE
- INSTRUCTIONS FOR USE(IFU)

TYPE OF APPLICATION/SUBMISSION

- ORIGINAL NDA/BLA
- IND
- EFFICACY SUPPLEMENT
- SAFETY SUPPLEMENT
- LABELING SUPPLEMENT
- PLR CONVERSION

REASON FOR LABELING CONSULT

- INITIAL PROPOSED LABELING
- LABELING REVISION

EDR link to submission:

<\\CDSESUB5\EVSPROD\NDA204141\204141.enx>

Please Note: There is no need to send labeling at this time. OPDP reviews substantially complete labeling, which has already been marked up by the CDER Review Team. After the disciplines have completed their sections of the labeling, a full review team labeling meeting can be held to go over all of the revisions. Within a week after this meeting, "substantially complete" labeling should be sent to OPDP. Once the substantially complete labeling is received, OPDP will complete its review within 14 calendar days.

COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: 11/2/12
Labeling Meetings: 11/5/12; 11/26/12; 12/3/12; 12/10/12
Wrap-Up Meeting: 1/14/13

SIGNATURE OF REQUESTER
J. Paul Phillips

SIGNATURE OF RECEIVER

METHOD OF DELIVERY (Check one)

- eMAIL DARRTS HAND

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

/s/

J P PHILLIPS
07/16/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR PATIENT LABELING REVIEW CONSULTATION			
TO: CDER-DMPP-PatientLabelingTeam			FROM: (Name/Title, Office/Division/Phone number of requestor) J. Paul Phillips/RPM, DDDP/x6-3935		
REQUEST DATE: 07/16/2012		NDA NO.: 204141	TYPE OF DOCUMENTS: (PLEASE CHECK OFF BELOW)		
NAME OF DRUG: (desoximetasone) Spray, 0.25%		PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE (Generally 2 Weeks after receiving substantially complete labeling) 1/4/2013	
SPONSOR: Taro Pharmaceuticals USA Inc.			PDUFA Date: 4/12/2013		
TYPE OF LABEL TO REVIEW					
TYPE OF LABELING: (Check all that apply) <input checked="" type="checkbox"/> PATIENT PACKAGE INSERT (PPI) <input type="checkbox"/> MEDICATION GUIDE <input type="checkbox"/> INSTRUCTIONS FOR USE (IFU)		TYPE OF APPLICATION/SUBMISSION <input checked="" type="checkbox"/> ORIGINAL NDA/BLA <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> SAFETY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> MANUFACTURING (CMC) SUPPLEMENT <input type="checkbox"/> PLR CONVERSION		REASON FOR LABELING CONSULT <input checked="" type="checkbox"/> INITIAL PROPOSED LABELING <input type="checkbox"/> LABELING REVISION	
EDR link to submission: \\CDSESUB5\EVSPROD\NDA204141\204141.enx					
Please Note: DMPP uses substantially complete labeling, which has already been marked up by the CDER Review Team, when reviewing MedGuides, IFUs, and PPIs. Once the substantially complete labeling is received, DMPP will complete its review within 14 calendar days. Please provide a copy of the sponsor's proposed patient labeling in Word format.					
COMMENTS/SPECIAL INSTRUCTIONS: Filing/Planning Meeting: 7/20/12 Mid-Cycle Meeting: 11/2/12 Labeling Meetings: 11/5/12; 11/26/12; 12/3/12; 12/10/12 Wrap-Up Meeting: 1/14/13					
SIGNATURE OF REQUESTER J. Paul Phillips					
SIGNATURE OF RECEIVER			METHOD OF DELIVERY (Check one) <input type="checkbox"/> eMAIL (BLAs Only) <input checked="" type="checkbox"/> DARRTS		

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

/s/

J P PHILLIPS
07/16/2012



NDA 204141

NDA ACKNOWLEDGMENT

Taro Pharmaceuticals USA, Inc.
Attention: Kavita Srivastava
Executive Director, Regulatory Affairs
3 Skyline Drive
Hawthorne, NY 10532

Dear Ms. Srivastava:

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

Name of Drug Product: (desoximetasone) Spray, 0.25%

Date of Application: June 11, 2012

Date of Receipt: June 12, 2012

Our Reference Number: NDA 204141

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on August 10, 2012, in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No. 110-85, 121 Stat. 904).

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Dermatology and Dental Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications.

If you have any questions, call me, at (301) 796-3935.

