CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-272

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 022272 SUPPL # HFD # 170

Trade Name OxyContin

Generic Name Oxycodone Hydrochloride Controlled-Release Tablets

Applicant Name Purdue Pharma L.P.

Approval Date, If Known April 5, 2010

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

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

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

YES ☒ NO ☐

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

505(b)(1)

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

YES ☐ NO ☒

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

This is a reformulation of the original OxyContin (under NDA 020553). The new formulation was compared to the original formulation in comparative bioavailability studies. This new formulation was shown to be bioequivalent to the original formulation. No clinical studies were performed.

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).

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
A040199	AA	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	CAPSULE; ORAL	500MG;5MG	OXYCODONE AND ACETAMINOPHEN	ACTAVIS TOTOWA
A040289	AA	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	CAPSULE; ORAL	500MG;5MG	OXYCODONE AND ACETAMINOPHEN	DURAMED PHARMS BARR
A040303	AA	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	CAPSULE; ORAL	500MG;5MG	OXYCODONE AND ACETAMINOPHEN	ENDO PHARMS
A040257	AA	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	CAPSULE; ORAL	500MG;5MG	OXYCODONE AND ACETAMINOPHEN	MALLINCKRODT
A088790	AA	Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	CAPSULE; ORAL	500MG;5MG	TYLOX	ORTHO MCNEIL JANSSEN
A040061	AA	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	CAPSULE; ORAL	500MG;5MG	ROXILOX	ROXANE
A040106	AA	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	CAPSULE; ORAL	500MG;5MG	OXYCODONE AND ACETAMINOPHEN	VINTAGE PHARMS
A040234	AA	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	CAPSULE; ORAL	500MG;5MG	OXYCODONE AND ACETAMINOPHEN	WATSON LABS
A040680	AA	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	SOLUTION; ORAL	325MG/5ML;5MG/5ML	OXYCODONE AND ACETAMINOPHEN	MALLINCKRODT
A089351	AA	Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	SOLUTION; ORAL	325MG/5ML;5MG/5ML	ROXICET	ROXANE
A040203	AA	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;5MG	OXYCODONE AND ACETAMINOPHEN	ACTAVIS TOTOWA
A040778	AA	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;10MG	OXYCODONE AND ACETAMINOPHEN	AMNEAL PHARMS NY

A040777	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;5MG	OXYCODONE AND ACETAMINOPHEN	AMNEAL PHARMS NY
A040789	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	500MG;7 5MG	OXYCODONE AND ACETAMINOPHEN	AMNEAL PHARMS NY
A040789	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	650MG;10MG	OXYCODONE AND ACETAMINOPHEN	AMNEAL PHARMS NY
A090177	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;10MG	OXYCODONE AND ACETAMINOPHEN	COASTAL PHARMS
A090177	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;2 5MG	OXYCODONE AND ACETAMINOPHEN	COASTAL PHARMS
A090177	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;5MG	OXYCODONE AND ACETAMINOPHEN	COASTAL PHARMS
A090177	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;7 5MG	OXYCODONE AND ACETAMINOPHEN	COASTAL PHARMS
A090177	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	500MG;7 5MG	OXYCODONE AND ACETAMINOPHEN	COASTAL PHARMS
A090177	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	650MG;10MG	OXYCODONE AND ACETAMINOPHEN	COASTAL PHARMS
A040434	**AA**	Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;10MG	PERCOCET	ENDO PHARMS
A040330	**AA**	Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;2 5MG	PERCOCET	ENDO PHARMS
A040330	**AA**	Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;5MG	PERCOCET	ENDO PHARMS
A040434	**AA**	Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;7 5MG	PERCOCET	ENDO PHARMS

A040341	**AA**	Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	500MG;7 5MG	PERCOCET	ENDO PHARMS
A040341	**AA**	Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	650MG;10MG	PERCOCET	ENDO PHARMS
A040545	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;10MG	OXYCODONE AND ACETAMINOPHEN	MALLINCKRODT
A087463	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;5MG	OXYCET	MALLINCKRODT
A040545	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;7 5MG	OXYCODONE AND ACETAMINOPHEN	MALLINCKRODT
A040550	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	500MG;7 5MG	OXYCODONE AND ACETAMINOPHEN	MALLINCKRODT
A040550	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	650MG;10MG	OXYCODONE AND ACETAMINOPHEN	MALLINCKRODT
A040608		Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	300MG;10MG	OXYCODONE AND ACETAMINOPHEN	MIKART
A040608		Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	300MG;2 5MG	OXYCODONE AND ACETAMINOPHEN	MIKART
A040608		Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	300MG;5MG	OXYCODONE AND ACETAMINOPHEN	MIKART
A040608		Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	300MG;7 5MG	OXYCODONE AND ACETAMINOPHEN	MIKART
A040692		Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	400MG;10MG	OXYCODONE AND ACETAMINOPHEN	MIKART
A040679		Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	400MG;2 5MG	OXYCODONE AND ACETAMINOPHEN	MIKART

