

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

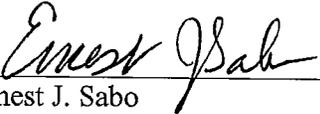
*APPLICATION NUMBER:*  
**201517Orig1s000**

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

Lannett Holdings, Inc.  
Morphine Sulfate Oral Solution, 20 mg/mL  
NDA: 201517  
Module: 1.3.5.2

Patent Certification (§ 21CFR 314.50(i)1(ii))

In the opinion of Lannett Holdings, Inc., and to the best of its knowledge there are no patents that claim the drug or drugs on which investigations that are relied upon in this application were conducted or that claim a use of such drug or drugs. A copy of the page from "The Approved Drug Products with Therapeutic Equivalence Evaluation, Website"(Orange Book, [www.fda.gov/cder/ob/default.htm](http://www.fda.gov/cder/ob/default.htm)) is enclosed demonstrating that no patents are listed for this product.

  
\_\_\_\_\_  
Ernest J. Sabo  
Vice President of Regulatory and Corporate Compliance

4/28/10  
Date

Exclusivity Statement

There is no unexpired exclusivity that claims the drug referred to in this application. A copy of the page from "The Approved Drug Products with Therapeutic Equivalence Evaluation, Website"(Orange Book, [www.fda.gov/cder/ob/default.htm](http://www.fda.gov/cder/ob/default.htm)) is enclosed demonstrating that no unexpired exclusivity is listed for this product.

  
\_\_\_\_\_  
Ernest J. Sabo  
Vice President of Regulatory and Corporate Compliance

4/28/10  
Date

[Quick Links: Skip to main page content](#) [Skip to Search](#) [Skip to Topics Menu](#) [Skip to Section Content Menu](#) [Skip to Common Links](#)

## Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Search results from the "OB\_Rx" table for query on "022195."

---

Active Ingredient: MORPHINE SULFATE  
Dosage Form;Route: SOLUTION; ORAL  
Proprietary Name: MORPHINE SULFATE  
Applicant: ROXANE  
Strength: 10MG/5ML  
Application Number: N022195  
Product Number: 001  
Approval Date: Mar 17, 2008  
Reference Listed Drug: No  
RX/OTC/DISCN: RX  
TE Code:  
Patent and Exclusivity Info for this product: [View](#)

---

Active Ingredient: MORPHINE SULFATE  
Dosage Form;Route: SOLUTION; ORAL  
Proprietary Name: MORPHINE SULFATE  
Applicant: ROXANE  
Strength: 20MG/5ML  
Application Number: N022195  
Product Number: 002  
Approval Date: Mar 17, 2008  
Reference Listed Drug: No  
RX/OTC/DISCN: RX  
TE Code:  
Patent and Exclusivity Info for this product: [View](#)

---

Active Ingredient: MORPHINE SULFATE  
Dosage Form;Route: SOLUTION; ORAL  
Proprietary Name: MORPHINE SULFATE  
Applicant: ROXANE  
Strength: 100MG/5ML  
Application Number: N022195  
Product Number: 003  
Approval Date: Jan 25, 2010  
Reference Listed Drug: Yes  
RX/OTC/DISCN: RX  
TE Code:  
Patent and Exclusivity Info for this product: [View](#)

---

[Return to Electronic Orange Book Home Page](#)

---

FDA/Center for Drug Evaluation and Research

Office of Generic Drugs

Division of Labeling and Program Support

Update Frequency:

Orange Book Data - **Monthly**

Generic Drug Product Information & Patent Information - **Daily**

Orange Book Data Updated Through March, 2010

Patent and Generic Drug Product Data Last Updated: April 28, 2010

[Quick Links: Skip to main page content](#) [Skip to Search](#) [Skip to Topics Menu](#) [Skip to Section Content Menu](#) [Skip to Common Links](#)

## **Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations**

**Patent and Exclusivity Search Results from query on Appl No 022195 Product 001 in the OB\_Rx list.**

---

**There are no unexpired patents for this product in the Orange Book Database.**

**There is no unexpired exclusivity for this product.**

**[View a list of all patent use codes](#)**

**[View a list of all exclusivity codes](#)**

**[Return to Electronic Orange Book Home Page](#)**

---

FDA/Center for Drug Evaluation and Research

Office of Generic Drugs

Division of Labeling and Program Support

Update Frequency:

Orange Book Data - **Monthly**

Generic Drug Product Information & Patent Information - **Daily**

Orange Book Data Updated Through March, 2010

Patent and Generic Drug Product Data Last Updated: April 28, 2010

## EXCLUSIVITY SUMMARY

NDA # 201517

SUPPL #

HFD # 170

Trade Name Morphine Sulfate Oral Solution, 100 mg/5 mL (20 mg/mL)

Generic Name Morphine Sulfate Oral Solution, 100 mg/5 mL (20 mg/mL)

Applicant Name Lannett Holdings, Inc.

Approval Date, If Known June 23, 2011

### 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)(2)

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.

The Sponsor has submitted and defined the study as a comparative bridging bioavailability study. The Sponsor has not made any arguments that the study is not 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?

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# 020616 Kadian  
NDA# 021260 Avinza  
NDA# 022195 Morphine Oral Sol (See Orange Book for additional products)

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:

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"):

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

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

Investigation #1 !  
IND # YES  ! NO   
! Explain:

Investigation #2 !  
IND # YES  ! NO   
! Explain:

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

Investigation #1 !  
YES  ! NO

Explain:

! Explain:

Investigation #2

!

!

YES

! NO

Explain:

! 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: Diana L. Walker, Ph.D.

Title: Regulatory Health Project Manager

Date: June 23, 2011

Name of Office/Division Director signing form: Sharon H. Hertz, M.D.

Title: Deputy Division Director, Division of Anesthesia, Analgesia, and Addiction Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/  
-----

DIANA L WALKER  
06/23/2011

SHARON H HERTZ  
06/23/2011



LANNETT

LANNETT COMPANY INC.

9000 State Road, Philadelphia, PA 19136

Debarment Certification

Lannett Company, Inc. hereby certifies, under section 306 (a) or (b) of the Federal Food, Drug, and Cosmetic Act, that it did not and will not use, in any capacity, the services of a debarred person in connection with this application.

Arthur Bedrosian, J.D.  
President and CEO

Date



LANNETT COMPANY INC.  
9000 State Road, Philadelphia, PA 19136

List of Convictions

In accordance with sections 306 (a) and (b) of the Federal Food, Drug, and Cosmetic Act, Lannett Company, Inc. hereby certifies that it did not use any person that had any convictions described in subsections (a) and (b) within the previous 5 years in connection with this ANDA application.

  
\_\_\_\_\_  
Arthur Bedrosian, J.D.  
President and CEO

  
\_\_\_\_\_  
Date

# CODY LABORATORIES, INC.

## Debarment Statement

Cody Laboratories, Inc., hereby certifies under section 306 (a) or (b) of the Food Drug and Cosmetic Act, that it did not and will not use, in any capacity, the services of a debarred person in connection with this application.



Richard E. Asherman  
President and Chief Executive Officer

01/27/2010  
Date

# CODY LABORATORIES, INC.

## List of Convictions

In accordance with sections 306 (a) and (b) of the Federal Food, Drug and Cosmetic Act, Cody Laboratories, Inc. hereby certifies that it did not use any person that had any convictions described in subsections (a) and (b) within the previous 5 years in connection with this ANDA application.



Richard E. Asherman  
President and Chief Executive Officer

01/28/2010  
Date

# ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION <sup>1</sup>		
NDA # 201517 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Established/Proper Name: Morphine Sulfate Oral Solution Dosage Form: 100 mg per 5 mL (20 mg per mL)		Applicant: Lannett Holdings, Inc. Agent for Applicant (if applicable):
RPM: Diana Walker		Division: Division of Anesthesia, Analgesia and Addiction Products
<p><u>NDA's:</u> NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" 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> Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Morphine Sulfate Oral Solution, 20 mg/5 mL and 20 mg/mL, Roxane Laboratories, Inc., NDA 22195, and NDA 22195 S-002.</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p style="padding-left: 40px;">There is no difference. In explanation, when the Sponsor met with the Agency in July 2009, the filing of this NDA application was considered for a different strength of morphine sulfate solution (20 mg/mL); at that time the Agency agreed with the Sponsor's use of the approved 4 mg/mL (20 mg/ 5 mL) morphine sulfate solution as a reference for a 505(b)(2) application. (NDA 22-195 approved in March 2008). However, between the time of that meeting and the time the sponsor submitted this application (between July 2009 and March 2010); the Agency approved a 20 mg/mL morphine sulfate solution (supplement to NDA 22-195 approved in January 2010).</p> <p>If no listed drug, explain.</p> <p><input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> Other (explain)</p> <p><b><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></b></p> <p><b>Cleared June 7, 2011</b></p> <p><u>On the day of approval</u>, check the Orange Book again for any new patents or pediatric exclusivity.</p> <p><input checked="" type="checkbox"/> No changes    <input type="checkbox"/> Updated    Date of check: June 23, 2011</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		

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



❖ Exclusivity	
<ul style="list-style-type: none"> <li>Is approval of this application blocked by any type of exclusivity?</li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> <li>NDA and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <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></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <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></li> </ul>	<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"> <li>Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.</li> </ul>	<input type="checkbox"/> Verified <input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> <li>Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.</li> </ul>	21 CFR 314.50(i)(1)(i)(A) <input checked="" type="checkbox"/> Verified  21 CFR 314.50(i)(1) <input checked="" type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> <li>[505(b)(2) applications] If the application includes a <b>paragraph III</b> certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).</li> </ul>	<input checked="" type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> <li>[505(b)(2) applications] For <b>each paragraph IV</b> 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></li> </ul>	<input checked="" 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>	<p><input type="checkbox"/> Yes    <input type="checkbox"/> No</p>
---	--

**CONTENTS OF ACTION PACKAGE**

❖ Copy of this Action Package Checklist <sup>3</sup>	Included: June 29, 2011
<b>Officer/Employee List</b>	
❖ 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
<b>Action Letters</b>	
❖ Copies of all action letters ( <i>including approval letter with final labeling</i> )	Action(s) and date(s) Approval, June 23, 2011 CR, December 10, 2010
<b>Labeling</b>	
❖ Package Insert ( <i>write submission/communication date at upper right of first page of PI</i> )	
<ul style="list-style-type: none"> <li>• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	June 23, 2011
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	March 1, 2010
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	

<sup>3</sup> Fill in blanks with dates of reviews, letters, etc.  
Version: 8/25/10

<ul style="list-style-type: none"> <li>❖ 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>)</li> </ul>	<input checked="" type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	June 23, 2011
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	March 1, 2010
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	
<ul style="list-style-type: none"> <li>❖ Labels (<b>full color</b> carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)</li> </ul>	
<ul style="list-style-type: none"> <li>• Most-recent draft labeling</li> </ul>	Final: June 23, 2011 Original: March 1, 2010
<ul style="list-style-type: none"> <li>❖ Proprietary Name             <ul style="list-style-type: none"> <li>• Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)</li> <li>• Review(s) (<i>indicate date(s)</i>)</li> </ul> </li> </ul>	Applicant does not plan to submit a proprietary name
<ul style="list-style-type: none"> <li>❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)</li> </ul>	<input type="checkbox"/> RPM <input checked="" type="checkbox"/> DMEPA April 2, 2011 and October 21, 2010 <input checked="" type="checkbox"/> DRISK April 29, 2011 and see review, Risk Management section, November 1, 2010 <input checked="" type="checkbox"/> DDMAC October 27, 2010 and October 29, 2010 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
<b>Administrative / Regulatory Documents</b>	
<ul style="list-style-type: none"> <li>❖ Administrative Reviews (<i>e.g., RPM Filing Review<sup>4</sup>/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)</li> <li>❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte</li> <li>❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>)</li> </ul>	RPM Filing Review: April 22, 2010 <input type="checkbox"/> Not a (b)(2) AP – June 23, 2011 (Cleared by 505(b)(2) committee June 7, 2011) CR - November 24, 2010 <input type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> <li>❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)</li> </ul>	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> <li>❖ Application Integrity Policy (AIP) Status and Related Documents <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a></li> </ul>	
<ul style="list-style-type: none"> <li>• Applicant is on the AIP</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>• This application is on the AIP             <ul style="list-style-type: none"> <li>○ If yes, Center Director’s Exception for Review memo (<i>indicate date</i>)</li> <li>○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No  <input type="checkbox"/> Not an AP action

<sup>4</sup> Filing reviews for scientific disciplines should be filed behind the respective discipline tab.  
Version: 8/25/10

❖ Pediatrics ( <i>approvals only</i> ) <ul style="list-style-type: none"> <li>• Date reviewed by PeRC _____ If PeRC review not necessary, explain: <u>Does not fall under PREA</u></li> <li>• Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>)</li> </ul>	<input type="checkbox"/> Included
❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent ( <i>include certification</i> )	<input checked="" type="checkbox"/> Verified, statement is acceptable
❖ Outgoing communications ( <i>letters (except action letters), emails, faxes, telecons</i> )	included
❖ 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 type="checkbox"/> No mtg    Combination Pre-IND/Pre-NDA, July 27, 2009
• 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)	
• 48-hour alert or minutes, if available ( <i>do not include transcript</i> )	
<b>Decisional and Summary Memos</b>	
❖ Office Director Decisional Memo ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
Division Deputy Director Summary Review ( <i>indicate date for each review</i> )	<input type="checkbox"/> None June 23, 2011 December 10, 2010
Cross-Discipline Team Leader Review ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
PMR/PMC Development Templates ( <i>indicate total number</i> )	<input checked="" type="checkbox"/> None
<b>Clinical Information<sup>5</sup></b>	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) ( <i>indicate date for each review</i> )	N/A
• Clinical review(s) ( <i>indicate date for each review</i> )	N/A
• 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> )	Addressed in Summary Review
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers ( <i>indicate date of each review</i> )	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation ( <i>indicate date of each review</i> )	<input type="checkbox"/> Not applicable November 10, 2010