Sincerely,

{See appended electronic signature page}

J. Paul Phillips, MS
Regulatory Health Project Manager
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

J P PHILLIPS
07/11/2012

Jennings, Kerri-Ann

From: Jennings, Kerri-Ann
Sent: Friday, July 06, 2012 12:07 PM
To: 'kavita.srivastava@taro.com'; 'marina.fatakhova@taro.com'
Cc: Phillips, J. Paul
Subject: NDA 204141

Good afternoon,

Re: NDA 204141

Per our discussion on yesterday, the following summarizes the manufacturing clarification required:

- Clarify which of the (b) (4) contract testing facilities listed in Section 3.2.P.3.1 may be involved in the release/stability testing of the finished drug product or drug substance, and provide a statement of readiness for inspecting for each testing facility that may be involved.
- Provide FDA Drug Establishment Registration Numbers for (b) (4)
- Provide the correct FDA Drug Establishment Registration Number for Taro Pharmaceuticals Inc. located at 130 East Drive, Brampton, Ontario, Canada.
- Clarify the name of the facility located at (b) (4)
- Provide the correct FDA Drug Establishment Registration Number for (b) (4)
- Revise the attachment to Form 356h, Section 3.2.S.2.1 and Section 3.2.P.3.1 for the aforementioned items. Those contract testing facilities that may be involved in the testing of drug substance and/or drug product should be added to the attachment to Form 356h.

In addition, please submit an amendment to NDA 204141.

Please let me know if you have any questions.

Regards,

Kerri-Ann E. Jennings, MS, BSN, RN
LT, United States Public Health Service
Regulatory Health Project Manager
FDA/CDER/OPS/ONDQA
Division of New Drug Quality Assessment II
Phone (301) 796-2919

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

/s/

KERRI-ANN JENNINGS
07/10/2012



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 101789

MEETING MINUTES

Taro Pharmaceuticals U.S.A., Inc.
Attention: Kavita Srivastava
Executive Director, Regulatory Affairs
3 Skyline Drive
Hawthorne, NY 10532

Dear Ms. Srivastava:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for (desoximetasone) Spray, 0.25%.

We also refer to the teleconference between representatives of your firm and the FDA on July 20, 2011. The purpose of the meeting was to discuss the content and format of the proposed New Drug Application (NDA) submission for (desoximetasone) Spray, 0.25%.

A copy of the official minutes of the teleconference is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, contact Paul Phillips, Regulatory Project Manager, at (301) 796-3935.

Sincerely,

{See appended electronic signature page}

Stanka Kukich, M.D.
Deputy Director
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE:
Meeting Minutes

MEMORANDUM OF MEETING MINUTES

Meeting Type: Type B
Meeting Category: Pre-NDA

Meeting Date and Time: July 20, 2011, 9:00 am
Meeting Location: Teleconference

Application Number: IND 101789
Product Name: (desoximetasone) Spray, 0.25%
Proposed Indication: relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses

Sponsor/Applicant Name: Taro Pharmaceuticals U.S.A., Inc.

Meeting Chair: Stanka Kukich, M.D.
Meeting Recorder: Cristina Attinello, M.P.H.

FDA ATTENDEES

Stanka Kukich, M.D., Deputy Director, DDDP
Gordana Diglicic, M.D., Clinical Team Leader, DDDP
Melinda McCord, M.D., Clinical Reviewer, DDDP
Barbara Hill, Ph.D., Pharmacology Supervisor, DDDP
Renqin Duan, Ph.D., Pharmacology Reviewer, DDDP
Cristina Attinello, M.P.H., Regulatory Health Project Manager, DDDP
Mohamed Alosch, Ph.D., Biostatistics Team Leader, DB III
Kate Dwyer, Ph.D., Biostatistics Reviewer, DB III
Shulin Ding, Ph.D., Pharmaceutical Assessment Lead, DNDQA II
Doanh Tran, Ph.D., Clinical Pharmacology Team Leader, DCP3
Abimbola Adebawale, Ph.D., Clinical Pharmacology Reviewer, DCP 3
Roy Blay, Ph.D., Regulatory Specialist, OC/DSI/GCPBII
Douglas Warfield, Regulatory Information Specialist, OPI/OBI/DRRS

SPONSOR ATTENDEES

Derek Ganes, Ph.D., VP Clinical, Taro
Kavita Srivastava, M.S., Executive Director, Regulatory Affairs, Taro
Jerzy Zadykowicz, Ph.D., Director, Research and Development, Taro

(b) (4)

Purpose of the Meeting:

To discuss the content and format of the proposed New Drug Application (NDA) submission for (desoximetasone) Spray, 0.25%.