A040687		Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	400MG;5MG	OXYCODONE AND ACETAMINOPHEN	MIKART
A040698		Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	400MG;7 5MG	OXYCODONE AND ACETAMINOPHEN	MIKART
A040676		No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	500MG;10MG	OXYCODONE AND ACETAMINOPHEN	MIKART
A087003	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;5MG	ROXICET	ROXANE
A089775		Yes	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	500MG;5MG	ROXICET 5/500	ROXANE
A040105	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;5MG	OXYCODONE AND ACETAMINOPHEN	VINTAGE PHARMS
A040535	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;10MG	OXYCODONE AND ACETAMINOPHEN	WATSON LABS
A040171	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;5MG	OXYCODONE AND ACETAMINOPHEN	WATSON LABS
A040535	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;7 5MG	OXYCODONE AND ACETAMINOPHEN	WATSON LABS
A040371	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	500MG;7 5MG	OXYCODONE AND ACETAMINOPHEN	WATSON LABS
A040371	**AA**	No	ACETAMINOPHEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	650MG;10MG	OXYCODONE AND ACETAMINOPHEN	WATSON LABS
N007337		Yes	ASPIRIN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	325MG;4 8355MG	PERCODAN	ENDO PHARMS
N007337	**AA**	Yes	ASPIRIN; OXYCODONE HYDROCHLORIDE; OXYCODONE TEREPHTHALATE	TABLET; ORAL	325MG;4 5MG;0 38MG	PERCODAN	ENDO PHARMS

A040255	**AA**	No	ASPIRIN; OXYCODONE HYDROCHLORIDE; OXYCODONE TEREPHTHALATE	TABLET; ORAL	325MG;4 5MG;0 38MG	OXYCODONE AND ASPIRIN	WATSON LABS
A078769	**AB**	No	IBUPROFEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	400MG;5MG	OXYCODONE HYDROCHLORIDE AND IBUPROFEN	ACTAVIS ELIZABETH
A078316	**AB**	No	IBUPROFEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	400MG;5MG	OXYCODONE HYDROCHLORIDE AND IBUPROFEN	BARR
N021378	**AB**	Yes	IBUPROFEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	400MG;5MG	COMBUNOX	FOREST LABS
A078394	**AB**	No	IBUPROFEN; OXYCODONE HYDROCHLORIDE	TABLET; ORAL	400MG;5MG	OXYCODONE HYDROCHLORIDE AND IBUPROFEN	WATSON LABS
A077822	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET, EXTENDED RELEASE; ORAL	10MG	OXYCODONE HYDROCHLORIDE	MALLINCKRODT
A077822	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET, EXTENDED RELEASE; ORAL	20MG	OXYCODONE HYDROCHLORIDE	MALLINCKRODT
A077822	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET, EXTENDED RELEASE; ORAL	40MG	OXYCODONE HYDROCHLORIDE	MALLINCKRODT
A077822	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET, EXTENDED RELEASE; ORAL	80MG	OXYCODONE HYDROCHLORIDE	MALLINCKRODT
N020553	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET, EXTENDED RELEASE; ORAL	10MG	OXYCONTIN	PURDUE PHARMA LP
N020553		No	OXYCODONE HYDROCHLORIDE	TABLET, EXTENDED RELEASE; ORAL	15MG	OXYCONTIN	PURDUE PHARMA LP
N020553	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET, EXTENDED RELEASE; ORAL	20MG	OXYCONTIN	PURDUE PHARMA LP

N020553		No	OXYCODONE HYDROCHLORIDE	TABLET, EXTENDED RELEASE; ORAL	30MG	OXYCONTIN	PURDUE PHARMA LP
N020553	**AB**	Yes	OXYCODONE HYDROCHLORIDE	TABLET, EXTENDED RELEASE; ORAL	40MG	OXYCONTIN	PURDUE PHARMA LP
N020553		No	OXYCODONE HYDROCHLORIDE	TABLET, EXTENDED RELEASE; ORAL	60MG	OXYCONTIN	PURDUE PHARMA LP
N020553	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET, EXTENDED RELEASE; ORAL	80MG	OXYCONTIN	PURDUE PHARMA LP
A076636	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	15MG	OXYCODONE HYDROCHLORIDE	ACTAVIS TOTOWA
A076636	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	30MG	OXYCODONE HYDROCHLORIDE	ACTAVIS TOTOWA
A091393	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	10MG	OXYCODONE HYDROCHLORIDE	AVANTHI INC
A091393	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	15MG	OXYCODONE HYDROCHLORIDE	AVANTHI INC
A091393	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	20MG	OXYCODONE HYDROCHLORIDE	AVANTHI INC
A091393	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	30MG	OXYCODONE HYDROCHLORIDE	AVANTHI INC
A091393	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	5MG	OXYCODONE HYDROCHLORIDE	AVANTHI INC
A090895	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	15MG	OXYCODONE HYDROCHLORIDE	COREPHARMA
A090895	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	30MG	OXYCODONE HYDROCHLORIDE	COREPHARMA
A090895	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	5MG	OXYCODONE HYDROCHLORIDE	COREPHARMA