<sup>5</sup> Filing reviews should be filed with the discipline reviews.  
Version: 8/25/10

<ul style="list-style-type: none"> <li>❖ Risk Management           <ul style="list-style-type: none"> <li>• REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>)</li> <li>• REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)</li> <li>• 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>)</li> </ul> </li> </ul>	<p>REMS submissions: March 1, 2010, March 26, 2010, and November 17, 2010</p> <p>REMS Elimination Memo- June 23, 2011</p> <p>REMS Memo –December 10, 2010</p> <p><input type="checkbox"/> None</p> <p>REMS review: November 1, 2010</p>
<ul style="list-style-type: none"> <li>❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)</li> </ul>	<input checked="" type="checkbox"/> None requested
<b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None	
<ul style="list-style-type: none"> <li>❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Clinical Microbiology Review(s) (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<b>Biostatistics</b> <input checked="" type="checkbox"/> None	
<ul style="list-style-type: none"> <li>❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Statistical Team Leader Review(s) (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Statistical Review(s) (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<b>Clinical Pharmacology</b> <input type="checkbox"/> None	
<ul style="list-style-type: none"> <li>❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Clinical Pharmacology review(s) (<i>indicate date for each review</i>)</li> </ul>	<input type="checkbox"/> None Final and Filing review: October 25, 2010
<ul style="list-style-type: none"> <li>❖ DSI Clinical Pharmacology Inspection Review Summary (<i>include copies of DSI letters</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<b>Nonclinical</b> <input type="checkbox"/> None	
<ul style="list-style-type: none"> <li>❖ Pharmacology/Toxicology Discipline Reviews</li> </ul>	
<ul style="list-style-type: none"> <li>• ADP/T Review(s) (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Supervisory Review(s) (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)</li> </ul>	<input type="checkbox"/> None Final: November 4, 2010 Filing: April 26, 2010
<ul style="list-style-type: none"> <li>❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> No carc
<ul style="list-style-type: none"> <li>❖ ECAC/CAC report/memo of meeting</li> </ul>	<input checked="" type="checkbox"/> None Included in P/T review, page
<ul style="list-style-type: none"> <li>❖ DSI Nonclinical Inspection Review Summary (<i>include copies of DSI letters</i>)</li> </ul>	<input checked="" type="checkbox"/> None requested

<b>Product Quality</b> <input type="checkbox"/> None	
<b>❖ Product Quality Discipline Reviews</b>	
• 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 type="checkbox"/> None CMC #5: June 14, 2011 CMC #4: May 20, 2011 CMC #3: December 7, 2010 CMC #2: September 20, 2010 CMC #1: September 14, 2010 Filing: April 26, 2010
<b>❖ Microbiology Reviews</b> <input checked="" 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 (DMPQ/MAPCB/BMT) <i>(indicate date of each review)</i>	<input type="checkbox"/> Not needed May 10, 2011 September 1, 2010  N/A
<b>❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer</b> <i>(indicate date of each review)</i>	<input type="checkbox"/> None ONDQA-Statistics Review: May 13, 2011
<b>❖ Environmental Assessment (check one) (original and supplemental applications)</b>	
<input checked="" type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>	In CMC reviews
<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>	
<b>❖ Facilities Review/Inspection</b>	
<input checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) <i>(date completed must be within 2 years of action date) (only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites<sup>6</sup>)</i>	Date completed: November 10, 2010 (1 <sup>st</sup> cycle- Withhold) June 8, 2011 (2 <sup>nd</sup> cycle- Acceptable) <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) (original and supplemental BLAs)</i>	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
<b>❖ NDAs: Methods Validation</b> <i>(check box only, do not include documents)</i>	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input checked="" type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

<sup>6</sup> 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.

## Appendix to Action Package Checklist

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

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

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

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

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

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

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

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

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

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

/s/  
-----

DIANA L WALKER  
06/29/2011

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Wednesday, June 15, 2011 9:42 AM  
**To:** Walker, Diana; 'Denise Fairman'  
**Subject:** RE: NDA 201517 Labeling Revisions 15jun11  
**Attachments:** Morphine Sulfate-package-insert 15jun11-track changes.pdf; Morphine Sulfate-package-insert 15jun11-track changes.doc

Dear Denise,

I apologize that I did not change the date on the files I sent to today's date. Please use these files.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

---

**From:** Walker, Diana  
**Sent:** Wednesday, June 15, 2011 9:37 AM  
**To:** 'Denise Fairman'  
**Subject:** NDA 201517 Labeling Revisions 15jun11

Dear Denise,

Please find attached both a track-changes Word version and a PDF version of the Package Insert revisions requested by the Division. If you have questions or would like to discuss any particular revision, please contact me and I will set up a teleconference with the reviewers. If you concur with all of the revisions, please reply to this email stating your concurrence. If you concur, there is no need to submit a revised label at this time, as the label attached to any action letter that is issued will reflect the agreed upon changes.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

19 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS)  
immediately following this page.

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

/s/  
-----

DIANA L WALKER  
06/15/2011

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Wednesday, June 08, 2011 3:55 PM  
**To:** 'Denise Fairman'  
**Subject:** NDA 201517 Morphine Sulfate Package Insert - Revisions 08jun11  
**Attachments:** Morphine Sulfate-package-insert 08jun11-track changes.doc; Morphine Sulfate-package-insert 08jun11-track changes.pdf

Dear Denise,

After review of your submission May 24, 2011, we have several revisions to the package insert (please see pages 1, 2, 5, 12 and 17). I am attaching the Word version and PDF version in track changes.

If you concur with the changes, you don't need to resubmit the Package Insert to your NDA, as we would attach any final, agreed upon version of the labeling to any action letter that is issued.

At this point, I have not received any further revisions for the Medication Guide or Carton and Container labels. I believe that the reviewers have found them acceptable, but I caution you not to have anything printed or finalized until you receive a final action letter.

Please send me your concurrence or your changes to these revisions to the Package Insert via email this week or early next week if possible.

Please feel free to contact me if you have questions.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

---

**From:** Denise Fairman [mailto:dfairman@lannett.com]  
**Sent:** Tuesday, May 24, 2011 4:45 PM  
**To:** Walker, Diana  
**Cc:** Kristie Stephens; Ernest Sabo  
**Subject:** NDA 201517 Morphine Sulfate Labeling response

Hello Diana,

Attached please find one package insert with track changes and one accepting track changes,

one Medication Guide with track changes and one accepting track changes, three container labels (one 30 mL, one 120 mL and one 240 mL) and three carton labels (one 30 mL, one 120 mL and one 240 mL).

In the email Lannett received on April 8, 2011, the DMEPA reviewer requested Lannett to “include a statement on the oral syringe, “For Oral Use Only” which communicates the route of administration”. Lannett commits to have the statement “For Oral Use Only” on the oral syringe.

Should Lannett submit this labeling through ESG? Please confirm receipt. Thank you very much.

Regards,  
Denise

Denise K. Fairman, MS, RAC  
Senior Regulatory Affairs Associate  
Lannett Company, Inc.  
13200 Townsend Road  
Philadelphia, PA 19154-1014  
Phone: 215-333-9000, ext 2101  
Fax: 215-624-2126  
Email: [dfairman@lannett.com](mailto:dfairman@lannett.com)

19 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS)  
immediately following this page.

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

/s/  
-----

DIANA L WALKER  
06/09/2011

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Friday, May 20, 2011 11:56 AM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** RE: NDA 201517 Labeling Comments Morphine Sulfate  
**Attachments:** Working draft Morphine Sulfate-package-insert 20may11.doc; Working draft Morphine Sulfate-package-insert 20may11.pdf

Dear Denise,

Thank you for pointing out the inconsistencies that you found in the package insert. We have reviewed the package insert, and hopefully corrected these inconsistencies. Please review the attached package insert in Word and PDF. If you concur with the changes, you can accept all changes and email the document back to me. If you do not concur or have questions, please accept all changes except those with which you do not concur, and send back your revisions in track changes in a Word document, and we will review your comments.

Regards,

Diana

---

**From:** Denise Fairman [mailto:dfairman@lannett.com]  
**Sent:** Friday, May 13, 2011 2:46 PM  
**To:** Jani, Parinda; Walker, Diana  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** NDA 201517 Labeling Comments Morphine Sulfate

Reviewing the package insert received from FDA on 22Nov10, we are finding inconsistencies in the way the dosage strength is presented. Throughout the insert, the strength is listed as either 20 mg per mL or 20 mg/mL. In section 17, Patient Counseling Information, bullet statement two and four were changed by FDA to 100 mg/5mL and 100 mg per 5 mL. Lannett thinks this may be confusing to the patient switching to 100 mg/5mL with no mention of the 20 mg/mL. Please advise how the FDA would like the dosage strength presented in the PI. Thank you.

Regards,  
Denise

Denise K. Fairman, MS, RAC  
Senior Regulatory Affairs Associate  
Lannett Company, Inc.  
13200 Townsend Road  
Philadelphia, PA 19154-1014  
Phone: 215-333-9000, ext 2101  
Fax: 215-624-2126  
Email: [dfairman@lannett.com](mailto:dfairman@lannett.com)

19 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS)  
immediately following this page.

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

/s/  
-----

DIANA L WALKER  
06/09/2011

## Walker, Diana

---

**From:** Walker, Diana  
**Sent:** Friday, April 29, 2011 1:13 PM  
**To:** 'Denise Fairman'  
**Cc:** Kristie Stephens  
**Subject:** NDA 201517 Labeling Comments 29apr11

**Attachments:** NDA 201517 Morphine Sulfate Oral Solution MG Comments.doc



NDA 201517  
Morphine Sulfate O

Dear Denise,

I am sending you comments concerning the **Carton and Container** labeling and the **Medication Guide/Patient Instructions for Use** in two formats.

A. Two comments for the Medication Guide are in the attached track-changes document, with one deletion on page 3, and one change on page 4 (the change on page 4 is accompanied by a comment from the review team for your information).

B. I am also sending some comments in the body of this email (see immediately below) that apply to either or both the Carton/Container labels and the Patient Instructions for Use. Comment #1 is a general comment and sent just to ensure that this has been corrected in all locations.

1. Confirm that (b) (4) has been changed to “**Morphine Sulfate Oral Solution**” wherever it appears in the Package Insert and Medication Guide.
  
2. The diagram of the syringe in the Medication Guide/Patient Instructions for Use should match the diagram of the syringe on the Carton/Container labels.
  
3. Some of the sentences below are already on your labels, and some should be added as requested below.
  - 1) **ADD** the two sentences (**a and d**) and **ADD "the inside of"** for sentence **c** to the Carton and Container Labels.
  - 2) **ADD all of the sentences (a through f)** to the Medication Guide/Patient Instructions for Use. Incorporate appropriately with the existing instructions.
    - a. After filling syringe, remove excess liquid from the outside of the syringe by touching it to the inside rim of the bottle.
    - b. Do not place oral syringe directly into mouth.
    - c. Do not rinse the inside of the oral syringe with water.
    - d. Rinse the outside of the oral syringe with water or wipe with a damp cloth or tissue after use.

- e. Do not rinse the inside of the oral syringe with water.
- f. Close the bottle after each use.

If you have any questions, please feel free to contact me.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: [Diana.Walker@fda.hhs.gov](mailto:Diana.Walker@fda.hhs.gov)

11 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS)  
immediately following this page.

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

/s/  
-----

DIANA L WALKER  
05/24/2011

## MEMORANDUM OF TELECON

DATE: May 12, 2011

APPLICATION NUMBER: NDA 201517

BETWEEN:

Name: **Lannett Company, Inc:**

Denise Fairman, Sr. Reg. Affairs Associate  
Kristie Stephens, Manager

AND

Name: **FDA**

Swati Patwardhan, Regulatory Project Manager, ONDQA

SUBJECT: Testing site related to stability and release of the drug product

This is a memo to file regarding telephone conversation on May 12, 2011, with Lannett Company Inc. to clarify the testing responsibilities of the Cody laboratories for the release and stability testing of the drug product. In the original and subsequent amendments, the specification sheet for preservative had discrepancy in the footnote for the acceptance criteria.

During the teleconference, Lanett was informed that the footnote in the specification sheet submitted in the latest amendment, dated April 29, 2011, infers that Cody Labs is not responsible for drug product stability testing, which is contradictory to the original submission. The applicant agreed to submit an amendment to clarify this discrepancy by removing Cody Labs as drug product stability testing site.

---

Swati Patwardhan  
Regulatory Project Manager

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

/s/  
-----

SWATI A PATWARDHAN  
05/19/2011

## REQUEST FOR CONSULTATION

TO (Office/Division): Yi Tsong-301-796-1013

FROM (Name, Office/Division, and Phone Number of Requestor): Swati Patwardhan, ONDQA, Division of Post-Marketing Assessment, 301-796-4085

DATE  
5/5/2011

IND NO.

NDA NO.  
201-517

TYPE OF DOCUMENT  
N-000

DATE OF DOCUMENT

NAME OF DRUG  
morphine sulfate oral  
solution 20 mg/mL

PRIORITY CONSIDERATION  
Standard

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE  
5/16/2011

NAME OF FIRM: Lanett Holdings

### 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: Please provide statistical evaluation by using an appropriate SAS program to determine the expiration date. The acceptance criterion is (b) (4)

At the time this was not the parameter that was determining the expiration date. Another parameter gave a shorter expiration date but the applicant changed the acceptance criteria (appropriately) so that it then passed with an expiration date of 18 months.