Regulatory Correspondence History

We have sent the following correspondences:

- 05/09/2008: Adv/IR letter
- 07/06/2009: Adv/IR letter
- 11/04/2009: Adv/IR letter
- 01/21/2010: Adv/IR letter

Clinical/Biostatistics

General

Your studies might lack components of well-designed and conducted clinical trials necessary for establishing efficacy. You indicated that your studies were multicenter trials; however, it is not clear from your protocols or submission the number of centers in each study nor the number of subjects planned and enrolled per center; so that an investigation of site-to-site variability can be made. It is not clear whether randomization was stratified by site to ensure reasonable number of subjects per treatment arm per site so that comparison of the response rates across sites can be made and stratification of the statistical analysis by site is meaningful. Your proposed approach for handling missing data might not be scientifically justifiable. In terms of study conduct, you stated in the submission that there were 35 patients common among your trials DSXS-0906 (Phase 2), DSXS-0808 (now Phase 3) and DSXS-0914 (Phase 3). You are reminded that replication of study findings from independent and well-controlled trials is needed for establishing an efficacy claim. You should clarify how enrollment of these patients occurred twice and the centers in which enrollment of the same patients in multiple trials occurred, so that an analysis can be carried out to investigate the impact of such double enrollment on the efficacy findings in your trials (which are relatively small to start with--about 120 patients in each).

The NDA submission should include the following items:

- Study protocols including the statistical analysis plan, protocol amendments and their dates.
- The generated treatment assignment lists and the actual treatment allocations (along with date of enrollment) from the trials.
- For the interpretation of study results, the statistical methodology for analysis needs to follow that pre-specified in the protocol and ensures control of the Type I error rate.

For each of the trials submitted for establishing an efficacy claim, your submission should include:

- Analysis for success on the Physician Global assessment (PGA), defined as score of 0 or 1. It should be noted that this success criterion along with a score of 3 or 4 for enrollment implies 2 grades improvement on the PGA at a minimum.
- Efficacy analysis based on the Cochran-Mantel-Haenszel (CMH) test stratified by site as a sensitivity analysis. Investigate the impact of extreme centers, if any, on the efficacy results by considering site-to-site variability in the efficacy findings. Investigate the impact of your proposed approach for handling missing data, the last observation carried forward (LOCF),

by considering other approaches for handling missing data such as multiple imputations and modeling the response over time using models for longitudinal data analysis.

ISE and ISS should be submitted to the FDA in accordance with the regulations for NDA submissions (21 CFR 314.50(d)(5)(v) and 21 CFR 314.50(d)(5)(vi)(a), respectively).

- For information about the content of the ISE, the sponsor is referred to the Agency Guidance: *Guidance for Industry Integrated Summary of Effectiveness* which is available at the FDA website.
(<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079803.pdf>)
- For information about the location of ISS and ISE in the CTD, the sponsor is referred to the Agency Guidance: *Guidance for Industry Integrated Summaries of Effectiveness and Safety: Location Within the Common Technical Document at the FDA website*.
(<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM136174.pdf>)

For each of the 3 clinical trials:

- Provide the Agency with SAS transport files in electronic form. In addition to submitting data sets using the Study Data Tabulation Model (SDTM), the Agency also requests the sponsor submit ADaM data sets.
- The data sets should include demographic and baseline data as well as efficacy and safety data.
 - i. The database should include both raw variables (from the CRF) and derived variables suitable for conducting primary and secondary efficacy analyses.
 - ii. Each data set should include the treatment assignments. For each of the primary and secondary endpoints, an indicator variable that denotes whether measurements are actual or imputed should be included.
 - iii. The submission should include adequate documentation for the data sets including definitions of each variable in the data set, formulas for derived variables and decodes for any factor variables so that all categories are well-defined in the documentation.

Meeting Discussion:

The sponsor was asked to carefully consider Agency concerns provided above prior to submitting the NDA, specifically concerns regarding study design and conduct.

Question 12:

Does the Division agree that the adequate and well-controlled studies described in Section 6.3 adequately demonstrate the efficacy of Desoximetasone Spray, 0.25%? Specifically, are studies that were limited to patients with moderately severe to severe psoriasis appropriate to allow a claim for the treatment of corticosteroid responsive dermatoses (the indication for the other approved Topicort[®] products)?

Response:

No, we do not agree.

