

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**022272Orig1s027**

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

## EXCLUSIVITY SUMMARY

NDA # 022272

SUPPL # S-027

HFD # 170

Trade Name: OXYCONTIN

Generic Name: oxycodone extended-release tablets

Applicant Name: Purdue Pharma L.P.

Approval Date, If Known: August 13, 2015

### 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

#### SE5

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

YES  NO

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

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

d) Did the applicant request exclusivity?

YES  NO

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

**6 months of pediatric exclusivity** (b)(4) **based on the conduct of clinical trials essential for approval of this application.**

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

(b)(4)

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?

(b)(4)

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). **Many NDAs and ANDAs.**

NDA#

NDA#

NDA#

2. Combination product.

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

YES  NO

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:
- i. A Multicenter, Inpatient, Open-Label, Dose-Ranging Study to Characterize the Pharmacokinetics and Safety of an Oral Liquid Formulation of Oxycodone in Patients From Birth to 4 Years, Who Require Opioid Analgesia
  - ii. Multicenter, Double Blind, Randomized, Dose Ranging Study, in Pediatric Patients 5 to  $\leq$  16 Years of Age Receiving Morphine As Standard Supplemental Pain Medication, to Evaluate Pharmacokinetics, Efficacy and Safety of Oxy Pediatric Liquid (1 mg/mL) Versus Placebo in the Treatment of Acute Moderate to Severe Pain
  - iii. An Open-label, Multicenter Study of the Safety of Twice Daily Oxycodone Hydrochloride Controlled-release Tablets in Opioid Experienced Children from Ages 6 to 16 Years Old, Inclusive, with Moderate to Severe Malignant and/or Nonmalignant Pain Requiring Opioid Analgesics

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

Investigation #3

YES

NO

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

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

Investigation #3

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"):

- i. A Multicenter, Inpatient, Open-Label, Dose-Ranging Study to Characterize the Pharmacokinetics and Safety of an Oral Liquid Formulation of Oxycodone in Patients From Birth to 4 Years, Who Require Opioid Analgesia
- ii. Multicenter, Double Blind, Randomized, Dose Ranging Study, in Pediatric Patients 5 to ≤ 16 Years of Age Receiving Morphine As Standard Supplemental Pain Medication, to Evaluate Pharmacokinetics, Efficacy and Safety of Oxy Pediatric Liquid (1 mg/mL) Versus Placebo in the Treatment of Acute Moderate to Severe Pain
- iii. An Open-label, Multicenter Study of the Safety of Twice Daily Oxycodone Hydrochloride Controlled-release Tablets in Opioid Experienced Children from Ages 6 to 16 Years Old, Inclusive, with Moderate to Severe Malignant and/or Nonmalignant Pain Requiring Opioid Analgesics

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



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Name of person completing form: Diana L. Walker, PhD  
Title: Senior Regulatory Health Project Manager, DAAAP  
Date: August 12, 2015

Name of Division Director signing form: Sharon Hertz, MD  
Title: Director, DAAAP

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

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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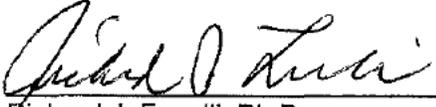
/s/  
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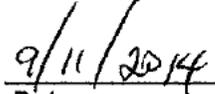
DIANA L WALKER  
08/13/2015

SHARON H HERTZ  
08/13/2015

### 1.3.3 DEBARMENT CERTIFICATION

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

  
Richard J. Fanelli, Ph.D.  
Head of Regulatory Affairs

  
Date

# ACTION PACKAGE CHECKLIST

## APPLICATION INFORMATION<sup>1</sup>

NDA # 22272 BLA #	NDA Supplement # 027 BLA Supplement #	If NDA, Efficacy Supplement Type: SE5 <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: OxyContin Established/Proper Name: oxycodone hydrochloride Dosage Form: extended-release tablets		Applicant: Purdue Pharma Agent for Applicant (if applicable):
RPM: Diana Walker		Division: DAAAP
NDA Application Type: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)  BLA Application Type: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a) Efficacy Supplement: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a)		<p><b>For ALL 505(b)(2) applications, two months prior to EVERY action:</b></p> <ul style="list-style-type: none"> <li>• Review the information in the 505(b)(2) Assessment and submit the draft<sup>2</sup> to CDER OND IO for clearance.</li> <li>• Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)           <ul style="list-style-type: none"> <li><input type="checkbox"/> No changes</li> <li><input type="checkbox"/> New patent/exclusivity (notify CDER OND IO)</li> </ul> </li> </ul> <p>Date of check:</p> <p><i>Note: 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.</i></p>
Actions <ul style="list-style-type: none"> <li>• Proposed action</li> <li>• User Fee Goal Date is June 10, 2015. Action taken August 13, 2015</li> <li>• Previous actions (specify type and date for each action taken)</li> </ul>		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR  <input checked="" type="checkbox"/> None
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf</a> ). If not submitted, explain _____		<input type="checkbox"/> Received
❖ Application Characteristics <sup>3</sup>		

<sup>1</sup> The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

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

<sup>3</sup> Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA.

Review priority:  Standard  Priority  
 Chemical classification (new NDAs only):  
*(confirm chemical classification at time of approval)*

- |   |   |
|---|---|
| <input type="checkbox"/> Fast Track                       | <input type="checkbox"/> Rx-to-OTC full switch    |
| <input type="checkbox"/> Rolling Review                   | <input type="checkbox"/> Rx-to-OTC partial switch |
| <input type="checkbox"/> Orphan drug designation          | <input type="checkbox"/> Direct-to-OTC            |
| <input type="checkbox"/> Breakthrough Therapy designation |   |

NDAs: Subpart H  
 Accelerated approval (21 CFR 314.510)  
 Restricted distribution (21 CFR 314.520)

BLAs: Subpart E  
 Accelerated approval (21 CFR 601.41)  
 Restricted distribution (21 CFR 601.42)

Subpart I  
 Approval based on animal studies

Subpart H  
 Approval based on animal studies

- Submitted in response to a PMR
- Submitted in response to a PMC
- Submitted in response to a Pediatric Written Request

- REMS:  MedGuide  
 Communication Plan  
 ETASU  
 MedGuide w/o REMS  
 REMS not required

Comments:

❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 <i>(approvals only)</i>	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications <i>(approvals only)</i>	
• Office of Executive Programs (OEP) liaison has been notified of action	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
• Indicate what types (if any) of information were issued	<input type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input checked="" type="checkbox"/> CDER Q&As <input checked="" type="checkbox"/> Other CDER Conversation piece
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)?	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
• If so, specify the type	
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<b>CONTENTS OF ACTION PACKAGE</b>	
<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

### Action Letters

❖ Copies of all action letters <i>(including approval letter with final labeling)</i>	Action and date: Approval: August 13, 2015
Labeling	
❖ Package Insert <i>(write submission/communication date at upper right of first page of PI)</i>	
• Most recent draft labeling <i>(if it is division-proposed labeling, it should be in track-changes format)</i>	<input checked="" type="checkbox"/> Included Approved August 13, 2015
• Original applicant-proposed labeling	<input checked="" type="checkbox"/> Included Original proposed December 2014
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling <i>(write submission/communication date at upper right of first page of each piece)</i>	<input 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
• Most-recent draft labeling <i>(if it is division-proposed labeling, it should be in track-changes format)</i>	<input checked="" type="checkbox"/> Included: Approved August 13, 2015
• Original applicant-proposed labeling	<input checked="" type="checkbox"/> Included: Original proposed December 2014
❖ 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>	
• Most-recent draft labeling	<input type="checkbox"/> Included
❖ Proprietary Name	
• Acceptability/non-acceptability letter(s) <i>(indicate date(s))</i>	
• Review(s) <i>(indicate date(s))</i>	
❖ Labeling reviews <i>(indicate dates of reviews)</i>	RPM: <input checked="" type="checkbox"/> None DMEPA: <input checked="" type="checkbox"/> None DMPP/PLT: <input type="checkbox"/> None May 27, 2015 OPDP: <input type="checkbox"/> None May 21, 2015 SEALD: <input checked="" type="checkbox"/> None CSS: <input checked="" type="checkbox"/> None Product Quality <input checked="" type="checkbox"/> None Other: <input type="checkbox"/> None PMHS labeling review dated June 11, 2015
Administrative / Regulatory Documents	
❖ RPM Filing Review <sup>4</sup> /Memo of Filing Meeting <i>(indicate date of each review)</i>	February 4, 2015
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	<input checked="" type="checkbox"/> Not a (b)(2)
❖ NDAs only: Exclusivity Summary <i>(signed by Division Director)</i>	<input checked="" type="checkbox"/> Included
❖ 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>	

<sup>4</sup> Filing reviews for scientific disciplines are NOT required to be included in the action package.

<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 <u>May 13, 2015</u> If PeRC review not necessary, explain: _____</li> </ul> </li> </ul>	
<ul style="list-style-type: none"> <li>Breakthrough Therapy Designation</li> </ul>	<input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> <li>Breakthrough Therapy Designation Letter(s) (granted, denied, an/or rescinded)</li> </ul>	
<ul style="list-style-type: none"> <li>CDER Medical Policy Council Breakthrough Therapy Designation Determination Review Template(s) (<i>include only the completed template(s) and not the meeting minutes</i>)</li> </ul>	
<ul style="list-style-type: none"> <li>CDER Medical Policy Council Brief – Evaluating a Breakthrough Therapy Designation for Rescission Template(s) (<i>include only the completed template(s) and not the meeting minutes</i>)</li> </ul> <p>(<i>completed CDER MPC templates can be found in DARRTS as clinical reviews or on the MPC SharePoint Site</i>)</p>	
<ul style="list-style-type: none"> <li>Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, Formal Dispute Resolution Request decisional letters, etc.) (<i>do not include previous action letters, as these are located elsewhere in package</i>)</li> </ul>	Included
<ul style="list-style-type: none"> <li>Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)</li> </ul>	(b) (4)
<ul style="list-style-type: none"> <li>Minutes of Meetings</li> </ul>	
<ul style="list-style-type: none"> <li>If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)</li> </ul>	<input checked="" type="checkbox"/> N/A or no mtg
<ul style="list-style-type: none"> <li>Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)</li> </ul>	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> <li>EOP2 meeting (<i>indicate date of mtg</i>)</li> </ul>	<input checked="" type="checkbox"/> No mtg
<ul style="list-style-type: none"> <li>Mid-cycle Communication (<i>indicate date of mtg</i>)</li> </ul>	<input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> <li>Late-cycle Meeting (<i>indicate date of mtg</i>)</li> </ul>	<input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> <li>Other milestone meetings (e.g., EOP2a, CMC focused milestone meetings) (<i>indicate dates of mtgs</i>)</li> </ul>	PeRC: May 26, 2015
<ul style="list-style-type: none"> <li>Advisory Committee Meeting(s)</li> </ul>	<input checked="" type="checkbox"/> No AC meeting
<ul style="list-style-type: none"> <li>Date(s) of Meeting(s)</li> </ul>	
<b>Decisional and Summary Memos</b>	
<ul style="list-style-type: none"> <li>Office Director Decisional Memo (<i>indicate date for each review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> <li>Division Director Summary Review (<i>indicate date for each review</i>)</li> </ul>	<input type="checkbox"/> None August 13, 2015
<ul style="list-style-type: none"> <li>Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)</li> </ul>	<input type="checkbox"/> None May 26, 2015
<ul style="list-style-type: none"> <li>PMR/PMC Development Templates (<i>indicate total number</i>)</li> </ul>	<input type="checkbox"/> None 2 templates, both dated August 13, 2015
<b>Clinical</b>	