The attached data are for an unknown impurity. If it goes above (b) (4) then it has to be qualified. Note that the data are reported to 2 decimal places. This permits more accurate calculation of the trending. However the acceptance criterion is (b) (4), not (b) (4). This might make a difference. Note that if you calculate the linear regression using the rounded values, the curve is not linear.

The PDFUA goal date is : 6/23/2011

SIGNATURE OF REQUESTOR <b>Swati Patwardhan</b>		METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <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/  
-----

SWATI A PATWARDHAN  
05/05/2011

## Walker, Diana

---

**From:** Walker, Diana  
**Sent:** Monday, April 18, 2011 3:43 PM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** NDA 201517 Response to question about labeling 18apr11

Dear Denise,

You called to ask a question about the Medication Guide, and whether it needs to be printed immediately following the last section of the labeling, or as a separate document/page. According to this guidance (see page 15), it appears you have either option, but please read this section in detail to make sure I am answering the specific question you had.

<<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075082.pdf>>

You should also read the regulations in 21 CFR 208.24, which goes into detail about distributing and dispensing Medication Guides.

<<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcr/CFRSearch.cfm?fr=208.24>>

Please let me know if the response above answers your question, or if I should look into this further.

During our conversation, you mentioned that the reason for your questions was that your firm wanted to work with your contractors on Carton and Container label printing. I want to reiterate that we advise against printing Carton and Container labeling and other labeling until an application is actually approved. As I mentioned in our telephone conversation, there is always the possibility that labeling changes can be negotiated at any time throughout the review cycle, up until the application is approved; therefore, it would be a risk to finalize any label printing until that time.

Feel free to contact me with any other questions.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: [Diana.Walker@fda.hhs.gov](mailto:Diana.Walker@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/

-----  
DIANA L WALKER  
04/19/2011

## Walker, Diana

---

**From:** Walker, Diana  
**Sent:** Friday, April 08, 2011 9:49 AM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo  
**Subject:** NDA 201517 Morphine Sulfate CMC information request 08apr11

Dear Denise,

I received your response to our previous CMC information request and have forwarded that on to the review team. Today I received a new request from the CMC reviewer. This request is to assist in evaluating any other labeling instructions that might be necessary concerning the viscosity of the solution and the syringe.

**Please provide several bottle of placebo solution with the syringes.**

Please send these samples to me at the following address:

Diana L. Walker  
Regulatory Health Project Manager  
Food and Drug Administration  
10903 New Hampshire Ave.  
Bldg. 22, Room 3209  
Silver Spring, MD 20993

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@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/  
-----

DIANA L WALKER  
04/19/2011

## Walker, Diana

---

**From:** Walker, Diana  
**Sent:** Friday, April 08, 2011 10:42 AM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo  
**Subject:** NDA (b) (4) Carton and Container Labeling Comments 08apr11

Dear Denise,

I have received the following comments on the Carton and Container labeling for NDA 201517, morphine sulfate. Please submit your responses to comments/requests #2 and # 3 below to your NDA.

- 1. The Agency acknowledges and has reviewed your comments concerning the presentation of the dosage strength and your request for a (b) (4) presentation; however, based on current information, the dosage strength labeling will retain the 100 mg/5 mL presentation.**
- 2. Include a statement on the oral syringe, "For Oral Use Only" which communicates the route of administration.**
- 3. Revise the calibrated syringe statement that is presented in conjunction with storage recommendation (b) (4) to read, "Dispense only with the enclosed, calibrated syringe."**

I do want to remind you that, as the NDA review is still in progress, that there could potentially be further labeling comments forthcoming; however, I did want to get the current comments out to you as soon as possible.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@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/  
-----

DIANA L WALKER  
04/19/2011

## Walker, Diana

---

**From:** Walker, Diana  
**Sent:** Friday, April 08, 2011 10:23 AM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo  
**Subject:** NDA 201517 Package Insert draft comments 08apr11

**Attachments:** Working draft Morphine Sulfate-package-insert April 8 2011.pdf; Working draft Morphine Sulfate-package-insert April 8 2011.doc



Working draft  
Morphine Sulfate...



Working draft  
Morphine Sulfate...

Dear Denise,

I am attaching a track changes and pdf version of the most recent revisions to the morphine sulfate label. The changes are in Highlights, and sections 9 and 10. Please review these changes, and then email me either your concurrence, or email me the label with your revisions/comments in track changes. At this point, it is not necessary to submit a new version of the label to your NDA.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

19 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS)  
immediately following this page.

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

/s/  
-----

DIANA L WALKER  
04/19/2011

## Walker, Diana

---

**From:** Walker, Diana  
**Sent:** Wednesday, March 30, 2011 3:02 PM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo  
**Subject:** NDA 201517 Request for CMC Information 30mar11

**Importance:** High

Dear Denise,

In reviewing your responses in your December 21, 2010, submission to our Advice/Information Request letter dated December 10, 2010, our chemist noted revisions that were not made as well as new information that is necessary. Please respond to the following information request by submitting your responses to your NDA as soon as possible.

- 1. Revise 3.2.P.7 to reflect the changes in the table describing the Oral Doser that were included in the cover letter to the December 21, 2010 submission.**
- 2. Revise Sections 3.2.P.5.1 and 3.2.P.8.1 to include the revised acceptance criteria for the preservative limits.**
- 3. Explain how the [REDACTED] <sup>(b) (4)</sup> is used and whether this material is new or has been used throughout development.**

If you have any questions regarding this request, please feel free to contact me.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@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/

-----  
DIANA L WALKER  
04/05/2011

## REQUEST FOR CONSULTATION

TO (Office/Division):

**Controlled Substances Staff (CSS)**  
Attention: Corrine Moody  
HFD-009

FROM (Name, Office/Division, and Phone Number of Requestor):

**Bob Rappaport, M.D.**  
Director, Division of Anesthesia and Analgesia Products  
(DAAP), HFD-170

DATE  
February 8, 2011

IND NO.  
N/A

NDA NO.  
201517

TYPE OF DOCUMENT  
NDA - Complete  
Response submission

DATE OF DOCUMENT  
December 23, 2010

NAME OF DRUG  
**Morphine Sulfate Oral  
Solution, 20 mg/mL**

PRIORITY CONSIDERATION  
**Priority**

CLASSIFICATION OF DRUG  
**opioid**

DESIRED COMPLETION DATE  
**May 23, 2011**  
Date Primary reviews due

NAME OF FIRM: **Lannett**

### 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:**

**Application:**

This is a resubmission of a CR (CR action was December 10, 21010). This is a 505(b)(2) application, an opioid analgesic for the relief of moderate to severe acute and chronic pain.

EDR Location: \\CDSESUB1\EVSPROD\NDA201517\201517.enx

**Request:**

Please review and provide your assessment of the abuse potential or other potential CS issues for Morphine Sulphate.

Also, please comment on the labeling if necessary. Previous review team: Alicja Lerner and Lori Love.

February 23, 2011 (labeling meeting)

Reference ID: A292408  
Application ID: 292408

For questions, please contact Diana Walker, DAARP Project Manager, at 301-796-4029.

SIGNATURE OF REQUESTOR  
Diana L. Walker, PhD  
Regulatory Project Manager  
FDA/CDER/ODE II/DAARP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

METHOD OF DELIVERY (Check one)  
 DFS       EMAIL       MAIL       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/  
-----

DIANA L WALKER  
02/08/2011



NDA 201517

**ACKNOWLEDGE –  
CLASS 2 RESPONSE**

Lannett Holdings, Inc.  
13200 Townsend Road  
Philadelphia, PA 19154-1014

Attention: Ernest Sabo  
Vice President, Regulatory and Corporate Compliance

Dear Mr. Sabo:

We acknowledge receipt on December 23, 2010, of your December 22, 2010, submission to your new drug application (NDA) for Morphine Sulfate Oral Solution, 20 mg/mL.

We consider this a complete, class 2 response to our December 10, 2010, action letter. Therefore, the user fee goal date is June 23, 2011.

If you have any questions, call Diana L. Walker, Ph.D., Regulatory Health Project Manager, at (301) 796-4029.

Sincerely,

*{See appended electronic signature page}*

Parinda Jani  
Chief, Project Management Staff  
Division of Anesthesia and Analgesia Products  
Office of Drug Evaluation II  
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/  
-----

PARINDA JANI  
01/06/2011

# ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION <sup>1</sup>		
NDA # 201517 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Established/Proper Name: Morphine Sulfate Oral Solution Dosage Form: 20 mg per mL		Applicant: Lannett Holdings, Inc. Agent for Applicant (if applicable):
RPM: Diana Walker		Division: Division of Anesthesia and Analgesia Products
<p><b><u>NDAs:</u></b>                      NDA Application Type: <input type="checkbox"/> 505(b)(1) <input checked="" 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><b><u>505(b)(2) Original NDAs and 505(b)(2) NDA supplements:</u></b>                      Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s)):</p> <p>Morphine Sulfate Oral Solution, 20 mg/mL, Roxane Laboratories, Inc., NDA 22195, and NDA 22195 S-002.</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p style="padding-left: 40px;">There is no difference. In explanation, when the Sponsor met with the Agency in July 2009, the filing of this NDA application was considered for a different strength of morphine sulfate solution (20 mg/mL); at that time the Agency agreed with the Sponsor's use of the approved 5 mg/mL (20 mg/ 5 mL) morphine sulfate solution as a reference for a 505(b)(2) application. (NDA 22-195 approved in March 2008). However, between the time of that meeting and the time the sponsor submitted this application (between July 2009 and April 2010); the Agency approved a 20 mg/mL morphine sulfate solution (supplement to NDA 22-195 approved in January 2010) and this product was used as a component in the bridging BA study.</p> <p>If no listed drug, explain.</p> <p><input type="checkbox"/> This application relies on literature.  <input type="checkbox"/> This application relies on a final OTC monograph.  <input type="checkbox"/> Other (explain)</p> <p><b><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></b></p> <p><b><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></b></p> <p><input type="checkbox"/> No changes    <input type="checkbox"/> Updated    Date of check:</p> <p><b>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.</b></p>
❖ Actions		

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



❖ Exclusivity	
<ul style="list-style-type: none"> <li>Is approval of this application blocked by any type of exclusivity?</li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> <li>NDA and BLAs: Is there existing orphan drug exclusivity for the “same” drug or biologic for the proposed indication(s)? <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></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>(b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? <i>(Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.)</i></li> </ul>	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> <li>NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? <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></li> </ul>	<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"> <li>Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions.</li> </ul>	<input type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> <li>Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent.</li> </ul>	21 CFR 314.50(i)(1)(i)(A) <input checked="" type="checkbox"/> Verified  21 CFR 314.50(i)(1) <input checked="" type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> <li>[505(b)(2) applications] If the application includes a <b>paragraph III</b> certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval).</li> </ul>	<input checked="" type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> <li>[505(b)(2) applications] For <b>each paragraph IV</b> 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></li> </ul>	<input checked="" 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 <sup>3</sup>	Included – December 15, 2010
<b>Officer/Employee List</b>	
❖ 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 type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input type="checkbox"/> Included
<b>Action Letters</b>	
❖ Copies of all action letters ( <i>including approval letter with final labeling</i> )	Action(s) and date(s) CR, December 10, 2010
<b>Labeling</b>	
❖ Package Insert ( <i>write submission/communication date at upper right of first page of PI</i> )	
<ul style="list-style-type: none"> <li>• Most recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	Sent to Sponsor November 23, 2010
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	March 1, 2010
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	

<sup>3</sup> Fill in blanks with dates of reviews, letters, etc.  
Version: 8/25/10

<ul style="list-style-type: none"> <li>❖ 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>)</li> </ul>	<input checked="" type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> <li>• Most-recent draft labeling. If it is division-proposed labeling, it should be in track-changes format.</li> </ul>	Sent to Sponsor November 23, 2 010
<ul style="list-style-type: none"> <li>• Original applicant-proposed labeling</li> </ul>	March 1, 2010
<ul style="list-style-type: none"> <li>• Example of class labeling, if applicable</li> </ul>	
<ul style="list-style-type: none"> <li>❖ Labels (<b>full color</b> carton and immediate-container labels) (<i>write submission/communication date on upper right of first page of each submission</i>)</li> </ul>	
<ul style="list-style-type: none"> <li>• Most-recent draft labeling</li> </ul>	original: March 1, 2010
<ul style="list-style-type: none"> <li>❖ Proprietary Name             <ul style="list-style-type: none"> <li>• Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)</li> <li>• Review(s) (<i>indicate date(s)</i>)</li> </ul> </li> </ul>	Applicant does not plan to submit a proprietary name
<ul style="list-style-type: none"> <li>❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>)</li> </ul>	<input type="checkbox"/> RPM <input checked="" type="checkbox"/> DMEPA 10/21/2010 <input checked="" type="checkbox"/> DRISK see review, Risk Management section, 11/1/2010 <input checked="" type="checkbox"/> DDMAC 10/27/2010 and 10/29/2010 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
<b>Administrative / Regulatory Documents</b>	
<ul style="list-style-type: none"> <li>❖ Administrative Reviews (<i>e.g., RPM Filing Review<sup>4</sup>/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>)</li> <li>❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte</li> <li>❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>)</li> </ul>	RPM Filing Review: April 22, 2010 <input type="checkbox"/> Not a (b)(2) CR - November 24, 2010 <input type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> <li>❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>)</li> </ul>	<input type="checkbox"/> Included
<ul style="list-style-type: none"> <li>❖ Application Integrity Policy (AIP) Status and Related Documents <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a></li> </ul>	
<ul style="list-style-type: none"> <li>• Applicant is on the AIP</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<ul style="list-style-type: none"> <li>• This application is on the AIP             <ul style="list-style-type: none"> <li>○ If yes, Center Director's Exception for Review memo (<i>indicate date</i>)</li> <li>○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No  <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> <li>❖ Pediatrics (<i>approvals only</i>)             <ul style="list-style-type: none"> <li>• Date reviewed by PeRC _____ If PeRC review not necessary, explain: <u>Does not fall under PREA</u></li> <li>• Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Included
<ul style="list-style-type: none"> <li>❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>)</li> </ul>	<input checked="" type="checkbox"/> Verified, statement is acceptable