To receive approval to market a product for a specific indication, an applicant must present substantial evidence of the safety and efficacy of their product for that indication. The indication garnered will be based upon the population studied in the Phase 3 trials and for whom safety and effectiveness is established.

The two clinical trials (DSXS-0808 and DSXS-0914) enrolled subjects with moderate to severe psoriasis. Therefore, these trials are not sufficient to support the proposed indication of "relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses."

As previously noted, it is not clear whether your study design and randomization was stratified by sites to enable assessing site to site variability and enable analysis stratified by site. Also, the proposed LOCF method for handling missing data might not be scientifically justified.

We remind you of the Pediatric Research Equity Act of 2007 which requires all applications for a new active ingredient, new dosage form, new indication, new route of administration, or new dosing regimen to contain an assessment of the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations unless this requirement is waived or deferred. As a part of drug development for your product, it is anticipated that safety and efficacy information will be necessary for subjects 2 years of age and older, unless there is a clear safety concern in younger subjects. Refer to Guidance for Industry; How to Comply with the Pediatric Research Equity Act www.fda.gov/cder/guidance/6215dft.pdf - 09-07-2005.

Meeting Discussion:

The sponsor proposed (b) (4) The sponsor was advised to submit a protocol for Agency review and comment. The sponsor asked if they needed to conduct an HPA axis suppression study as part of the development plan in the pediatric population. The Agency responded that an HPA axis suppression study in pediatrics is needed as part of the safety evaluation of their product.

Question 13:

Across all eight Taro-sponsored studies (further described in Section 6.4.1), 617 unique subjects (11 patients were exposed in two separate studies) have been exposed to at least one dose of Desoximetasone Spray, 0.25% (identical to that proposed for marketing). Is this safety database adequate to allow review of the NDA?

Response:

The adequacy of the safety database is a review issue.

Question 14:

Are the plans for the ISS, described in Section 3.5 and further detailed in the Statistical Analysis Plan and the sample tables in Appendix 6.4.3, acceptable? Does the Division have any additional recommendations?

Response:

The Agency agrees with your approach.

In addition, you should provide the following:

- Subject narratives for all deaths, all serious adverse events (AEs), and AEs resulting in discontinuation from the trials conducted with desoximetasone spray, 0.25%.
- Case report forms (CRFs)
 - for all serious AEs, all severe AEs, and for all subjects who discontinued from the studies for any reason. A study's CRFs should be placed in a CRF folder under the applicable study with a file tag of "case-report-forms." Also provide the following:
 - Electronic links for:
 - a. all serious AEs
 - b. all severe AEs
 - c. all patients discontinued regardless of reason
 - d. all deaths
 - CRFs should be referenced under the study in which it belongs and tagged as "casereport-forms" in that study's stf.xml file.
 - CRFs that are not submitted should be readily available upon request.
- Adverse event tables $\geq 1\%$ regardless of causality.
- Adverse reaction tables (adverse reactions defined as those AEs with possible or probable causality) $\geq 1\%$.
- Line listings for all safety data.
- Group means for irritancy safety study results.
- Frequency tables for sensitivity safety study results. Define and justify the threshold for calling a score positive (or negative) for sensitization.
 - The generated treatment assignment lists and the actual treatment allocations (along with date of enrollment) from the trials.

Question 15:

Taro believes that there will be no REMS required for this drug due to the fact that desoximetasone is approved for the same route of administration and for the same potency in cream, gel and ointment dosage forms. The labeling of Taro's approved product does not include a medication guide and the product does not present a high risk profile. Taro's desoximetasone products have been in use for over two decades, in multiple formulations and the addition of an additional formulation is not judged as altering the risk. Does the Agency agree with this assessment?

Response:

This is a review issue. However, at this time we are not aware of a safety signal that would necessitate a REMS.

Question 16:

There are no ongoing studies, therefore, the 120-day safety update will focus on providing an update of the published literature and spontaneously reported adverse events for Taro's marketed products. Is this acceptable?

Response:

Your approach appears to be acceptable. However, if the spray formulation is approved in any other jurisdiction, provide a worldwide safety update in addition to the 120 day safety update for the Phase 3 trials.

Chemistry, Manufacturing and Controls (CMC)

Question 4:

Are the completed (and planned) container closure suitability studies and delivery pump functionality studies presented in Section 4.2.2 adequate to support the NDA?

Response:

They are adequate to support the filing of the NDA. Their adequacy to support NDA approval is a review issue.