❖ Clinical Reviews	
• Clinical Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> No separate review
• Clinical review(s) (indicate date for each review)	February 2 and May 18, 2015
• Social scientist review(s) (if OTC drug) (indicate date for each review)	<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 (indicate date of review/memo)	Included in Clinical Review dated May 18, 2015.
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (indicate date of each review)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (indicate date of each review)	<input checked="" type="checkbox"/> N/A
❖ Risk Management <ul style="list-style-type: none"> <li>• REMS Documents and REMS Supporting Document (indicate date(s) of submission(s))</li> <li>• REMS Memo(s) and letter(s) (indicate date(s))</li> <li>• Risk management review(s) and recommendations (including those by OSE and CSS) (indicate date of each review and indicate location/date if incorporated into another review)</li> </ul>	July 31, 2015 (see approval letter – attached)  N/A  <input type="checkbox"/> None August 13, 2015
❖ OSI Clinical Inspection Review Summary(ies) (include copies of OSI letters to investigators)	<input type="checkbox"/> None requested April 30 and June 1 and 4, and August 7, 2015
<b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None	
Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input type="checkbox"/> No separate review
Clinical Microbiology Review(s) (indicate date for each review)	<input type="checkbox"/> None
<b>Biostatistics</b> <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> No separate review
Statistical Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> No separate review
Statistical Review(s) (indicate date for each review)	<input type="checkbox"/> None February 2 and May 7, 2015
<b>Clinical Pharmacology</b> <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> No separate review
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> No separate review
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None February 4 and May 15, 2015
❖ OSI Clinical Pharmacology Inspection Review Summary (include copies of OSI letters)	<input checked="" type="checkbox"/> None requested

<b>Nonclinical</b> <input checked="" type="checkbox"/> None	
<b>Pharmacology/Toxicology Discipline Reviews</b>	
• ADP/T Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> No separate review
• Supervisory Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> No separate review
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>	<input type="checkbox"/> None
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer <i>(indicate date for each review)</i>	<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies <i>(indicate date for each review)</i>	<input type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input type="checkbox"/> None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary <i>(include copies of OSI letters)</i>	<input type="checkbox"/> None requested
<b>Product Quality</b> <input type="checkbox"/> None	
<b>Product Quality Discipline Reviews</b>	
• Tertiary review <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Secondary review (e.g., Branch Chief) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) <i>(indicate date for each review)</i>	<input type="checkbox"/> None May 11, 2015
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>	July 15, 2015
<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 type="checkbox"/> Facilities inspections <i>(action must be taken prior to the re-evaluation date) (only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change)</i>	<input type="checkbox"/> Acceptable Re-evaluation date: <input type="checkbox"/> Withhold recommendation <input checked="" type="checkbox"/> Not applicable

### Day of Approval Activities

❖ For all 505(b)(2) applications: <ul style="list-style-type: none"> <li>• Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)</li> </ul>	<input type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity ( <i>Notify CDER OND IO</i> )
<ul style="list-style-type: none"> <li>• Finalize 505(b)(2) assessment</li> </ul>	<input type="checkbox"/> Done
❖ For Breakthrough Therapy (BT) Designated drugs: <ul style="list-style-type: none"> <li>• Notify the CDER BT Program Manager</li> </ul>	<input type="checkbox"/> Done <i>(Send email to CDER OND IO)</i>
❖ For products that need to be added to the flush list (generally opioids): <u>Flush List</u> <ul style="list-style-type: none"> <li>• Notify the Division of Online Communications, Office of Communications</li> </ul>	<input type="checkbox"/> Done
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	<input checked="" type="checkbox"/> Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	<input checked="" type="checkbox"/> Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	<input type="checkbox"/> Done
❖ Ensure Pediatric Record is accurate	<input type="checkbox"/> Done
❖ Send approval email within one business day to CDER-APPROVALS	<input checked="" type="checkbox"/> Done

**From:** [Walker, Diana](#)  
**To:** ["Connelly, Beth \(Beth.Connelly@pharma.com\)"](#)  
**Cc:** ["Richard" "Fanelli \(Richard.Fanelli@pharma.com\)"](#)  
**Subject:** Addendum: sNDA 22272 S-027 REMS information request 30jul15  
**Date:** Thursday, July 30, 2015 11:18:25 AM  
**Attachments:** [OxyContin 022272 Blueprint \(7.30.15\).doc](#)  
**Importance:** High

---

Dear Beth,

Please note the following comments in reference to our request below:

- **Please note the track changes in the following ER/LA REMS materials:**
  - **Drug Specific Information regarding OxyContin in the FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics**
  - **ER/LA REMS website**
  - **Patient Counselling Document**
- **Please ensure that the ER/LA REMS materials match the final label for NDA 22272.**
- **The REMS materials are not appropriate for use in a promotional manner.**

---

**From:** Walker, Diana  
**Sent:** Thursday, July 30, 2015 11:15 AM  
**To:** Connelly, Beth (Beth.Connelly@pharma.com)  
**Cc:** Richard 'Fanelli' (Richard.Fanelli@pharma.com)  
**Subject:** sNDA 22272 S-027 REMS information request 30jul15

Dear Beth,

Please find attached the proposed revised REMS blueprint. Please review this document. Accept all of the changes with which you agree, and if there are changes for which you do not agree or wish to propose alternative language, please make these revisions in track changes. Please submit your new REMS to your NDA as soon as possible. Please submit both clean and track-changes versions (submit the track changes version only if you have any track changes revisions for us to review).

If you have any questions, feel free to contact me. Kindly acknowledge receipt of this email.

Warm regards,

Diana

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

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/s/  
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DIANA L WALKER  
08/11/2015

**From:** [Walker, Diana](#)  
**To:** [Connelly, Beth](#)  
**Subject:** Follow-up request - RE: Response to : sNDA 022272 S-027 Clinical Information Request 26may15  
**Date:** Friday, May 29, 2015 5:00:54 PM  
**Importance:** High

---

Dear Beth,

I have received the following follow-up information request from our review team in regard to the information you sent us in the email below. Please submit the following information to your NDA along with your previous responses.

Please respond to the following request:

**In addition to what you have already provided in your response to the information request dated May 26, 2015, for Study OXP1005, provide narratives for the individual patients with low oxygen saturations.**

34020  
34021  
34022  
34025  
34026  
34016

Warm regards,

Diana

---

**From:** Connelly, Beth [mailto:[Beth.Connelly@pharma.com](mailto:Beth.Connelly@pharma.com)]  
**Sent:** Friday, May 29, 2015 1:56 PM  
**To:** Walker, Diana  
**Subject:** Response to : sNDA 022272 S-027 Clinical Information Request 26may15

Hi Diana,  
One more! Attached above is our response to the information requested in the May 26, 2015 IR below. This information is also being submitted officially through the electronic gateway. If you have any questions, please let me know.  
Have a good weekend!  
Best regards,  
Beth

***Beth Connelly***  
*Associate Director, Regulatory Affairs*  
*Purdue Pharma L. P.*  
*Telephone: 203-588-7289*  
*email: [beth.connelly@pharma.com](mailto:beth.connelly@pharma.com)*

---

**From:** Walker, Diana [<mailto:Diana.Walker@fda.hhs.gov>]  
**Sent:** Tuesday, May 26, 2015 10:41 AM  
**To:** Connelly, Beth  
**Subject:** sNDA 022272 S-027 Clinical Information Request 26may15  
**Importance:** High

Dear Beth,

I have received the following request for information from our clinical review team. Please send me your response via email as soon as possible but no later than close of business **Friday, May 29, 2015**, followed by a submission to your application.