<sup>4</sup> Filing reviews for scientific disciplines should be filed behind the respective discipline tab.  
Version: 8/25/10

❖ Outgoing communications ( <i>letters (except action letters), emails, faxes, telecons</i> )	included
❖ 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 type="checkbox"/> No mtg   Combination Pre-IND/Pre-NDA, July 27, 2009
• 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)	
• 48-hour alert or minutes, if available ( <i>do not include transcript</i> )	
<b>Decisional and Summary Memos</b>	
❖ Office Director Decisional Memo ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
Division Deputy Director Summary Review ( <i>indicate date for each review</i> )	<input type="checkbox"/> None   December 10, 2010
Cross-Discipline Team Leader Review ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
PMR/PMC Development Templates ( <i>indicate total number</i> )	<input checked="" type="checkbox"/> None
<b>Clinical Information<sup>5</sup></b>	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) ( <i>indicate date for each review</i> )	N/A
• Clinical review(s) ( <i>indicate date for each review</i> )	N/A
• 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> )	Addressed in Summary Review
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers ( <i>indicate date of each review</i> )	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation ( <i>indicate date of each review</i> )	<input type="checkbox"/> Not applicable November 10, 2010
❖ Risk Management <ul style="list-style-type: none"> <li>• REMS Documents and Supporting Statement (<i>indicate date(s) of submission(s)</i>)</li> <li>• REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)</li> <li>• 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>)</li> </ul>	March 1, 2010, March 26, 2010, and November 17, 2010 REMS Memo –December 10, 2010 <input type="checkbox"/> None November 1, 2010
❖ DSI Clinical Inspection Review Summary(ies) ( <i>include copies of DSI letters to investigators</i> )	<input checked="" type="checkbox"/> None requested

<sup>5</sup> Filing reviews should be filed with the discipline reviews.  
Version: 8/25/10

<b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
<b>Biostatistics</b> <input checked="" type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
<b>Clinical Pharmacology</b> <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None October 25, 2010
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)	<input checked="" type="checkbox"/> None
<b>Nonclinical</b> <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Supervisory Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None Final: November 4, 2010 Filing: April 26, 2010
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (include copies of DSI letters)	<input checked="" type="checkbox"/> None requested
<b>Product Quality</b> <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Product quality review(s) including ONDQA biopharmaceutics reviews (indicate date for each review)	<input type="checkbox"/> None CMC #3: December 7, 2010 CMC #2: September 20, 2010 CMC #1: September 14, 2010 Filing: April 26, 2010
❖ Microbiology Reviews	<input type="checkbox"/> Not needed September 1, 2010
<input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (indicate date of each review)	
<input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) (indicate date of each review)	N/A
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)	<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> )	In CMC reviews
<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 sites<sup>6</sup></i> )	Date completed: November 10, 2010 <input type="checkbox"/> Acceptable <input checked="" 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 checked="" type="checkbox"/> Not yet requested <input type="checkbox"/> Not needed (per review)

<sup>6</sup> 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.

## Appendix to Action Package Checklist

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

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

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

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

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

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

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

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

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

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

/s/  
-----

DIANA L WALKER  
12/15/2010

## Walker, Diana

---

**From:** Walker, Diana  
**Sent:** Tuesday, December 14, 2010 9:48 AM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** NDA 201517 Morphine Sulfate CMC Clarification of Stability Calculation 14Dec10

Dear Denise,

I have received a response from our CMC review team as follows:

**The method used was linear regression analysis and calculated "...the earliest time at which the 95 percent confidence limit for the mean intersects the proposed acceptance criterion."**

**See Guidance for Industry: Q1E Evaluation of Stability Data**

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073380.pdf>

Regards,

Diana

---

From: Denise Fairman [<mailto:dfairman@lannett.com>]  
Sent: Monday, December 13, 2010 4:53 PM  
To: Walker, Diana  
Cc: Ernest Sabo; Kristie Stephens  
Subject: NDA 201517 Morphine Sulfate Action Letter 10Dec10  
Importance: High

Dear Diana,

We appreciate if you would provide the statistical analysis of the data the reviewer used to determine the (b) (4) expiration date. It would be helpful to us to understand, in order to respond to the question below. If possible, would you please forward the requested information this week. Thank you very much.

5. Based on a statistical analysis of the data provided the expiration period should be (b) (4). This is based on an acceptance criterion of NLT (b) (4) for sodium benzoate (30 mL package size, Batch 09801017). We note that you have proposed to test batches on stability for antimicrobial effective testing if the values of any preservative is between (b) (4) and (b) (4). However this type of testing is not applicable to determining an expiration date.

Regards,

Denise

Denise K. Fairman  
Senior Regulatory Affairs Associate  
Lannett Company, Inc.  
9000 State Road  
Philadelphia, PA 19136  
Phone: 215-333-9000, ext 2101  
Fax: 215-624-2126

APPEARS THIS WAY ON  
ORIGINAL.

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

/s/  
-----

DIANA L WALKER  
12/14/2010

**Walker, Diana**

**From:** Walker, Diana  
**Sent:** Friday, December 10, 2010 4:03 PM  
**To:** 'Denise Fairman'  
**Subject:** RE: NDA 201517 Morphine Sulfate 30 mL container label revised 11\_23\_2010

Dear Denise,

I received the following response from the DMEPA review team regarding your request in the email below, and in reference to the prior DMEPA request that Lannett implement a flag label for the 30-mL container:

**Given the severity of the outcomes that could occur with administration errors for this product, DMEPA considers the flag label, which allows for more detailed instructions, to be important for safe use. We acknowledge that these instructions are on the carton labeling; however, it is likely that practitioners or patients could discard the carton label after the initial use. Please submit a draft mock-up for review prior to finalizing this label.**

If you have further questions, please let me know and I will convey them to the review team.

Regards,

Diana

---

**From:** Denise Fairman [mailto:dfairman@lannett.com]  
**Sent:** Monday, December 06, 2010 6:43 PM  
**To:** Walker, Diana  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** RE: NDA 201517 Morphine Sulfate 30 mL container label revised 11 23 2010

Dear Diana,

Thank you for getting back to me concerning the 30 mL container label. Lannett would not like to have a flag label.

Would DMPEA be agreeable if Lannett's wording on the container label is similar to the RLD, Roxane?

Only have the statements (b) (4)  
 Store at Controlled Room Temperature 15° to 30°C (59° to 86° F).” Elimination of the bullet statements currently on the draft I sent in under Pharmacist/Nurse/Patient and picture of oral syringe would create much more space and the font size of the wording would be able to be made larger. I have attached the Roxane label you sent to me. I appreciate it if you can get some feedback from the reviewers. Thank you very much.

Regards,  
 Denise

Denise K. Fairman  
 Senior Regulatory Affairs Associate  
 Lannett Company, Inc.  
 9000 State Road  
 Philadelphia, PA 19136  
 Phone: 215-333-9000, ext 2101  
 Fax: 215-624-2126

---

**From:** Reference ID: 2876125 Walker@fda.hhs.gov  
**Sent:** Monday, December 06, 2010 2:28 PM

12/10/2010

**To:** Denise Fairman

**Subject:** RE: NDA 201517 Morphine Sulfate 30 mL container label revised 11 23 2010

Dear Denise,

After review of your revisions for the carton and container labels, the DMEPA review team asked me to pass on to you that your revisions all appear to be adequate, with the exception that they would like to hear from you regarding the comment concerning the flag labels, and whether you have looked into this option. The review team feels that the flag label would be a very appropriate and effective option for your 30-mL bottle, and therefore would like to emphasize the importance of this comment.

Please let me know your response to this item.

Regards,

Diana

---

**From:** Denise Fairman [mailto:dfairman@lannett.com]

**Sent:** Thursday, December 02, 2010 12:03 PM

**To:** Walker, Diana

**Cc:** Ernest Sabo; Kristie Stephens

**Subject:** RE: NDA 201517 Morphine Sulfate 30 mL container label revised 11 23 2010

Dear Diana,

Have you heard anything from the reviewer concerning the 30 mL draft container label revision I sent on Nov 23rd?

Regards,  
Denise

Denise K. Fairman  
Senior Regulatory Affairs Associate  
Lannett Company, Inc.  
9000 State Road  
Philadelphia, PA 19136  
Phone: 215-333-9000, ext 2101  
Fax: 215-624-2126

---

**From:** Walker, Diana [mailto:Diana.Walker@fda.hhs.gov]

**Sent:** Monday, November 29, 2010 10:12 AM

**To:** Denise Fairman

**Cc:** Ernest Sabo; Kristie Stephens

**Subject:** RE: NDA 201517 Morphine Sulfate 30 mL container label revised 11 23 2010

Dear Denise,

The comments were sent to the review team, but I will likely not receive feedback until the middle of this week. I will let you know once I do. One question however, in case he reviewer asks, comment #3 concerned ALL of the labels. Do you plan to revise the other labels along with the 30-mL label revision you sent here when you make the final submission? I just wanted to check so I can inform the review team.

3. **For all Carton and Container labels, this was the original comment:**

**“It is essential that the strength box be large and prominent. Although it seems large when viewing from the computer, keep in mind that this will be on a shelf with 20 or 30 other oral solution containers. We recommend making the color box a bit larger, for example by extending the upper border close to the “Oral Solution” text, shifting the text within the black box lower, and extending the lower border of the color box toward the black box. This would allow the text to be larger within the box as well.”**

Reference ID: 2876425

12/10/2010

**After review of your revised labels, the review team reiterates that you still need to enlarge the color box and have it extend further across the principal display panel.**

Regards,

Diana

---

**From:** Denise Fairman [mailto:dfairman@lannett.com]  
**Sent:** Tuesday, November 23, 2010 3:09 PM  
**To:** Walker, Diana  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** NDA 201517 Morphine Sulfate 30 mL container label revised 11 23 2010  
**Importance:** High

Dear Diana,

Attached is a draft label incorporating the requested changes. If possible, would you please let me know today if the most recent changes address all of FDA's concerns. Thank you very much.

Regards,  
Denise

Denise K. Fairman  
Senior Regulatory Affairs Associate  
Lannett Company, Inc.  
9000 State Road  
Philadelphia, PA 19136  
Phone: 215-333-9000, ext 2101  
Fax: 215-624-2126

Reference ID: 2876125

12/10/2010

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

/s/  
-----

DIANA L WALKER  
12/10/2010

**Walker, Diana**

**From:** Walker, Diana  
**Sent:** Wednesday, December 08, 2010 11:53 AM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo  
**Subject:** NDA 201517 CMC Advice and Information Request 08Dec10

Dear Denise,

I have received the following Advice and Information Request Comments from our CMC review team regarding your NDA 201517 for Morphine Sulfate Oral Solution, 20 mg/mL.

1. DMF (b) (4) for morphine sulfate held by (b) (4) was found deficient and the holder notified on December 2, 2010.
2. Provide the source and qualification procedures for the (b) (4) reference standards.
3. Submit a revision to Section 3.2.P.5.6 to include the revised acceptance criterion for (b) (4)
4. Explain why the (b) (4) for the Oral Doser Barrel is different for the 30 mL package size (b) (4) from the (b) (4) for the 120 mL and 240 mL package sizes (b) (4)
5. Explain why the CFR citations for the Colorant used in the Oral Dosers include sections that are not usually associated with colorants for plastics:

176.170 Components of paper and paperboard in contact with aqueous and fatty foods  
 175.105 Adhesives  
 175.300 Resinous and polymeric coatings  
 175.320 Resinous and polymeric coatings for polyolefin films

6. Based on a statistical analysis of the data provided the expiration period should be (b) (4). This is based on an acceptance criterion of NLT (b) (4) for sodium benzoate (30 mL package size, Batch 09801017). We note that you have proposed to test batches on stability for antimicrobial effective testing if the values of any preservative is between (b) (4). However this type of testing is not applicable to determining an expiration date.

Please contact me if you have any questions.

Regards,

Diana

Diana L. Walker, Ph.D.  
 Regulatory Health Project Manager  
 FDA/CDER/ODE II/DAAP  
 Tel: 301-796-4029  
 Fax: 301-796-9723/9713  
 Email: Diana.Walker@fda.hhs.gov

Reference ID: 2874271

12/8/2010

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

/s/  
-----

DIANA L WALKER  
12/08/2010

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Tuesday, November 23, 2010 9:30 AM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** NDA 201517 Labeling Comments 23Nov10  
**Importance:** High  
**Attachments:** NDA 201517 Draft package-insert for Lannett 22Nov10-clean.doc; NDA 201517 Draft package-insert for Lannett 22Nov10-tracked.doc; NDA 201517 Draft medication-guide for Lannett 22Nov10-clean.doc; NDA 201517 Draft medication-guide for Lannett 22Nov10-tracked.doc

Dear Denise,

Please find attached the first round of draft comments for the Morphine Sulfate Package Insert and Medication Guide. I have attached both track changes and clean versions. Please note that these comments may not be final, as they have not cleared the Division management final review yet, but we wanted you to be able to review and comment on the current working draft labels.

Please review these labels. Accept any changes that you agree with, and for any changes you don't agree with, edit them (using track changes) and then return both labels to me in track changes so we can see your edits. You can include comments/explanations to explain your rationale. Also, please review the labels carefully for things like typos, formatting, etc., as we may not have caught everything on this first round. As we are still working in draft, you do not have to submit through the ESG, but just send the labels to me via email.