We noticed that you chose

(b) (4)

(b) (4) Since the proposed formulation contains a significant amount of isopropyl alcohol, we recommend that you include alcohol as a challenge solvent in the extractables studies.

Question 5:

Taro requests confirmation that the tests and specifications proposed in Section 4.2.5 are adequate to support the NDA.

Response:

They are adequate to support the filing of the NDA. Their adequacy to support NDA approval is a review issue. We noticed the omission of (b) (4) (b) (4) from the proposed product specification. You will need to provide adequate justification to support their omissions. We may have other comments regarding drug product specification in the NDA review.

Question 6:

Are the stability data described in Table 4:14 and the stability protocol outlined in Table 4:13 adequate to support the proposed 24-month expiration dating period?

Response:

They are adequate to support the filing of the NDA. Their adequacy to support the proposed expiration dating period is a review issue.

Question 7:

Taro requests confirmation that the CMC data generated to date (or planned) as outlined in Section 3.2 and Section 4 are sufficient to support the NDA and no more information is required.

Response:

They are adequate to support the filing of the NDA, but may not be sufficient for NDA approval. Please see the additional comments given below. We may have other comments during NDA review.

Meeting Discussion:

The sponsor asked for the acceptability of the following proposal:

- 18 months of in-use stability data from one batch at time of NDA submission
- 3 months of in-use stability data from two batches to be manufactured at the time of the 120-day Safety Update

The Agency responded that the sponsor should submit a written proposal to the IND for review.

Additional CMC Comments

1. Provide in-use stability data on the bottles assembled with the to-be-marketed pump head to support the proposed "in-use expiration dating period" for the product. We recommend that you include at least three registration stability batches in the in-use stability studies, and at least one of the registration stability batches should be near the end of the expiration dating period. The pump heads used should be those that went through the same storage condition for the same period as the bottles.

The testing plan of the in-use stability studies should include pump performance, and weight loss in addition to those tests listed in Section 4.2.5. The storage conditions investigated should include both long term and accelerated storage conditions.

2. Pump performance evaluation should include (but not limit to) the following tests: dose volume, total deliverable, actuation pressure, number of prime, etc.
3. Since you propose to [REDACTED] ^{(b) (4)} labeling should require that the assembly of the bottle with the pump be carried out by pharmacists before dispensing to patients.

Pharmacology/Toxicology

Question 8:

Does the Division agree that no additional nonclinical studies, other than those described in Section 5.2.1, are required at the time of the NDA submission?

Response:

You indicated in Section 5.2.1 that you have conducted a 28-day dermal bridging study in minipigs, bacterial reverse mutation test, *in vitro* mammalian chromosome aberration test in CHO cells, and mammalian erythrocyte micronucleus test by gavage in Swiss Albino mice with plasma exposure assessment. We agree that no additional nonclinical studies other than those described in section 5.2.1 are required at the time of the NDA submission. You should provide the time line for conduct of your carcinogenicity study as a post-marketing requirement with the NDA. A photocarcinogenicity study is no longer recommended by the Agency per the revised ICH M3(R2) guidance.

Meeting Discussion:

The sponsor proposed a timeline for conduct of a dermal rat carcinogenicity study as a postmarketing study. The Agency responded that the sponsor could submit the timeline to the IND for review or with the NDA submission. The Agency clarified that the dermal rat carcinogenicity study could be conducted with the solution formulation used for the spray drug product. However, the sponsor should submit a proposal for the dermal rat carcinogenicity study for review.

Question 9:

Is the plan for updating the labeling, including information from the completed battery of genotoxicity studies of desoximetasone and relevant data from literature review, acceptable as described in Section 3.3?

Response:

Your plan for updating the labeling appears acceptable. However, the adequacy of the content and format will be a review issue under the NDA.

Question 10:

In the NDA submission, newly conducted studies will be summarized in detail per eCTD contents and format whereas only an overview of the pharmacology and toxicology studies from the NDAs that Taro now owns will be included. Is this acceptable to the Division?

Response:

In the NDA submission, you should provide full study reports including individual animal data for the newly conducted studies per eCTD content and format.

Clinical Pharmacology/Biopharmaceutics

Question 11:

The five Phase 1 studies sponsored by Taro are described in Section 6.1 and Section 6.2. Does the Division agree that no additional Biopharmaceutics/Clinical Pharmacology studies are required?