A077290	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	10MG	OXYCODONE HYDROCHLORIDE	KV PHARM
A077290	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	15MG	OXYCODONE HYDROCHLORIDE	KV PHARM
A077290	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	20MG	OXYCODONE HYDROCHLORIDE	KV PHARM
A077290	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	30MG	OXYCODONE HYDROCHLORIDE	KV PHARM
A077290	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	5MG	OXYCODONE HYDROCHLORIDE	KV PHARM
A076758	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	15MG	OXYCODONE HYDROCHLORIDE	MALLINCKRODT
A076758	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	30MG	OXYCODONE HYDROCHLORIDE	MALLINCKRODT
A090659	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	15MG	OXYCODONE HYDROCHLORIDE	SUN PHARM INDS INC
A090659	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	30MG	OXYCODONE HYDROCHLORIDE	SUN PHARM INDS INC
A090659	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	5MG	OXYCODONE HYDROCHLORIDE	SUN PHARM INDS INC
A078206	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	5MG	OXYCODONE HYDROCHLORIDE	TYCO HLTHCARE
A077712	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	15MG	OXYCODONE HYDROCHLORIDE	VINTAGE PHARMS
A077712	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	30MG	OXYCODONE HYDROCHLORIDE	VINTAGE PHARMS
A077712	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	5MG	OXYCODONE HYDROCHLORIDE	VINTAGE PHARMS
N021011	**AB**	Yes	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	15MG	ROXICODONE	XANODYNE PHARMS
N021011	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	30MG	ROXICODONE	XANODYNE PHARMS

N021011	**AB**	No	OXYCODONE HYDROCHLORIDE	TABLET; ORAL	5MG	ROXICODONE	XANODYNE PHARMS	

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: Lisa Basham
Title: Senior Regulatory Health Project Manager
Date: 3/31/10

Name of Office/Division Director signing form: Bob A. Rappaport, MD
Title: Director, Division of Anesthesia and Analgesia Products

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

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/s/

LISA E BASHAM
04/05/2010

BOB A RAPPAPORT
04/05/2010

Basham, Lisa

From: Basham, Lisa
Sent: Monday, April 26, 2010 3:19 PM
To: 'Connelly, Beth'
Subject: Correction to March 18, 2010 REMS comments.
Attachments: revised survey comments.doc

Beth, Regarding the REMS comments that were sent to you on March 18, 2010, those comments included detailed plans to be used to evaluate patients', prescribers', and pharmacists' understanding about the risks associated with and safe use of OxyContin. Upon further review, we have determined that a pharmacist survey is not necessary because the target audience for the mailing and educational materials includes only prescribers. Therefore, the pharmacist survey will not be necessary. Attached is a revised assessment tool that has the word "pharmacist" removed.

Warm Regards,

Lisa Basham, MS
Senior Regulatory Health Project Manager
Division of Anesthesia and Analgesia Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research
301-796-1175
email: lisa.basham@fda.hhs.gov

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

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/s/

LISA E BASHAM
04/27/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022272 **ACKNOWLEDGE CLASS 1 COMPLETE RESPONSE**

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

Attention: Craig Landau, M.D.
CMO & VP Clinical, Medical & Regulatory Affairs

Dear Dr. Landau:

We acknowledge receipt on February 5, 2010, of your February 5, 2010, resubmission to your new drug application for OxyContin (oxycodone hydrochloride) Controlled-Release Tablets.

We consider this a complete, class 1 response to our December 30, 2009, action letter. Therefore, the user fee goal date is April 5, 2010.

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

Sincerely,

{See appended electronic signature page}

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

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/s/

LISA E BASHAM
02/21/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022272 **DISCIPLINE REVIEW LETTER**

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

Attention: Craig Landau, M.D.
CMO & VP Clinical, Medical & Regulatory Affairs

Dear Dr. Landau:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OxyContin (oxycodone hydrochloride) Controlled-Release Tablets.