Note that I will be away from the office for the rest of the week, but will return Monday, November 29 if you have any questions.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

59 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page.

Reference ID: 2874259

12/8/2010

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

/s/  
-----

DIANA L WALKER  
12/08/2010

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Friday, November 19, 2010 12:30 PM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** NDA 201517 Morphine Sulfate carton and container comments 19Nov10  
**Attachments:** Morphine Roxane 30 mL lable.pdf; flag label.jpg

Dear Denise,

Our Division management and the DMEPA review team have provided feedback to me on your draft responses to the requested carton and container labeling changes, as well as your requests to change the oral syringe terminology and to continue using your current label inventory.

1. **The decision remains that you should use the terminology “oral syringe”, which is currently being used in the RLD as well as other products. In order to be consistent with the Package Insert and Medication Guide labeling (to be sent by the end of the month), change all references on your Carton and Container labels from [REDACTED] (b) (4) or [REDACTED] (b) (4) or [REDACTED] (b) (4) to “oral syringe.”**
2. **Regarding your request to use the balance of your inventory of carton and container labels: No, we do not agree that the old labels and labeling should be used until the inventory runs out. We believe that the current labels do not sufficiently communicate pertinent information, especially for this potentially dangerous drug.**
3. **For all Carton and Container labels, this was the original comment:**

**“It is essential that the strength box be large and prominent. Although it seems large when viewing from the computer, keep in mind that this will be on a shelf with 20 or 30 other oral solution containers. We recommend making the color box a bit larger, for example by extending the upper border close to the “Oral Solution” text, shifting the text within the black box lower, and extending the lower border of the color box toward the black box. This would allow the text to be larger within the box as well.”**

**After review of your revised labels, the review team reiterates that you still need to enlarge the color box and have it extend further across the principal display panel.**

4. **For the 30 mL bottle:**
  - a. **The 'Rx Only' statement and 'Lannett' could be decreased in prominence so that other pertinent information (for example Medication Guide and note about the oral syringe) can be larger.**
  - b. **We recommend using a flag label (or peel open label), which allows for the information to remain on the back of the label. We are concerned that because this bottle is likely to be used in institutions and the carton and Medication Guide will not accompany the bottle, keeping this information on the label will be beneficial; however, it must be in larger and more readable text. A sample of a flag label is attached to this email as a jpg file.**

Reference ID: 2874257

- c. **Include volume markings on the label to assist institutions in estimating the volume in the bottle. The Roxane label for the 30 mL bottle is attached as an example of the markings.**

Please submit your changes to me via email as before (can be PDF versions and not proofs) for final review before submitting final labels to your NDA.

Regards,

Dian

---

**From:** Denise Fairman [mailto:dfairman@lannett.com]  
**Sent:** Friday, November 19, 2010 10:57 AM  
**To:** Walker, Diana  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** NDA 201517 Morphine Sulfate carton and container Information Request 25Oct10

Dear Diana,

On November 15, 2010 you stated you are still waiting on the reviewing teams' response to our request concerning the terminology "oral syringe". Have you heard any additional information from the reviewing team?

Please let me know when I should submit the container and cartons proofs (final proofs or word and pdf) through ESG.

You also forwarded our request to allow us to use the balance of inventory for container labels and cartons, approximately 3 months in order to not sustain a huge loss. We currently have approximately (b) (4) of current inventory in cartons and container labels. Will you please provide any update to this request.

Thank you very much.

Regards,

Denise K. Fairman  
Senior Regulatory Affairs Associate  
Lannett Company, Inc.  
9000 State Road  
Philadelphia, PA 19136  
Phone: 215-333-9000, ext 2101  
Fax: 215-624-2126

Reference ID: 2874257

12/8/2010

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

/s/  
-----

DIANA L WALKER  
12/08/2010

**Walker, Diana**

**From:** Walker, Diana  
**Sent:** Monday, November 08, 2010 4:01 PM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** RE: NDA 201517 Morphine Sulfate Oral Solution- Carton and Container Information Request 25Oct10  
**Importance:** High

Dear Denise,

I am enclosing comments from the review team regarding your proposed revised Carton and Container labels that were sent to us for review on October 28, 2010. Please note that there is one new comment, which you were not sent initially, concerning the oral syringe terminology. This terminology will be used for all of the labeling for the sake of consistency, and that is why we are sending you this additional comment for your Carton and Container labels. Note that you will see this change as well when you receive the Medication Guide and Package Insert labeling comments, to be sent within the next two weeks.

The DMEPA review team has provided feedback to me on your draft responses to the requested carton and container labeling changes, which you sent to us for review on October 28, 2010. Overall, they have said that there is great improvement in the labels, but have several comments.

**New Comment:**

In order to be consistent with the Package Insert, Medication Guide, and RLD labeling, change all references from (b) (4) or (b) (4) or (b) (4) to “**oral syringe**” on all of the Carton and Container labels.

**Comments regarding your proposed revisions to the Carton and Container labeling:**

1. It is essential that the strength box be large and prominent. Although it seems large when viewing from the computer, keep in mind that this will be on a shelf with 20 or 30 other oral solution containers. We recommend making the color box a bit larger, for example by extending the upper border close to the “Oral Solution” text, shifting the text within the black box lower, and extending the lower border of the color box toward the black box. This would allow the text to be larger within the box as well.
2. Lengthy descriptions are often not read carefully. Revise the lengthy “Pharmacist/Nurse/Patient” description on the back panel of the carton and container labeling into shorter sentences with more “white space” separation. For example,

(b) (4)  
 For Oral Use Only.

(b) (4)  
 Measure using ONLY the enclosed oral syringe.

(b) (4)  
 Measure dose from the widest part of the plunger, see picture of oral syringe.

(b) (4)

Syringe calibration: 0.5 mL = 10 mg and 1.0 mL = 20 mg.

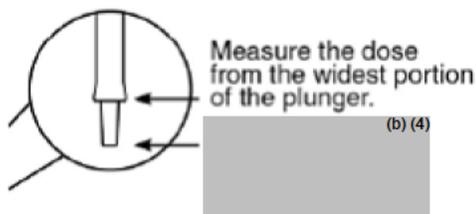
(b) (4)

Do not place oral syringe directly into mouth.

(b) (4)

Close the bottle after each use.

3. As much as possible, enlarge the pictures of the syringe and the directions on where to measure that appear on the side panels of the cartons. For the containers, one possibility, which may work for the 30 mL container as well, would be to only include the picture within the circle, arrows, and the measuring directions on the containers, and leave the full syringe diagram only on the cartons.



In this scenario, you could remove the circle, and only include the syringe tip, arrows, and instructions.

Please contact me if you have follow-up questions on the carton and container labeling.

Regards,

Diana

---

**From:** Denise Fairman [mailto:dfairman@lannett.com]

**Sent:** Thursday, October 28, 2010 2:49 PM

**To:** Walker, Diana

**Cc:** Ernest Sabo; Kristie Stephens

**Subject:** NDA 201517 Morphine Sulfate Oral Solution- Carton and Container Information Request 25Oct10

Hello Diana,

In our telephone conversation with you on October 26, 2010, we would like feedback from the reviewer concerning our draft carton and container labels. Attached please find draft labeling. Below are some additional changes we are submitting for review.

Container labels

The 30 mL container label is too small to have the picture of the oral dosing device, actual label size is 1-1/2" x 3-3/8" and the doser would not be legible. The picture of the oral dosing device has been added to the 120 mL and 240 mL container label, label size 2-1/2" x 4-5/8". Additional information has been added to the

PHARMACIST/NURSE/PATIENT information based on Lannett product history. For example, the text (b) (4) was added to minimize the risk of injection of this solution. The oral dosing device calibration information is provided to clarify dispensing instructions. The text that describes handling the oral dosing device ( (b) (4) etc.) was added to minimize the risk of contaminating the oral dosing device.

These statements enhance the safety of the drug product. A color box stretching across the principle display panel, only highlights the dose.

Reference ID: 2862132

11/9/2010

Carton labeling

Carton labeling has been updated with requested information. A picture of the oral dosing device is located on both side panels. Additional information has been added to the PHARMACIST/NURSE/PATIENT information based on Lannett product history. For example, the text [REDACTED]<sup>(b) (4)</sup>” was added to minimize the risk of injection of this solution. The oral dosing device calibration information is provided to clarify dispensing instructions. The text that describes handling the oral dosing device ([REDACTED]<sup>(b) (4)</sup>, etc.) was added to minimize the risk of contaminating the oral dosing device. These statements enhance the safety of the drug product. A color box stretching across the principle display panel, only highlights the dose.

If these changes are acceptable, I will prepare for submission through ESG.

Thank you very much.

Regards,

Denise K. Fairman  
Senior Regulatory Affairs Associate  
Lannett Company, Inc.  
9000 State Road  
Philadelphia, PA 19136  
Phone: 215-333-9000, ext 2101  
Fax: 215-624-2126

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

/s/  
-----

DIANA L WALKER  
11/09/2010

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Monday, November 08, 2010 4:45 PM  
**To:** 'Denise Fairman'  
**Subject:** RE: NDA 201517 Morphine Sulfate Oral Solution- Carton and Container Information Request 25Oct10

Dear Denise,

Thank you for the clarification. Here is what the DMEPA review team has said in response to your question, therefore it appears that they are amenable to your use of the current inventory.

Please verify that the oral syringe that states 'topical' is the oral syringe that is currently used with this product. If it is, then we are amenable to 3 more months to exhaust the supply. If it has not been included in the marketed concentrated morphine product, then we would propose not using it.

Regards,

Diana

---

**From:** Denise Fairman [mailto:dfairman@lannett.com]  
**Sent:** Monday, November 08, 2010 4:23 PM  
**To:** Walker, Diana  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** RE: NDA 201517 Morphine Sulfate Oral Solution- Carton and Container Information Request 25Oct10

Dear Diana,

The statements on the labels I referred to below were currently on the market until July 23, 2010.

Lannett currently has about (b) (4) oral dosing devices, approximately 3 month supply of dosers with the words "Oral" / "Topical" and would like to exhaust the remaining current inventory before going to the new dosers. The word "topical" will be removed from the oral dosing device. Is our request amenable?

Regards,  
Denise

Denise K. Fairman  
Senior Regulatory Affairs Associate  
Lannett Company, Inc.  
9000 State Road  
Philadelphia, PA 19136  
Phone: 215-333-9000, ext 2101  
Fax: 215-624-2126

---

**From:** Walker, Diana [mailto:Diana.Walker@fda.hhs.gov]  
**Sent:** Monday, November 08, 2010 3:30 PM  
**To:** Denise Fairman  
**Subject:** RE: NDA 201517 Morphine Sulfate Oral Solution- Carton and Container Information Request 25Oct10  
**Importance:** High

Dear Denise,

Reference ID: 2862129

I am working with the reviewer on finalizing the responses so send back to you concerning your carton and container labeling (I will

11/9/2010

be sending them to you today), but have one quick question regarding your question below. Just to clarify, are the labels you are referring to below what is currently out on the market, in other words currently in use?

If you can send me a response this afternoon, I could finalize and get the responses out to you by COB.

Regards,

Diana

---

**From:** Denise Fairman [mailto:dfairman@lannett.com]  
**Sent:** Thursday, November 04, 2010 9:05 AM  
**To:** Walker, Diana  
**Cc:** Ernest Sabo; Kristie Stephens  
**Subject:** RE: NDA 201517 Morphine Sulfate Oral Solution- Carton and Container Information Request 25Oct10

Good Morning Diana,

I was wondering if you received any feedback from the reviewer concerning the draft labeling I sent in last Thursday?

I also requested on Friday if we can use remaining inventory prior to implementing the comments listed in A1. Please see comment below.

The comment under Carton and Container Labeling Comments, A1 asked Lannett to remove the word "topical" from the oral dosing device. Lannett plans to implement the request however, we currently have about (b) (4) in inventory approximately 3 month supply and would like to use the remaining supply. Is this request amenable?

Thank you very much.

Regards,  
Denise

Denise K. Fairman  
Senior Regulatory Affairs Associate  
Lannett Company, Inc.  
9000 State Road  
Philadelphia, PA 19136  
Phone: 215-333-9000, ext 2101  
Fax: 215-624-2126

---

**From:** Walker, Diana [mailto:Diana.Walker@fda.hhs.gov]  
**Sent:** Friday, October 29, 2010 10:06 AM  
**To:** Denise Fairman  
**Subject:** RE: NDA 201517 Morphine Sulfate Oral Solution- Carton and Container Information Request 25Oct10

Dear Denise,

I sent this forward to the reviewer yesterday, and she has been actively looking at this. She said that these labels are much improved already, but she does have a couple of comments. She is running these comments past her team leader, and we should be able to send the feedback to you on Monday.

Also, can you update me on the status of your other information request submissions. I know you said previously that you planned to submit around November 8. I am just wondering whether it could be any earlier, or whether this is still your target? I am only asking, as the review team is working hard to finalize their reviews, and will need this information to finish up.

Thanks in advance for an update on your status.

Reference ID: 2862129

11/9/2010

Regards,

Diana

---

**From:** Denise Fairman [mailto:dfairman@lannett.com]

**Sent:** Thursday, October 28, 2010 2:49 PM

**To:** Walker, Diana

**Cc:** Ernest Sabo; Kristie Stephens

**Subject:** NDA 201517 Morphine Sulfate Oral Solution- Carton and Container Information Request 25Oct10

Hello Diana,

In our telephone conversation with you on October 26, 2010, we would like feedback from the reviewer concerning our draft carton and container labels. Attached please find draft labeling. Below are some additional changes we are submitting for review.