Please respond to the following request for information:

**Provide narratives for the following patients from Study OXP1005 discussing the determination that each patient met the inclusion/exclusion criteria regarding respiratory status.**

**34020**  
**34021**  
**34022**  
**34025**  
**34026**  
**34016**

Warm regards,

Diana

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

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/s/  
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DIANA L WALKER  
06/10/2015

**From:** [Walker, Diana](#)  
**To:** [Connelly, Beth \(Beth.Connelly@pharma.com\)](mailto:Beth.Connelly@pharma.com)  
**Subject:** NDA 22272 [REDACTED] (b) (4) 08Jun2015  
**Date:** Monday, June 08, 2015 2:51:56 PM

---

Dear Beth,

Although I am communicating this to you via email, this is the official communication to you concerning [REDACTED] (b) (4) with your recent supplement sNDA 22272/S-027; you will not receive an additional letter. Note that the action on your efficacy supplement sNDA 22272/S-027 is still pending.

(b) (4)

Regards,

Diana

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

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/s/  
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DIANA L WALKER  
06/10/2015

**MEMORANDUM**

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

**DATE:** June 8, 2015

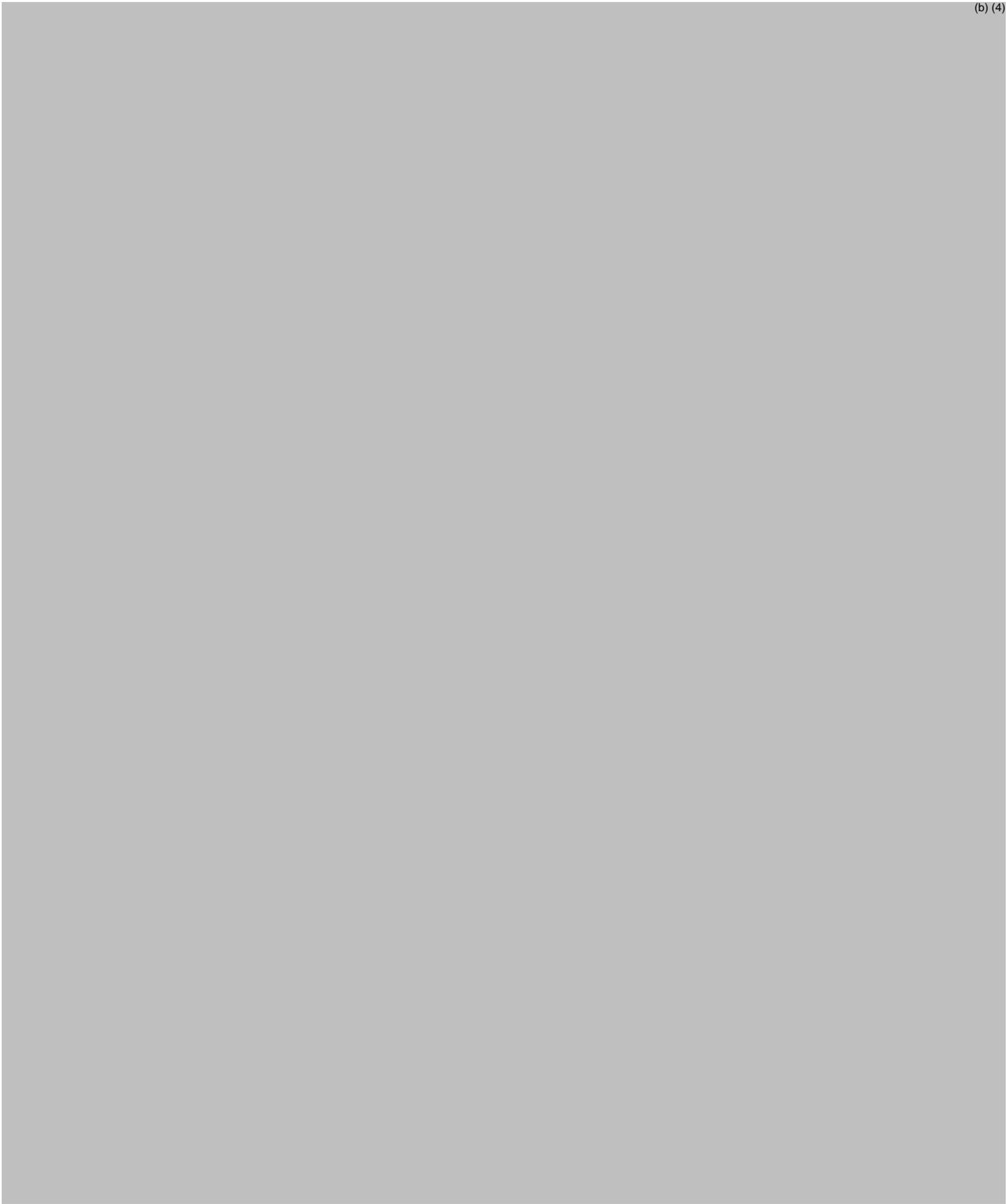
**FROM:** Pediatric Exclusivity Board

**SUBJECT:** (b) (4) Pediatric Exclusivity for OxyContin<sup>®</sup> (oxycodone hydrochloride extended-release tablets)

**TO:** NDA 022272/S-027

(b) (4)





## II. Summary of Factual Background

The WR was issued by FDA for oxycodone hydrochloride to obtain important dosing, efficacy, and safety information in pediatric patients with acute pain from birth through 16 years of age, and dosing, efficacy, and safety information in pediatric patients with chronic pain<sup>1</sup> age 6 through 16 years of age. Thus, the objective of the WR was to obtain information in pediatric patients for the use of oxycodone hydrochloride in both acute and chronic pain.<sup>2</sup>

The following facts summarize the interactions between FDA and Purdue concerning this WR:

- On August 28, 1998, Purdue submitted a Proposed Pediatric Study Request (PPSR) for oxycodone;
- On November 4, 1998, FDA issued a WR for oxycodone;
- On February 2, 2001, Purdue submitted an amended PPSR after an October 10, 2000, submission and teleconferences on December 19 and 28, 2000;

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<sup>1</sup> The WR refers to “severe pain requiring around-the-clock opioid therapy for an extended period of time;” however, we use for brevity the term “chronic pain” in this response.