Response:

We acknowledge the five Phase 1 studies described in the briefing package as follows:

1. Study 10715005: Vasoconstrictor Study
2. Study DSXS-0904: Phototoxicity Study
3. Study DSXS-0905: Photoallergenicity Study
4. Study DSXS-0804: Irritation and Sensitization Study
5. Study DSXS-0805: HPA Axis Suppression in Adult (n=24, Aged 18-74 years old) patients with moderate to severe plaque psoriasis (10-15% BSA affected (n=12) and > 15% affected (n=12) with determination of plasma concentrations of desoximetasone at baseline and 2 post treatment time points on Day 14 and Day 28

It is not clear whether your HPA axis suppression was conducted under maximal use conditions. For topical corticosteroid drug products we generally recommend that the HPA axis study be

conducted with the to-be-marketed formulation under maximal use conditions. (e.g. highest dose and frequency, upper level of disease severity, and total involved surface area) that is consistent with your clinical trials and your proposed labeling. You need to provide the details of how the design of your HPA Axis suppression study meets maximum use conditions studied in your clinical trials in your NDA.

The adequacy of the systemic exposure data obtained in your HPA axis suppression study will be a review issue.

See response to question #12 for additional information on the requirements for the pediatric population.

Regulatory/Administrative

Question 1:

Does the Division agree with the proposed eCTD organization as outlined in Section 3 and further detailed in Appendix 3.6.1?

Response:

Your proposed organization appears reasonable; however, you should refer to the eCTD guidance and instructions found on our website at the following location:
<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm>

In addition, you are encouraged to submit a test data set to the eSUB group to ensure that all files are accessible. To arrange a test submission, you may refer to the FDA website "Submit a Sample eCTD to the FDA"

<http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm174459.htm> for guidance on sending a test submission. You may request dataset(s) analysis for CDISC specifications compliance as part of a test submission. Please note that the scope of test submissions is limited. The Agency will give priority to testing electronic submissions made in preparation for actual submission for review. If requested, the Agency will provide reports of the dataset(s) CDISC compliance analyses of the eCTD test submission processing to the submitter. You should notify the Agency if you want feedback for SDTM formatted datasets submitted by sending an email to esub@fda.hhs.gov or cder-edata@fda.hhs.gov.

Question 2:

The clinical development program has been performed in adult subjects as the approved labeling for Topicort® products includes standard language pertaining to the use of potent corticosteroids in the pediatric patient population. None of the products, with the exception of the 0.25% ointment has any age limitation and hence a waiver from the need for pediatric studies will be requested. Is the plan to request a waiver from the need for pediatric studies acceptable?

Response:

See the response to Question 12.

Question 3:

Taro plans to request a categorical exclusion from the need for Environmental Assessment in Module 1, citing 21 CFR 25.31(a). The proposed product will not increase the use of desoximetasone. Rather, it will be an alternative to the currently approved Topicort® products. Is this acceptable to the Division?

Response:

You should submit your request for categorical exclusion along with supporting rationale, including any available data.

Administrative Comments

1. Comments shared today are based upon the contents of the briefing document, which is considered to be an informational aid to facilitate today's discussion. Review of information submitted to the IND or NDA might identify additional comments or information requests.
2. For applications submitted after February 2, 1999, the applicant is required either to certify to the absence of certain financial interests of clinical investigators or disclose those financial interests. For additional information, please refer to 21 CFR 54 and 21CFR 314.50(k).
3. Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products. You should refer to the Guidance for Industry: Qualifying for Pediatric Exclusivity for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request". FDA generally does not consider studies submitted to an NDA before issuance of a Written Request as responsive to the Written Request. Applicants should obtain a Written Request before submitting pediatric studies to an NDA.

PRESCRIBING INFORMATION

Proposed prescribing information (PI) submitted with your application must conform to the content and format regulations found at 21 CFR 201.56 and 201.57.

Summary of the Final Rule on the Requirements for Prescribing Information for Drug and Biological Products, labeling guidances, sample tool illustrating Highlights and Table of Contents, an educational module concerning prescription drug labeling, and fictitious prototypes of prescribing information are available at:
<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm>. We encourage you to review the information at this website and use it as you draft prescribing information for your application.

MANUFACTURING FACILITIES

To facilitate our inspectional process, the Division of Manufacturing and Product Quality in CDER's Office of Compliance requests that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility.

Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided in the attachment titled, "Product name, NDA/BLA 012345, Establishment Information for Form 356h."

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
1.				
2.				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
1.				
2.				

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

/s/

STANKA KUKICH
07/21/2011