Container labels

The 30 mL container label is too small to have the picture of the oral dosing device, actual label size is 1-1/2" x 3-3/8" and the doser would not be legible. The picture of the oral dosing device has been added to the 120 mL and 240 mL container label, label size 2-1/2" x 4-5/8". Additional information has been added to the PHARMACIST/NURSE/PATIENT information based on Lannett product history. For example, the text (b) (4) " was added to minimize the risk of injection of this solution. The oral dosing device calibration information is provided to clarify dispensing instructions. The text that describes handling the oral dosing device (b) (4) was added to minimize the risk of contaminating the oral dosing device. These statements enhance the safety of the drug product. A color box stretching across the principle display panel, only highlights the dose.

Carton labeling

Carton labeling has been updated with requested information. A picture of the oral dosing device is located on both side panels. Additional information has been added to the PHARMACIST/NURSE/PATIENT information based on Lannett product history. For example, the text (b) (4) was added to minimize the risk of injection of this solution. The oral dosing device calibration information is provided to clarify dispensing instructions. The text that describes handling the oral dosing device (b) (4) was added to minimize the risk of contaminating the oral dosing device. These statements enhance the safety of the drug product. A color box stretching across the principle display panel, only highlights the dose.

If these changes are acceptable, I will prepare for submission through ESG.

Thank you very much.

Regards,

Denise K. Fairman

Senior Regulatory Affairs Associate

Lannett Company, Inc.

9000 State Road

Philadelphia, PA 19136

Phone: 215-333-9000, ext 2101

Fax: 215-624-2126

Reference ID: 2862129

11/9/2010

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

/s/  
-----

DIANA L WALKER  
11/09/2010

**Walker, Diana**

**From:** Walker, Diana  
**Sent:** Thursday, November 04, 2010 4:36 PM  
**To:** 'Denise Fairman'; Ernest Sabo  
**Subject:** NDA 201517 REMS Information Request 03Nov10  
**Importance:** High  
**Attachments:** NDA 201517 Morphine Sulphate REMS Revisions 03Nov10.doc

Dear Denise,

Please see below for comments and advice concerning your proposed REMS. Also find attached the track-changes version of your proposed REMS, as referenced in Part A below. **Please submit your responses to Part A to your NDA as soon as possible.** Note the instructions in Part B, which state that those items need be submitted only at least 90 days prior to conducting the evaluation.

**Information Request: NDA 201517 Proposed REMS and REMS Assessment Plan**

**A. Comments concerning your Proposed REMS**

See the appended Morphine Sulfate Oral Solution REMS proposal for track changes corresponding to the comments in this Advice/Information Request Correspondence.

(b) (4)  
[Redacted]

[Redacted]

[Redacted]

**B. Comments concerning your REMS Assessment Plan.**

(b) (4)  
[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

2 Pages have been Withheld in Full as b4 (CCI/TS) immediately following this page.

(b) (4)

Kindly confirm receipt of this email, and that you have received and can open the attached document.  
Please contact me if you have any questions regarding this correspondence.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

2 Pages of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page.

Reference ID: 2862126

11/9/2010

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

/s/  
-----

DIANA L WALKER  
11/09/2010

**Walker, Diana**

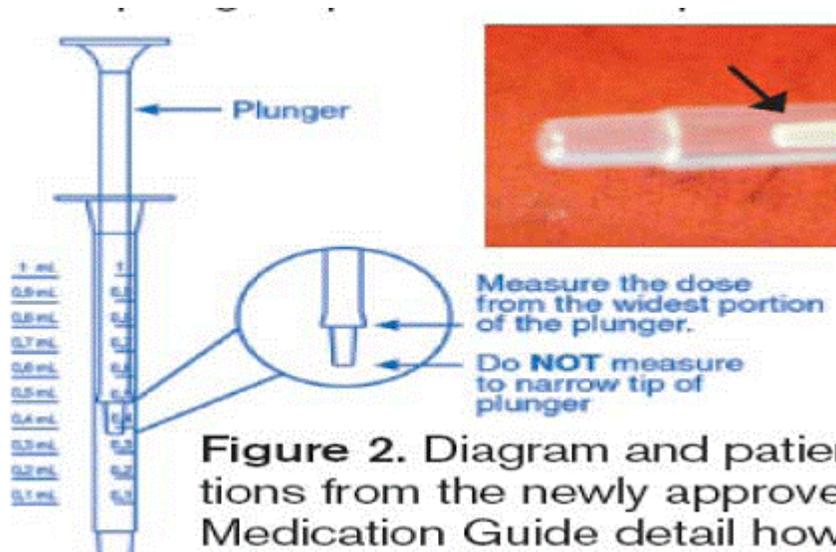
**From:** Walker, Diana  
**Sent:** Monday, October 25, 2010 5:30 PM  
**To:** 'Denise Fairman'; 'Ernest Sabo'  
**Subject:** NDA 201517 FDA Carton and Container Information Request 25Oct10  
**Importance:** High

Dear Denise and Ernest,

Our Division of Medication Error Prevention and Analysis has reviewed your carton and container labels, and has the following comments. Please address these comments, and submit your responses as soon as possible to your NDA, but no later than November 15, 2010. If you are able to submit sooner, it will greatly assist the reviewers in finalizing review of your application in a timely manner.

**Carton and Container Labeling Comments****A. Oral Dosing Device**

1. Medication errors described in a recent article which discussed confusion related to the oral dosing device used for concentrated Morphine Sulfate Oral Solution. The device involved in these errors is the same device that was submitted in your application. The plunger is all white and pointed and has caused confusion because practitioners are unsure if the dose should be measured from the narrow tip or the widest part of the plunger. These types of errors have resulted in overdose. We recommend adding a picture or diagram of the syringe and plunger with explicit instructions indicating what part of the plunger is used for measuring doses to mitigate this type of error. This picture or diagram should be included on the container label and the carton labeling (and retained in the Medication Guide). See picture below:



2. Remove the word, (b) (4) from the oral dosing device.

**B. Container Labels (30 mL, 120 mL and 240 mL bottle)**

1. Principal Display Panel

Reference ID: 2862123  
 a. Revise the presentations of strengths so that the 100 mg per 5 mL is more, and the 20 mg/mL statement so

that it is less prominently displayed and appears in parenthesis underneath the 100 mg per 5 mL statement.

Additionally, a large color box should stretch across the principle display panel which highlights the name and strength. This color should be chosen to ensure that it is visually well differentiated from the other morphine sulfate oral solution concentration because of the multiple similarities between the products, i.e. name, bottle shape and size.

- b. Remove the statement (b) (4) and replace with “Only for use in patients who are opioid tolerant”. This statement should appear in a box below the strength statements.
- c. Remove the statement, (b) (4) and replace it with the Medication Guide statement: “Pharmacist: Must dispense the enclosed Medication Guide to each patient”.
- d. Revise the (b) (4) statement so that it only displays the quantity, for example “120 mL”.
- e. Add a statement to the principal display panel that alerts patients, caregivers and practitioners to always use the oral dosing device provided to measure each dose of Morphine Sulfate Oral Solution.

## 2. Side Panel

- a. See comment A1
- b. Remove the (b) (4) statement on the side panel and replace with 100 mg per 5 mL so that the strength is consistently displayed throughout the label and labeling.
- c. Remove all of the text which appears under the title “Pharmacist/Nurse/Patient” and replace with a succinct description of how to properly measure a dose with the provided dosing device.
- d. Revise the dispense statement, the usual dose statement, and the storage statement on the **30 mL** bottle so that they appear horizontally oriented (b) (4) which will result in increased readability.

## C. Carton Labeling (30 mL, 120 mL and 240 mL)

### 1. Principle Display Panel

- a. See comments A1 and B1a through B1c.

### 2. Back Panel

- a. See comments A1, B2a and B2b.
- b. The back panel and principal display panel should mimic one another in the presentation of information which will ensure that the vital information regarding strength, opioid tolerance and Medication Guides are communicated regardless of which direction the carton is facing.

### 3. Side Panels

- a. See comment A1 (diagram can be placed on either back panel OR side panel).
- b. Add a statement which alerts practitioners that the carton contains both the morphine sulfate bottle and an oral dispenser.

Please contact me if you need any clarification on this information request.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@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/  
-----

DIANA L WALKER  
11/09/2010

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Monday, October 18, 2010 2:49 PM  
**To:** 'Denise Fairman'; 'Ernest Sabo'  
**Subject:** NDA 201517 CFR Citations Information Request 18Oct10  
**Importance:** High

Dear Denise,

I have received an information request from our review team. Please submit this information to me as soon as possible or by October 22, 2010, via email. If this information is already within your submission, there is no need to submit via ESG to you NDA; however, if it is not within your submission already, please submit via ESG as soon as possible, but no later than Monday, October 25, 2010.

**Please point out the location(s) within your NDA 201517 submission of the appropriate CFR citations for Indirect Food Additives in your Container-Closure System. If these citations are not within your current NDA submission, submit the appropriate citations to your NDA.**

If this is one of the items you were planning to send in by the week of November 8, 2010, please let me know, and we will expect it by that date. Otherwise, please submit this information as soon as possible

Please feel free to contact me if you have questions regarding this request.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

Reference ID: 2862121

11/9/2010

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

/s/  
-----

DIANA L WALKER  
11/09/2010



NDA 201517

**DISCIPLINE REVIEW LETTER**

Lannett Holdings, Inc.  
9000 State Road  
Philadelphia, PA 19136

Attention: Ernest Sabo  
Vice President, Regulatory and Corporate Compliance

Dear Mr. Sabo:

Please refer to your March 1, 2010, New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Morphine Sulfate Oral Solution, 20 mg/mL.

We also refer to your amendments dated June 23, and July 1, 14, 15 and 20, 2010.

Our review of the Product Quality section of your submission is complete, and we have identified the following deficiencies:

**A. The following comments pertain to the Drug Substance.**

1. Provide the specifications for testing incoming morphine sulfate in Section 3.2.S.4.1. (See Guidance for Industry M4Q: The CTD Quality <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073280.pdf> )
2. Explain how the information about the impurities obtained from injection of the Morphine Sensitivity Solution (MSS) is used.
3. Tighten the acceptance criterion for the precision in the test for Impurities (NMT (b) (4)) to reflect the actual measurements of the precision in the Methods Validation Report.
4. Provide the relative response factors for the impurities and the data to support the assignment of these values.
5. Tighten the acceptance criterion for the precision in the test for residual solvents (NMT (b) (4)) to reflect the actual measurements of the precision in the Methods Validation Report.

6. Provide the results of full testing for three batches of incoming drug substance from (b) (4)
7. Provide the source and qualification procedures for the impurity reference standards.
8. Explain how the stability data for the drug substance was obtained.
9. DMF (b) (4) submitted by (b) (4) for the manufacture of morphine sulfate is deficient and the holder has been notified.

**B. The following comments pertain to the Drug Product.**

10. Provide a description of the drug product in Section 3.2.P.1.  
(See Guidance for Industry M4Q: The CTD Quality <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073280.pdf>)
11. Explain the functionality of Edetate Disodium Dihydrate as a (b) (4)
12. Specify the testing performed by Bioscreen Testing Services.
13. Explain why the container/closure system is checked for defects only on stability and not at release.
14. Provide the methods validation data for evaluation of precision, linearity, accuracy and robustness for (b) (4)
15. Provide the determination of the Limits of Detection and Quantitation for the individual impurities.
16. Provide a justification for the acceptance criteria of the related substances based on the type of analysis discussed in the ICH Guidance for Industry: Q3B(R2) Impurities in New Drug Products  
(<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm073389.pdf>).
17. Provide the sources and specifications for the codeine sulfate used in the Morphine Sulfate test and the impurity standards used in the Related Substances test.
18. Provide the information requested in our Filing Communication dated June 18, 2010, on the compliance of all packaging materials to appropriate CFRs for indirect food additives.
19. Explain what investigations will be performed if the preservative levels fail but the Microbial Testing passes at a stability test station.

20. Provide stability data for an additional batch of drug product. Include appropriate statistical analysis to assist in setting an expiration date. Alternatively provide historical data from batches of drug product manufactured using the same formulation and container-closure system.
21. Explain why some of the values in the stability data reports are reported as (b) (4) some are reported as (b) (4) some are reported as “Not Detected,” and some are not reported at all (example for RRT (b) (4) at 18 months for the 30 mL bottle) in the stability data for Batch 08801017.
22. Explain why the 18 month time point for batch 08801017 submitted in the July 19, 2010 amendment was not included in the tables showing the most recent stability data submitted in the Electronic Document Room.
23. The following comments pertain to the structure determination of the Impurity eluting at RRT (b) (4)
- Provide further evidence that the impurity eluting at (b) (4) in M-Scan’s LC-MS chromatography system is the same as the unknown impurity eluting at RRT (b) (4) on stability in your chromatography system.
  - Identify the peak with (b) (4) in the mass spectrum provided as Figure 6 in the report from M-Scan.
  - Explain the relevance of the aryl-CH<sub>2</sub><sup>+</sup> ions in determining the structure of the unknown.
  - Provide the data and calculations to support the conclusion that the structure of the unknown is likely to be structures provided in the M-Scan’s report.
  - Provide a detailed explanation for the mass spectra in Figures 7 and 8.
  - Provide confirmatory data to support the assignment of the structure of the unknown impurity with RRT (b) (4).
  - If you wish to set an acceptance criterion for the impurity eluting at RRT (b) (4) that reflects the measured value at 18 months of (b) (4) with an expiration date of 18 months you must perform additional experiments to identify the impurity and you must provide data to qualify the impurity.
24. Explain why you state in the report “Summary of Impurity Investigation” in Section 3.2.P.8.3 that “Lannett concludes that this out-of-specification impurity level does not represent what happens with the more representative room temperature stability...” when, in fact, this out-of-specification impurity level occurs in Lot 7801005 when stored for eighteen months at room temperature.