<sup>2</sup> See amended WR issued by FDA on November 14, 2011.

- On December 31, 2001, FDA issued an amended WR;
- On November 11, 2003, Purdue submitted pediatric protocol changes based on FDA input made on November 14, 2002, and April 3, 2003;
- On February 4, 2004, Purdue terminated its pediatric program due to company issues;
- On December 18, 2008, Purdue submitted a PPSR that included the three prior studies and two additional studies;
- On May 13, 2009, FDA reissued a WR for oxycodone in response to the December 18, 2008, PPSR;
- On October 30, 2009, Purdue submitted written request for clarification;
- On May 14, 2010, FDA provided general advice;
- On June 4, 2010, Purdue submitted an amended PPSR;
- On November 18, 2010, FDA issued an amended WR;
- On September 21, 2011, Purdue submitted an amended PPSR to change the due date from December 10, 2011, to January 31, 2016;
- On November 14, 2011, FDA issued an amended WR;
- On December 10, 2014, Purdue submitted NDA 022272/S-027 with a request for a pediatric exclusivity determination for oxycodone.

(b) (4)





## IV. Conclusion

(b) (4)



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MATTHEW A BACHO  
06/08/2015

JOHN K JENKINS  
06/08/2015



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/s/  
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MATTHEW A BACHO  
06/05/2015

JOHN K JENKINS  
06/08/2015

## Jani, Parinda

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**From:** Jani, Parinda  
**Sent:** Thursday, June 04, 2015 10:50 AM  
**To:** Beth.Connelly@pharma.com  
**Cc:** Walker, Diana  
**Subject:** IR for NDA 22272/S-027

Hi Beth:

This is in reference to your submission dated June 3, 2015, in which you have provided narratives from Study OXP1005 for the individual patients with low oxygen saturation. We have additional request, **"Were any of these patients receiving supplemental oxygen? If so, summarize that experience for each patient at baseline and throughout the treatment period. Provide CRFs for the patients."**

Thanks

Parinda Jani  
Chief, Project Management Staff  
Division of Anesthesia, Analgesia, and Addiction Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research  
Tel # (301) 796-1232

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/s/  
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PARINDA JANI  
06/04/2015

**From:** [Walker, Diana](#)  
**To:** [Connelly, Beth \(Beth.Connelly@pharma.com\)](mailto:Beth.Connelly@pharma.com)  
**Subject:** sNDA22272 (S-027) Clinical Pharmacology Information Request 08may15  
**Date:** Friday, May 08, 2015 10:26:39 AM  
**Importance:** High

---

Dear Beth,

I have received the following information request from our Clinical Pharmacology review team. Please submit this as an amendment to your supplement as soon as possible.

Please respond to the following:

**With regard to Bioanalytical Report Number: OXP-P-003 supporting study “OXP3003”, submit the report titled “OXYR04-078:1, “Long-Term Stability of Oxycodone, Noroxycodone and Oxymorphone in Human Plasma and Spiking Solution”, X. Fang, 21 April 2005.”**

Warm regards,

Diana

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

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DIANA L WALKER  
05/08/2015

**From:** [Walker, Diana](#)  
**To:** [Connelly, Beth](#)  
**Subject:** sNDA22272 (S-027) Clinical Pharmacology/Labeling Information Request 05may15  
**Date:** Tuesday, May 05, 2015 9:16:49 AM  
**Importance:** High

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Dear Beth,

I have received the following information request from our review team concerning your proposed label. Please respond to me as soon as possible, or no later than Tuesday, May 12, via email. You can send me your revised section 12.3 as a Word document via email.

With regard to your proposed labeling in section 12.3 Pharmacokinetics, we note the proposed description of population pk. However, we want you to revise the section to describe pediatric experience (>6 years) with Oxycontin as follows:

As noted in adults, in a study comparing 10 mg of OXYCONTIN to 5 mg of immediate-release oxycodone in pediatric patients, the peak plasma concentrations (C<sub>max</sub>) of oxycodone were similar (**NOTE to sponsor: These are results shown by from study OC96-0602**).

Dose proportional PK was observed with OXYCONTIN 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, strengths for both peak plasma concentrations (C<sub>max</sub>) and extent of absorption (AUC) (see Table #) for age groups 6 -12 and 12 – 17 yrs (**NOTE to sponsor: Describe results from studies OTR1020 and OTR3001**).

**(NOTE to sponsor):** Arrange the table for the two age groups 6 -12 yrs and >12 – 17 yrs.

Regimen	Dosage Form	AUC (ng.hr/mL)	C <sub>max</sub> (ng/mL)
Single dose/steady- state	10 mg		
	15 mg		
	20 mg		
	40 mg		

**NOTE to sponsor:** Describe clearance and volume of distribution of oxycodone in the age groups 6 -12 yrs and >12 – 17 yrs.

Steady-state plasma concentrations of oxycodone were achieved within XXX hours of initiation of dosing with OXYCONTIN.

Warm regards,

Diana

Diana L. Walker, Ph.D.  
Sr. Regulatory Health Project Manager

FDA/CDER/ODE II/DAAAP  
Tel: 301-796-4029  
Email: [Diana.Walker@fda.hhs.gov](mailto:Diana.Walker@fda.hhs.gov)

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DIANA L WALKER  
05/06/2015

**From:** [Walker, Diana](#)  
**To:** [Connelly, Beth](#)  
**Subject:** sNDA22272 (S-027) Product Quality/CMC Information Request 05may15  
**Date:** Tuesday, May 05, 2015 1:07:39 PM  
**Importance:** High

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Dear Beth,

I have received the following information request from our Product Quality review team concerning your formulation development. Although some development reports were submitted on April 6, the review team has not been able to locate the specific information requested below. Please respond to me as soon as possible or by tomorrow, May 6, at noon, with your general response. If you do need to provide an additional technical report, please submit this as an amendment to your supplement as soon as possible.