25. The stability data provided do not support an expiration date of eighteen months for the following reasons:

Lot 08801017:

Sodium benzoate (Lower limit (b) (4)):

30 mL bottle:

(b) (4)

120 mL bottle:

(b) (4)

Impurity at RRT (b) (4)

30 mL bottle:

(b) (4)

120 mL bottle:

(b) (4)

240 mL bottle:

(b) (4)

Lot 7801005:

Impurity at RRT (b) (4)

30 mL bottle:

(b) (4)

120 mL bottle:

(b) (4)

240 mL bottle:

(b) (4)

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Diana Walker, Regulatory Health Project Manager at (301) 796-4029.

Sincerely,

*{See appended electronic signature page}*

Prasad Peri, Ph.D.  
Branch Chief (Acting), Branch VIII  
Division of New Drug Quality Assessment III  
Office of New Drug Quality Assessment  
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/

---

PRASAD PERI  
09/17/2010



NDA 201517

**DISCIPLINE REVIEW LETTER**

Lannett Holdings, Inc.  
9000 State Road  
Philadelphia, PA 19136

Attention: Ernest Sabo  
Vice President, Regulatory and Corporate Compliance

Dear Mr. Sabo:

Please refer to your March 1, 2010, New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Morphine Sulfate Oral Solution, 20 mg/mL.

We also refer to your submission dated July 15, 2010.

Our review of the Product Quality Microbiology section of your submission is complete, and we have identified the following deficiencies:

1. Provide test methods and acceptance criteria to demonstrate that the product is free of the objectionable microorganism *Burkholderia cepacia*. We recommend that potential sources are examined and sampled as process controls, and these may include raw materials and the manufacturing environment. A risk assessment for this species in the product and raw materials is recommended to develop sampling procedures and acceptance criteria. Your test method should be validated and a discussion of those methods should be provided. Test methods validation should address multiple strains of the species and cells that are acclimated to the environments (e.g., warm or cold water) that may be tested.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Diana Walker, Regulatory Health Project Manager at (301) 796-4029.

Sincerely,

*{See appended electronic signature page}*

Parinda Jani  
Chief, Project Management Staff  
Division of Anesthesia and Analgesia Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

---

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

---

/s/

---

PARINDA JANI  
09/08/2010

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Thursday, July 15, 2010 3:51 PM  
**To:** 'Denise Fairman'; Ernest Sabo  
**Subject:** FW: NDA 201517 CMC Information Request 13jul10  
**Importance:** High

Dear Denise and Ernest,

Following our telephone conversation regarding the information request sent July 13, 2010, shown below, I contacted our review team to discuss your concerns. The review team reviewed the original meeting minutes in the context of the current submission, and concluded that, as long as the syringe has been demonstrated to accurately deliver the drug product then that will satisfy the request. If you are able to demonstrate accuracy by performing an in vitro study as mentioned in item #3, and you submit this data and your analysis, that would be satisfactory.

Therefore, it is not necessary to submit a response to items #1 and #2.

Regards,

Diana

---

**From:** Walker, Diana  
**Sent:** Tuesday, July 13, 2010 9:58 AM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo  
**Subject:** NDA 201517 CMC Information Request 13jul10  
**Importance:** High

Dear Denise,

I have received an information request from our Chemistry, Manufacturing, and Controls (CMC) review team. Please submit these three information items to me via email followed by an official submission to your NDA as soon as possible, but no later than August 15, 2010.

**In our meeting minutes dated July 27, 2009, we provided you with advice regarding the oral dosing device to be co-packaged with the Morphine Sulfate Oral Solution, 20 mg/mL. Please provide the following information requested in the meeting minutes (note that the numbers in parenthesis correspond to the meeting minute numbers under "Comments on a Dosing Device"):**

- 1. (1.) Provide in-vitro data to show the accuracy of the device e.g., from in-use patient studies during clinical trials.**
- 2. (4.a.) Conduct usability studies on the proposed devices to validate the design and submit these findings accordingly. These usability studies must include patients, caregivers, and healthcare practitioners who may administer the product.**

**In addition provide the following information:**

- 3. Provide in vitro measurements of delivered volume using drug product similar to the data provided in the tables in the Container-Closure Section showing the delivery of water.**

**We remind you that all submissions must be paginated. We strongly recommend that all submissions be submitted as text rather than scanned images.**

Please contact me if you have questions or need clarification on this request.

8/4/2010

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: [Diana.Walker@fda.hhs.gov](mailto:Diana.Walker@fda.hhs.gov)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

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

/s/

DIANA L WALKER  
08/11/2010

## CMC MICRO & STERILITY ASSURANCE REVIEW REQUEST

TO (Division/Office): **New Drug Microbiology Staff**  
*E-mail to:* **CDER OPS IO MICRO**  
*Paper mail to:* **WO Bldg 51, Room 4193**

FROM:  
**Bob Rappaport, M.D.**  
Director, Division of Anesthesia and Analgesia Products  
(DAARP), HFD-170

PROJECT MANAGER (if other than sender): **Diana Walker, RPM**

REQUEST DATE  
**July 14, 2010**

IND NO.  
**N/A**

NDA NO  
**201517**

TYPE OF DOCUMENT  
**New NDA**

DATE OF DOCUMENT  
Submission via email (link below) to be  
submitted through Gateway in July..

NAMES OF DRUG  
**Morphine Sulfate**

PRIORITY CONSIDERATION  
**Standard**

PDUFA DATE  
Action goal date:  
**December 10, 2010**

DESIRED COMPLETION DATE  
**August 15, 2010**

NAME OF APPLICANT OR SPONSOR: **Lannett, Inc.**

### GENERAL PROVISIONS IN APPLICATION

- |   |   |
|---|---|
| <input type="checkbox"/> 30 DAY SAFETY REVIEW NEEDED        | <input type="checkbox"/> CBE 0 SUPPLEMENT                     |
| <input type="checkbox"/> NDA FILING REVIEW NEEDED BY: _____ | <input type="checkbox"/> CBE 30 SUPPLEMENT                    |
| <input type="checkbox"/> BUNDLED                            | <input type="checkbox"/> CHANGE IN DOSAGE, STRENGTH / POTENCY |
| <input type="checkbox"/> DOCUMENT IN EDR                    |   |

### COMMENTS / SPECIAL INSTRUCTIONS:

The submission is located in the EDR using the following link: <\\CDSESUB1\EVSPROD\NDA201517\0000>  
This is a marketed, unapproved product. It is 505(b)(2) referencing Roxane's product, NDA 22195.

After receipt of an information request response from the Sponsor, the CMC review team for this NDA requests a consult on Preservative Effectiveness Testing.

link to the raw data in the three files below

<<\\fdsfs01\ode2\Diana Walker\NDA 201517 Morphine sulfate\CMC submission for IR 12jul>>

USP 51 (b) (4) .pdf  
USP 51 (b) (4) .pdf  
USP 51 (b) (4) .pdf

**Please contact me if you have problems accessing the documents, or need further information. Thanks. Diana x6-4029**

For questions on this consult, please contact: Art Shaw, Product Quality Reviewer, x 6-1460  
Danae Christodoulou, CMC Team Leader x6-1342

### SIGNATURE OF REQUESTER

**Diana L. Walker, PhD**  
Regulatory Project Manager  
FDA/CDER/ODE II/DAARP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: [Diana.Walker@fda.hhs.gov](mailto:Diana.Walker@fda.hhs.gov)

### REVIEW REQUEST DELIVERED BY (Check one):

DARRTS  EDR  E MAIL  MAIL  HAND

### DOCUMENTS FOR REVIEW DELIVERED BY (Check one):

EDR  E MAIL  MAIL  HAND

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

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

/s/

DIANA L WALKER  
07/14/2010

**REQUEST FOR DDMAC LABELING REVIEW CONSULTATION**

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

TO: <b>CDER-DDMAC-RPM</b>	FROM: (Name/Title, Office/Division/Phone number of requestor) Diana Walker, RPM, for: Bob Rappaport, M.D. Director, Division of Anesthesia and Analgesia Products (DAARP), HFD-170
------------------------------	---

REQUEST DATE July 14, 2010	IND NO. N/A	NDA/BLA NO. 201517	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW) New NDA
-------------------------------	----------------	-----------------------	--

NAME OF DRUG Morphine Sulfate	PRIORITY CONSIDERATION Standard	CLASSIFICATION OF DRUG Opioid	DESIRED COMPLETION DATE (Generally 1 week before the wrap up meeting) November 4, 2010 Action goal date: December 10, 2010
----------------------------------	------------------------------------	----------------------------------	--

NAME OF FIRM: Lannett, Inc.	PDUFA Date: January 1, 2011
--------------------------------	-----------------------------

**TYPE OF LABEL TO REVIEW**

<b>TYPE OF LABELING:</b> (Check all that apply) <input checked="" type="checkbox"/> PACKAGE INSERT (PI) <input type="checkbox"/> PATIENT PACKAGE INSERT (PPI) <input checked="" type="checkbox"/> CARTON/CONTAINER LABELING <input checked="" type="checkbox"/> MEDICATION GUIDE <input type="checkbox"/> INSTRUCTIONS FOR USE(IFU)	<b>TYPE OF APPLICATION/SUBMISSION</b> <input checked="" type="checkbox"/> ORIGINAL NDA/BLA <input type="checkbox"/> IND <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> SAFETY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> PLR CONVERSION	<b>REASON FOR LABELING CONSULT</b> <input checked="" type="checkbox"/> INITIAL PROPOSED LABELING <input type="checkbox"/> LABELING REVISION
---	--	---

**EDR link to submission:**  
The submission is located in the EDR using the following link: <\\CDSESUB1\EVSPROD\NDA201517\0000>

This is a marketed, unapproved product. It is 505(b)(2) referencing Roxane's product, NDA 22195.

NOTE:  
**Red-line label will be sent to DDMAC reviewer October 13 or 21, 2010.** We ask that this review be completed by November 4, 2010 or sooner so that we can send comments to the Sponsor. For questions, please contact Diana Walker, DAARP Project Manager, at 301-796-4029.

**Please Note:** There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. The DDMAC reviewer will contact you at a later date to obtain the substantially complete labeling for review.

**COMMENTS/SPECIAL INSTRUCTIONS:**

Labeling Meetings: [Insert Dates] October 13, 2010, October 21, 2010, November 4, 2010: **Red-line label will be sent to DDMAC reviewer October 13 or 21, 2010.**

Wrap-Up Meeting: [Insert Date] October 18, 2010

**Please send me the name(s) of the reviewer(s) so I can add them to meetings. Thanks!**

SIGNATURE OF REQUESTER

Diana L. Walker, PhD

Regulatory Project Manager

FDA/CDER/ODE II/DAARP

Tel: 301-796-4029

Fax: 301-796-9723/9713

Email: Diana.Walker@fda.hhs.gov

SIGNATURE OF RECEIVER

METHOD OF DELIVERY (Check one)

eMAIL

HAND

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

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

/s/

DIANA L WALKER  
07/14/2010

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Tuesday, July 13, 2010 9:58 AM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo  
**Subject:** NDA 201517 CMC Information Request 13jul10  
**Importance:** High

Dear Denise,

I have received an information request from our Chemistry, Manufacturing, and Controls (CMC) review team. Please submit these three information items to me via email followed by an official submission to your NDA as soon as possible, but no later than August 15, 2010.

**In our meeting minutes dated July 27, 2009, we provided you with advice regarding the oral dosing device to be co-packaged with the Morphine Sulfate Oral Solution, 20 mg/mL. Please provide the following information requested in the meeting minutes (note that the numbers in parenthesis correspond to the meeting minute numbers under "Comments on a Dosing Device"):**

- 1. (1.) Provide in-vitro data to show the accuracy of the device e.g., from in-use patient studies during clinical trials.**
- 2. (4.a.) Conduct usability studies on the proposed devices to validate the design and submit these findings accordingly. These usability studies must include patients, caregivers, and healthcare practitioners who may administer the product.**

**In addition provide the following information:**

- 3. Provide in vitro measurements of delivered volume using drug product similar to the data provided in the tables in the Container-Closure Section showing the delivery of water.**

**We remind you that all submissions must be paginated. We strongly recommend that all submissions be submitted as text rather than scanned images.**

Please contact me if you have questions or need clarification on this request.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

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

/s/

DIANA L WALKER  
07/13/2010

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Monday, July 12, 2010 1:28 PM  
**To:** 'Denise Fairman'  
**Cc:** Ernest Sabo  
**Subject:** NDA 201517 CMC Information Request 12jul10  
**Importance:** High

Dear Denise,

I have received an information request from our Chemistry, Manufacturing, and Controls (CMC) review team. Please submit this information to me via email followed by an official submission to your NDA as soon as possible, but no later than August 15, 2010.

**Your formulation contains three preservatives: sodium benzoate, methylparaben (MP), and propylparaben (PP). In the pharmaceutical development report, you state that the comparator drug, Roxane's morphine sulfate oral solution contains sodium benzoate but no MP or PP.**

**Submit the following information:**

- 1. Provide justifications for the use of the preservatives in the amounts used in the drug product.**
- 2. Provide the results of preservative effectiveness testing.**

Please contact me if you have questions or need clarification on this request.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

---

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

---

/s/

---

DIANA L WALKER  
07/12/2010

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Thursday, April 15, 2010 3:20 PM  
**To:** 'Denise Fairman'  
**Cc:** 'esabo@lannett.com'  
**Subject:** NDA 201517 FDA Request for Device Information 15apr10

Dear Ms. Fairman,

I have received a request for information from our review team.

Please submit to me 6 sample Oral Dosing Devices (Oral Dosers).