Please respond to the following:

**On page 15 of the Annotated Detailed Responses to WR 03SEP14, the response states that**

(b) (4)



Warm regards,

Diana

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

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DIANA L WALKER  
05/06/2015

**From:** [Walker, Diana](#)  
**To:** [Connelly, Beth \(Beth.Connelly@pharma.com\)](mailto:Beth.Connelly@pharma.com)  
**Subject:** sNDA 022272 S-027 Clinical Information Request 26may15  
**Date:** Tuesday, May 26, 2015 10:41:09 AM  
**Importance:** High

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Dear Beth,

I have received the following request for information from our clinical review team. Please send me your response via email as soon as possible but no later than close of business **Friday, May 29, 2015**, followed by a submission to your application.

Please respond to the following request for information:

**Provide narratives for the following patients from Study OXP1005 discussing the determination that each patient met the inclusion/exclusion criteria regarding respiratory status.**

**34020**

**34021**

**34022**

**34025**

**34026**

**34016**

Warm regards,

Diana

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

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DIANA L WALKER  
05/27/2015

**PeRC Meeting Minutes  
May 13, 2015**

**PeRC Members Attending:**

Lynne Yao

Robert "Skip" Nelson

Wiley Chambers

Rosemary Addy

George Greeley

Peter Starke

Daiva Shetty (Did not review [REDACTED] (b) (4) and non-responsive )

Freda Cooner

Tom Smith

Karen Davis-Bruno

Daiva Shetty

Andrew Mulberg

Greg Reaman (Did not review [REDACTED] (b) (4) and non-responsive )

Adrienne Hornatko-Munoz

Andrew Mosholder (Did not review [REDACTED] (b) (4) and non-responsive )

Hari Cheryl Sachs

Julia Pinto

Shrikant Pagay

Lily Mulugeta

Kevin Krudys

Rachel Witten

Dianne Murphy

Maura O'Leary

Kristiana Brugger

## Agenda

(b) (4) and non-responsive

9:50	NDA	22272/27	Oxycontin	(b) (4) WR Review	Treatment of acute moderate to severe pain	(b) (4) and non-responsive
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(b) (4) and non-responsive



**Oxycontin** (b) (4) **WR Review**

- Indication studied: Treatment of acute moderate to severe pain
- The Division provided a summary of the data included in the application. Importantly, the Division does not agree that the sponsor has fairly met the terms of the WR because the sponsor failed to enroll sufficient numbers of patients 6-11 years of age in the oxycontin study (study 3 of the WR; a clinical trial of extended-release oxycodone in pediatric patients with chronic pain). The Division noted that only 14 patients 6 to 11 years of age (approximately 10%) were enrolled compared to 141 patients 12 to 17 years of age. Thus, the Division's current plan is to limit the approval of the indication to chronic pain in pediatric patients greater than 12 years of age.
- The Division also noted that PK data were obtained in studies 1 & 2 of the WR in patients 1-17years of age for the immediate release oxycodone product.

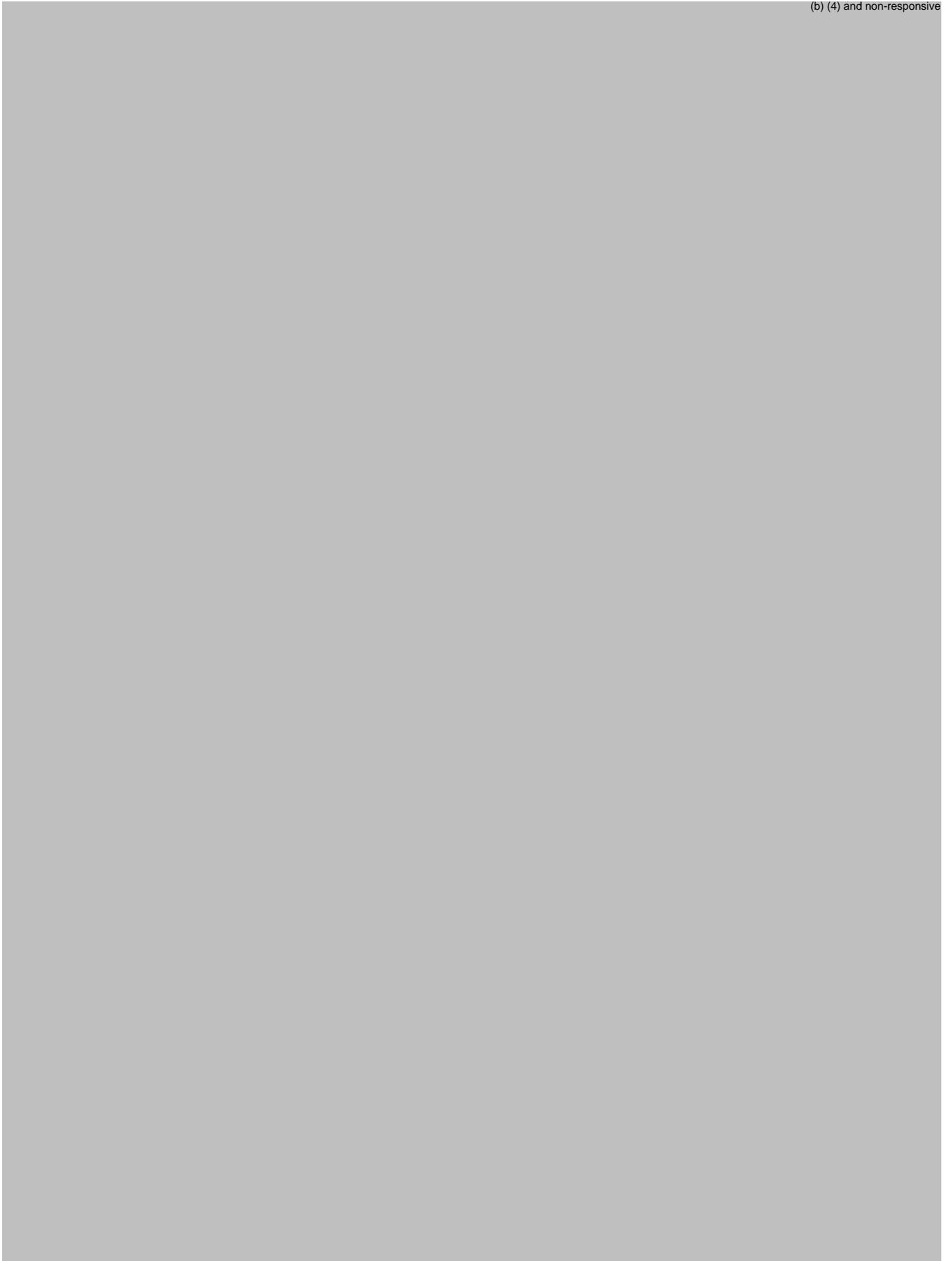
(b) (4)