You can submit the samples directly to me at the following address:

Diana L. Walker  
Regulatory Health Project Manager  
Food and Drug Administration  
10903 New Hampshire Ave.  
Bldg. 22, Room 3209  
Silver Spring, MD 20993

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

**Walker, Diana**

---

**From:** Walker, Diana  
**Sent:** Wednesday, March 24, 2010 11:55 AM  
**To:** 'dfairman@lannett.com'  
**Cc:** 'esabo@lannett.com'  
**Subject:** NDA 201517 REMS Information Request 24mar10  
**Importance:** High  
**Attachments:** REMS Document templates.doc

Dear Ms. Fairman,

It has come to our attention that your original Risk Management submission is not complete. You are required to submit both the REMS and the REMS Supporting Document. You have submitted the REMS, but not the REMS Supporting Document.

I am attaching a template for both of these documents. Appendix A (p. 1 and 2) is the REMS (you have already submitted this, so no need to do so again); Appendix B (p. 3) is the REMS Supporting Document. You can use Appendix B as a template for what to submit.

Please submit the REMS Supporting Document as an amendment to your NDA 201517 as soon as possible.

Regards,

Diana

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
FDA/CDER/ODE II/DAAP  
Tel: 301-796-4029  
Fax: 301-796-9723/9713  
Email: Diana.Walker@fda.hhs.gov

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

---

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

---

/s/

---

DIANA L WALKER  
05/20/2010



NDA 201517

**FILING COMMUNICATION**

Lannett Holdings, Inc.  
9000 State Road  
Philadelphia, PA 19136

Attention: Ernest Sabo  
Vice President, Regulatory and Corporate Compliance

Dear Mr. Sabo:

Please refer to your new drug application (NDA) dated February 26, 2010, received March 1, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Morphine Sulfate Oral Solution, 20 mg/mL.

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 January 1, 2011.

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 November 26, 2010.

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

1. Your NDA does not contain adequate information to justify the safety of the drug product formulation. Specifically, your NDA must include justification for the safety of each excipient should individuals consume up to 2 grams per day of morphine via this formulation. Please refer to the FDA Guidance for Industry: Nonclinical Studies for Safety Evaluation of Pharmaceutical Excipients (May 2005) which is available on the

CDER web page at the following:

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

2. Your proposed drug substance specification for (b) (4) an impurity that contains an (b) (4) structural alert for genotoxicity, is not adequately justified for safety. As noted in the preNDA meeting minutes, impurities with structural alerts for genotoxicity must be reduced to NMT (b) (4) mcg/day or adequate safety qualification must be provided. Adequate safety qualification for this impurity must include a minimal genetic toxicology screen (two in vitro genetic toxicology studies, e.g., one point mutation assay and one chromosome aberration assay) with the isolated impurity, tested up to the limit dose for the assay.
3. You have not provided adequate justification for the safety of the container closure system in terms of the safety assessment of potential leachables extractables into the drug product solution. The safety assessment should be specifically discussed in module 2.6.6.8 (Toxicology Written Summary/Other Toxicity) of the NDA submission.

In addition, to support compatibility of your drug product with the proposed container/closure system, provide information on the compliance of all packaging components to appropriate CFRs for indirect food additives, in Module 3.2.P.7 (Quality, Container/Closure system).

4. Provide a summary of the stability data and the proposed expiration date in Section 8.1.
5. Provide in-use stability data, to support in-use shelf life and conditions for the multi-dose presentations of your oral solution.
6. Provide a photostability study for the drug product, as per ICH Q1B.
7. Information is being requested from the holder of DMF (b) (4)

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 have not already done so, you must 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>. The content of labeling must be in the Prescribing Information (physician labeling rule) format.

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

If you have any questions, contact Diana Walker, Ph.D., Regulatory Health Project Manager, at (301) 796-4029.

Sincerely,

*{See appended electronic signature page}*

Bob A. Rappaport, M.D.  
Director  
Division of Anesthesia and Analgesia Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

---

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

---

/s/

---

BOB A RAPPAPORT  
05/17/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		<b>REQUEST FOR CONSULTATION</b>		
TO (Office/Division): Patrick Marroum/Angelica Dorantes CDER/OPS/ONDQA		FROM (Name, Office/Division, and Phone Number of Requestor): Don Henry Project Manager, ONDQA, 301-796-4227 on behalf of Danae Christodoulou		
DATE April 14, 2010	IND NO.	NDA NO. 201517	TYPE OF DOCUMENT NDA submission	DATE OF DOCUMENT February 26, 2010
NAME OF DRUG Morphine sulfate oral solution 20 mg/ml		PRIORITY CONSIDERATION priority requested	CLASSIFICATION OF DRUG DAAP	DESIRED COMPLETION DATE July 26, 2010
NAME OF FIRM: Lannett Holdings, Inc.				
<b>REASON FOR REQUEST</b>				
<b>I. GENERAL</b>				
<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				
<b>II. BIOMETRICS</b>				
<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):				
<b>III. BIOPHARMACEUTICS</b>				
<input type="checkbox"/> DISSOLUTION <input type="checkbox"/> DEFICIENCY LETTER RESPONSE <input type="checkbox"/> BIOAVAILABILTY STUDIES <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS <input type="checkbox"/> PHASE 4 STUDIES <input checked="" type="checkbox"/> IN-VIVO WAIVER REQUEST				
<b>IV. DRUG SAFETY</b>				
<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				
<b>V. SCIENTIFIC INVESTIGATIONS</b>				
<input type="checkbox"/> CLINICAL <input type="checkbox"/> NONCLINICAL				
COMMENTS / SPECIAL INSTRUCTIONS: The applicant has requested a waiver of the in vivo studies. A justification is included in module 1.12. A review of the information is requested.				
SIGNATURE OF REQUESTOR {See appended electronic signature page}			METHOD OF DELIVERY (Check one) <input type="checkbox"/> DFS <input checked="" type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND	
PRINTED NAME AND SIGNATURE OF RECEIVER			PRINTED NAME AND SIGNATURE OF DELIVERER	

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

---

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

---

/s/

---

DON L HENRY  
04/14/2010

DANAE D CHRISTODOULOU  
04/14/2010

## REQUEST FOR CONSULTATION

TO (Office/Division):  
Chris Wheeler, OSE  
Abolade Adeolu, OSE  
WO22, Rm 3408 (796-0151)

FROM (Name, Office/Division, and Phone Number of Requestor):  
Diana Walker, RPM, for:  
Bob Rappaport, M.D.  
Director, Division of Anesthesia and Analgesia Products  
(DAAP), HFD-170

DATE  
March 23, 2010

IND NO.  
N/A

NDA NO.  
201517

TYPE OF DOCUMENT  
New NDA

DATE OF DOCUMENT  
March 1, 2010

NAME OF DRUG  
Morphine Sulfate Oral  
Solution, 20 mg/mL

PRIORITY CONSIDERATION  
Standard

CLASSIFICATION OF DRUG  
opioid

DESIRED COMPLETION DATE  
October 31, 2010  
Action goal date:  
December 10, 2010

NAME OF FIRM: Lannett

### 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:

Application:

This is a 505(b)(2) application, an opioid analgesic for the relief of moderate to severe acute and chronic pain.

Request:

The Division requests that you please review this NDA submission labeling in Module 1.14, including the Package insert, carton and container, and Medication Guide and provide feedback by October 31, 2010. If you require additional items or clarification from the sponsor, please send those requests to me as soon as you are aware of them. Please notify me of any reviewers for this consult who need to be invited to the team meetings.

The submission is located in the EDR using the following link: \\CDSESUB1\EVSPROD\NDA201517

Filing Meeting Date: April 15, 2010/Action Goal Date: December 10, 2010 / PDUFA Date: January 1, 2011

NOTE:

We ask that this review be completed by October 18, 2010. Rob Shibuya will be the MO (301-796-1292). For questions, please contact Diana Walker, DAARP Project Manager, at 301-796-4029.

SIGNATURE OF REQUESTOR

Diana L. Walker, PhD

Regulatory Project Manager

FDA/CDER/ODE II/DAAP

Tel: 301-796-4029

Fax: 301-796-9723/9713

Email: Diana.Walker@fda.hhs.gov

METHOD OF DELIVERY (Check one)

DFS

EMAIL

MAIL

HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

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

/s/

DIANA L WALKER  
03/23/2010

## REQUEST FOR CONSULTATION

TO (Office/Division):  
Chris Wheeler, OSE  
Abolade Adeolu, OSE  
WO22, Rm 3408 (796-0151)

FROM (Name, Office/Division, and Phone Number of Requestor):  
Diana Walker, RPM, for:  
Bob Rappaport, M.D.  
Director, Division of Anesthesia and Analgesia Products  
(DAAP), HFD-170

DATE  
March 23, 2010

IND NO.  
N/A

NDA NO.  
201517

TYPE OF DOCUMENT  
New NDA

DATE OF DOCUMENT  
March 1, 2010

NAME OF DRUG  
Morphine Sulfate Oral  
Solution, 20 mg/mL

PRIORITY CONSIDERATION  
Standard

CLASSIFICATION OF DRUG  
opioid

DESIRED COMPLETION DATE  
October 31, 2010  
Action goal date:  
December 10, 2010

NAME OF FIRM: Lannett

### 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:**

**Application:**

This is a 505(b)(2) application, an opioid analgesic for the relief of moderate to severe acute and chronic pain.

**Request:**

The Sponsor has submitted a MedGuide and Timetable for assessments only REMS. The Division requests that you please review this NDA submission REMS in Module 1.16 (Med Guide is in Module 1.14), and provide feedback, both ongoing at team meetings, and a final review by October 31, 2010.

The submission is located in the EDR using the following link: \\CDSESUB1\EVSPROD\NDA201517

Please let me know who to invite for team meetings.

Filing Meeting Date: April 15, 2010/Action Goal Date: December 10, 2010 / PDUFA Date: January 1, 2011  
NOTE:  
We ask that this review be completed by October 18, 2010. Rob Shibuya will be the MO (301-796-1292). For questions, please contact Diana Walker, DAARP Project Manager, at 301-796-4029.

SIGNATURE OF REQUESTOR Diana L. Walker, PhD Regulatory Project Manager FDA/CDER/ODE II/DAAP Tel: 301-796-4029 Fax: 301-796-9723/9713 Email: Diana.Walker@fda.hhs.gov	METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS <input checked="" type="checkbox"/> EMAIL <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
--	---

PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER
--	---

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

---

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

---

/s/

---

DIANA L WALKER  
03/23/2010

## REQUEST FOR CONSULTATION

TO (Office/Division):

**Controlled Substances Staff (CSS)**  
Attention: Corrine Moody  
HFD-009

FROM (Name, Office/Division, and Phone Number of Requestor):

**Bob Rappaport, M.D.**  
Director, Division of Anesthesia and Analgesia Products  
(DAAP), HFD-170

DATE March 18, 2010	IND NO. N/A	NDA NO. 201517	TYPE OF DOCUMENT New NDA	DATE OF DOCUMENT March 1, 2010
------------------------	----------------	-------------------	-----------------------------	-----------------------------------

NAME OF DRUG <b>Morphine Sulfate Oral Solution, 20 mg/mL</b>	PRIORITY CONSIDERATION <b>Standard</b>	CLASSIFICATION OF DRUG <b>opioid</b>	DESIRED COMPLETION DATE <b>October 18, 2010</b>  Action goal date: <b>December 10, 2010</b>
---	---	---	---

NAME OF FIRM: **Lannett**

### 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:**

**Application:**

This is a 505(b)(2) application, an opioid analgesic for the relief of moderate to severe acute and chronic pain.

**Request:**

Please review and provide your assessment of the abuse potential or other potential CS issues for Morphine Sulphate. The submission is located in the EDR using the following link: \\CDSesub1\evsprod\NDA201517

Filing Meeting Date: April 15, 2010/Action Goal Date: December 10, 2010 / PDUFA Date: January 1, 2011

**NOTE:**

We ask that this review be completed by October 18, 2010 (Date of the Wrap-up meeting). Rob Shibuya will be the MO (301-796-1292). For questions, please contact Diana Walker, DAARP Project Manager, at 301-796-4029.

<p>SIGNATURE OF REQUESTOR Diana L. Walker, PhD Regulatory Project Manager FDA/CDER/ODE II/DAARP Tel: 301-796-4029 Fax: 301-796-9723/9713 Email: Diana.Walker@fda.hhs.gov</p>	<p>METHOD OF DELIVERY (Check one) <input checked="" type="checkbox"/> DFS      <input checked="" type="checkbox"/> EMAIL      <input type="checkbox"/> MAIL      <input type="checkbox"/> HAND</p>
<p>PRINTED NAME AND SIGNATURE OF RECEIVER</p>	<p>PRINTED NAME AND SIGNATURE OF DELIVERER</p>

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

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

/s/

DIANA L WALKER  
03/18/2010



NDA 201517

**NDA ACKNOWLEDGMENT**

Lannett Holdings, Inc.  
9000 State Road  
Philadelphia, PA 19136

Attention: Ernest Sabo  
Vice President, Regulatory and Corporate Compliance

Dear Mr. Sabo:

We have received your new drug application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Morphine Sulfate Oral Solution, 20 mg/mL

Date of Application: February 26, 2010

Date of Receipt: March 1, 2010

Our Reference Number: NDA 201517

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 April 30, 2010, 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.

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 Anesthesia and Analgesia 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>

If you have any questions, call me at (301) 796-4029.

Sincerely,

*{See appended electronic signature page}*

Diana L. Walker, Ph.D.  
Regulatory Health Project Manager  
Division of Anesthesia and Analgesia Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-201517	ORIG-1	LANNETT HOLDINGS INC	morphine sulfate oral solution 20 mg/mL

---

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

---

/s/

---

DIANA L WALKER  
03/18/2010