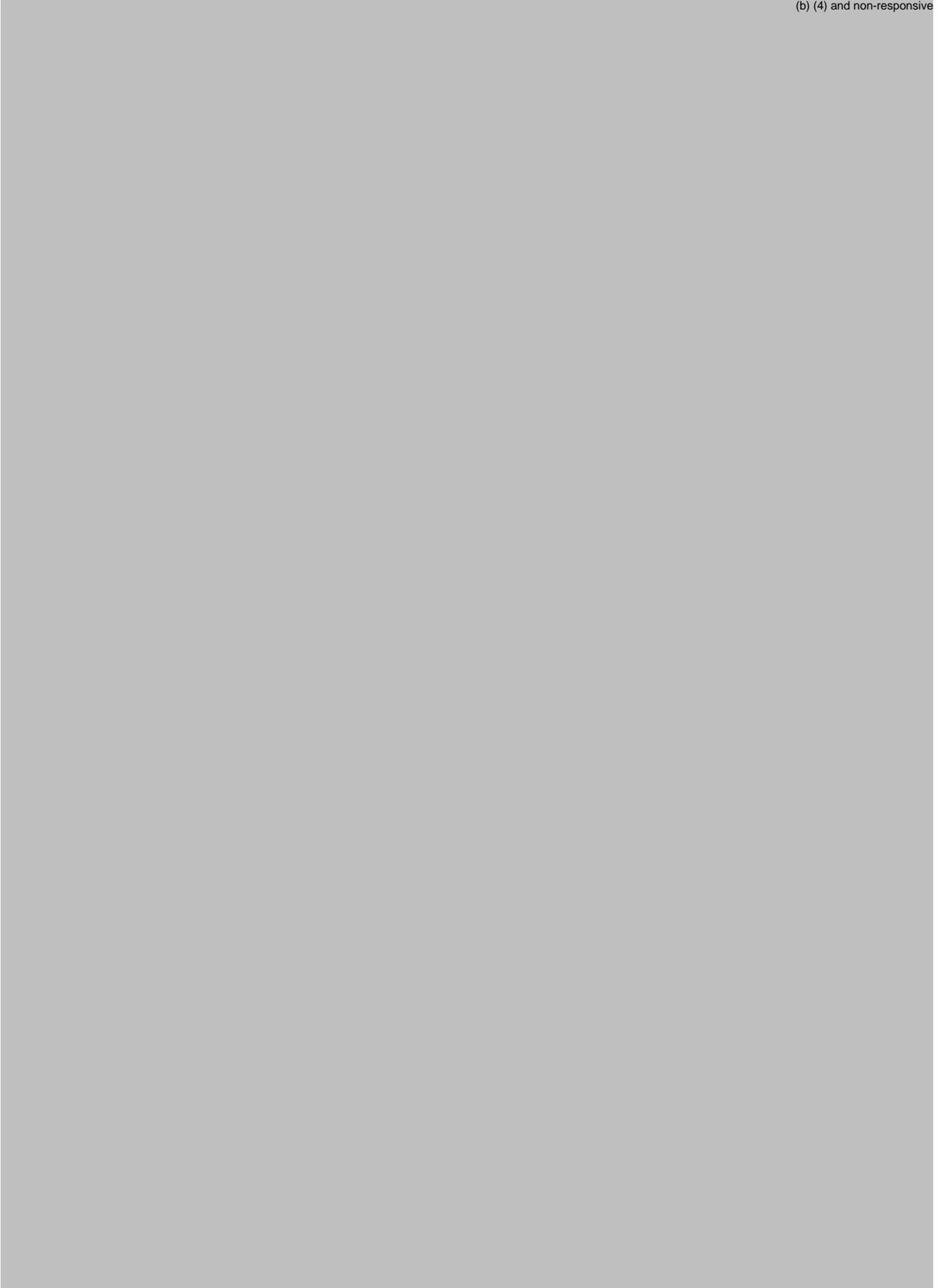
The Division questioned whether this PK information should be placed in the labeling for Oxycontin. The PeRC recommended that this information **NOT** be placed in Oxycontin labeling because it may lead the false assumption that these data relate to Oxycontin rather than to the immediate release form of oxycodone. However, because this information is of public health benefit the PeRC recommended that

(b) (5)

- *PeRC Recommendations:*
- The PeRC agreed with the Division's assessment.









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GEORGE E GREELEY  
05/26/2015

**From:** [Walker, Diana](#)  
**To:** [Connelly, Beth \(Beth.Connelly@pharma.com\)](mailto:Beth.Connelly@pharma.com)  
**Subject:** sNDA 022272 S-027 Clinical Information Request 20 may15  
**Date:** Wednesday, May 20, 2015 5:45:32 PM  
**Importance:** High

---

Dear Beth,

I have received the following request for information from our clinical review team. Please send me your response via email as soon as possible but no later than **Friday, May 29, 2015**, followed by a submission to your application.

Please respond to the following request for information:

**The specific reason(s) for prescribing chronic pain medication(s) to patients participating in OTR3001 is not clear to us. We understand that the CRF collects medical condition(s) and/or surgical procedure(s) during screening. It then asks if the condition/surgery is “current at the start of the study”. It is our understanding that these relevant conditions are used to populate the MH dataset. However, at least half of the patients have 9 or more conditions and a quarter of them have 14 or more, making it difficult or impossible for us to decipher which of these listed reasons is the primary for requiring the treatment provided. One case, subject OTR3001-1843A-0006001, does not have any relevant medical history. Provide the primary condition for which treatment with OxyContin was required for all subjects in the safety population of Study OTR3001.**

Warm regards,

Diana

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

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DIANA L WALKER  
05/21/2015

**From:** [Walker, Diana](#)  
**To:** [Connelly, Beth](#)  
**Subject:** CMC Information Request sNDA 22272 (S-027) 27mar15  
**Date:** Friday, March 27, 2015 12:57:26 PM  
**Importance:** High

---

Dear Beth,

I have received a request from our review team. Please submit to me via email as soon as possible or no later than next Thursday April 2, 2015, the following requested information. You can follow this with an official amendment to your NDA 22272 S-027.

**Submit the pharmaceutical development report and any documentation on development work conducted to develop** (b) (4)

Thank you for your assistance.

Warm regards,

Diana

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

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/s/  
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DIANA L WALKER  
05/14/2015

**From:** [Walker, Diana](#)  
**To:** [Connelly, Beth \(Beth.Connelly@pharma.com\)](mailto:Beth.Connelly@pharma.com)  
**Subject:** sNDA 22272/S-027 Information Request 11may15  
**Date:** Monday, May 11, 2015 11:20:29 AM  
**Importance:** High

---

Dear Beth,

I have received the following information request from our review team. Please respond to the two questions below as soon as possible via email by May 13, 2015, or earlier if possible, followed by an amendment to your sNDA.

In several places in your annotated detailed response to the PWR you indicated that:

- **For Studies 1 and 2 (OXP1005 and OXP3003, respectively), an oral (20 mg/ml) solution was diluted to the appropriate strength with cherry syrup.**
- **This diluted solution was administered to patients orally using a 1 cc syringe (CSR OXP1005, Section 9.4.1 and Section 9.4.2; CSR OXP3003, Section 9.4.1 and Section 9.4.2).**
- **All Chemical Manufacturing and Controls information (stability, packaging, storage, etc.) were submitted to IND 029038, Serial No. 025 on October 28, 2002.**

**1. Please provide the composition of the Pediatric Oxycodone formulation.**

You also indicate that:

- **The age appropriate formulation (for trials OXP1005, OXP3003) of oxycodone hydrochloride was an oral solution (20 mg/ml) diluted to the appropriate strength with cherry syrup.**
- **A generic liquid form of oxycodone suitable for use with pediatric patients is available commercially from other manufacturers. Purdue does not plan to develop its own liquid formulation.**
- **No separate BA or BE studies were undertaken in this development program for oxycodone IR solution in pediatric patients**

In this regard, we note that you resubmitted study report OC94-0101 comparing the bioavailability of Roxicodone, Endone and OxyContin. However, we are not certain if your pediatric oxycodone oral solution bridging/comparability to other generic forms of oxycodone is supported by this study.

**2. Indicate whether any other bridging data is available to show that the pediatric**

**oxycodone oral solution used in your clinical trials (EXP1005 and EXP3003) is similar or inter-changeable with the generic liquid oral dosage forms of oxycodone available in market.**

Warm regards,

Diana

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

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/s/  
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DIANA L WALKER  
05/14/2015



NDA 022272/S-027

**FILING COMMUNICATION –  
NO FILING REVIEW ISSUES IDENTIFIED**

Purdue Pharma L.P.  
One Stamford Forum  
Stamford, CT 06901-3431

Attention: Beth Connelly  
Associate Director, Regulatory Affairs

Dear Ms. Connelly:

Please refer to your supplemental New Drug Application (sNDA) dated December 8, 2014, received December 10, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for OXYCONTIN (oxycodone hydrochloride) extended-release tablets.

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 **Priority**. Therefore, the user fee goal date is June 10, 2015.

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, mid-cycle, 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 requirement/commitment requests by May 25, 2015. This date conforms to the 21<sup>st</sup> Century Review timeline for your application. If our review continues on an expedited timeline, we may communicate revised dates for labeling and postmarketing requirement/commitment requests.

At this time, we are notifying you that, we have not identified any potential review issues. Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

## **PRESCRIBING INFORMATION**

Your proposed prescribing information (PI) must conform to the content and format regulations found at 21 [CFR 201.56\(a\) and \(d\)](#) and [201.57](#). We encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of 42 important format items from labeling regulations and guidances.

At the end of labeling discussions, use the SRPI checklist to ensure that the PI conforms with format items in regulations and guidances.

## **PROMOTIONAL MATERIAL**

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

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

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

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

If you have any questions, call Lisa Basham, Senior Regulatory Health Project Manager, at (301) 796-1175.

Sincerely,

*{See appended electronic signature page}*

Sharon Hertz, MD  
Acting Director  
Division of Anesthesia, Analgesia,  
and Addiction Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

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/s/  
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SHARON H HERTZ  
02/05/2015



NDA 022272/S-027

**ACKNOWLEDGEMENT --  
PRIOR APPROVAL SUPPLEMENT**

Purdue Pharma L.P.  
One Stamford Forum  
Stamford, CT 06901-3431

Attention: Beth Connelly  
Associate Director, Regulatory Affairs

Dear Ms. Connelly:

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

**NDA NUMBER:** 022272  
**SUPPLEMENT NUMBER:** 027  
**PRODUCT NAME:** OXYCONTIN (oxycodone hydrochloride) extended-release tablets  
**DATE OF SUBMISSION:** December 8, 2014  
**DATE OF RECEIPT:** December 10, 2014

This supplemental application proposes the inclusion of language in the Full Prescribing Information for oxycodone in pediatric patients.

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 February 8, 2015, in accordance with 21 CFR 314.101(a).

If the application is filed, the goal date will be June 10, 2015.

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.

## **FDAAA TITLE VIII RESPONSIBILITIES**

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

## **SUBMISSION REQUIREMENTS**

Cite the application number listed above 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, Analgesia,  
and Addiction 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, see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

If you have questions, call me at (301) 796-1175.

Sincerely,

*{See appended electronic signature page}*

Lisa E. Basham, MS  
Senior Regulatory Health Project Manager  
Division of Anesthesia, Analgesia,  
and Addiction Products  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

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/s/  
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LISA E BASHAM  
12/16/2014