We also refer to your February 5, 2010, response to our December 30, 2009, Complete Response Letter.

Our review of the package insert and carton and container labels from the Chemistry, Manufacturing and Controls perspective is complete, and we have identified the following deficiencies:

1. Revise the DESCRIPTION section of the labeling to state that the new OxyContin formulations (b) (4) Alternately, remove the statement completely as you are not using the name from the official monograph.

2. For each strength of the drug product, revise and resubmit the mock-ups of the bottle labels such that it is clear where the lot number and expiration date will be located. Although the location had been clear in earlier versions of the bottle labels, it is not clear in the latest version supplied with the February 4, 2010, amendment.

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 Lisa Basham, Senior Regulatory Project Manager, at (301) 796-1175.

Sincerely,

{See appended electronic signature page}

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

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/s/

PARINDA JANI
02/19/2010

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022272 **DISCIPLINE REVIEW LETTER**

Purdue Pharma LP
One Stamford Forum
Stamford, CT 06901-3431

Attention: Craig Landau, M.D.
CMO & VP Clinical, Medical & Regulatory Affairs

Dear Dr. Landau:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets.

We also refer to your February 5, 2010, resubmission, submitted in response to our December 30, 2009, Complete Response letter.

Our review of your February 5, 2010, REMS proposal is complete, and we have the following comments:

Please see **Appendix A** (**Appendix B** – clean version) for our revisions to the proposed REMS which is consistent with current Agency standards. The REMS Supporting Document must reflect the below changes to be consistent with the REMS document. Please incorporate the necessary revisions and include all current versions of materials in appendices in the next submission.

A. Goals

The Goals have been reviewed and found to be acceptable. We have minor editorial revisions.

B. Medication Guide

The Medication Guide has been reviewed and found to be acceptable.

C. Communication Plan

A communication plan is not a requirement of this proposed REMS; therefore, the proposed communication plan has been removed from the REMS document and applicable sections have been moved to corresponding sections in the "Elements to Assure Safe Use" in the REMS.

D. Elements to Assure Safe Use

1. The Dear Healthcare Professional (DHCP) Letter, previously submitted under the communication plan, will be included in the REMS under elements to assure safe use to inform healthcare professionals of the OxyContin REMS and the need for Healthcare Provider training. The previously submitted DHCP letter with minor edits is attached as **Appendix C**.

2. The DHCP letter must be mailed within 60 days of the approval of OxyContin® to prescribers most experienced in treating chronic pain with opioid agonists, including, pain specialists, physiatrists, and primary care physicians. This letter is designed to convey and reinforce the risks of abuse, misuse, overdose, and addiction of OxyContin®. The mailings must also include the OxyContin® REMS Educational Program materials.

   Additional printed educational material should be made available through field-force distribution, by calling the toll free number, and available for download at the OxyContin® website.

3. The Agency finds the submitted revisions to the Healthcare Professional Guide to be acceptable.

4. As part of the healthcare provider training, develop a form that healthcare providers will return to the sponsor confirming they have completed the educational training. This form may request the following Prescriber Information:
   (1) Prescriber name and credentials
   (2) DEA Registration Number
   (3) Specialty
   (4) Affiliation
   (5) Address
   (6) Office Phone
   (7) Office Fax
   (8) Email
   (9) Date form completed

We recommend that you include questions that can verify prescriber's understanding of the risks associated with OxyContin, the indication for use proper dosing, safety information about proper administration and storage of OxyContin, and the need for patient counseling

This form should include the following statement: "***Completion of this form does not affect your ability to prescribe OxyContin.***" Additionally, we require that you maintain a list of all prescribers that have completed the OxyContin® REMS Educational Program training and provide a report on the status of the training program as part of your REMS assessment.

E. Timetable for Submission of Assessment

The proposed timetable for submission of assessment is acceptable.

F. REMS Supporting Document

1. All Changes in REMS Document should be reflected in the REMS Supporting Document.

2. The following information needs to be included in your REMS Supporting Document under "Information Needed for Assessment:"

   (1) An evaluation of patients' understanding of the serious risks of OxyContin.

   (2) A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24.

   (3) A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance.

   (4) A report on the status of the training program for healthcare providers.

   (5) An evaluation of healthcare providers' awareness and understanding of the serious risks associated with OxyContin (for example, through surveys of healthcare providers).

   (6) Specification of measures that would be taken to increase awareness if surveys of healthcare providers indicate that healthcare provider awareness is not adequate.

   (7) An analysis and summary of surveillance and monitoring activities for abuse, misuse, overdose, and addiction and any intervention taken resulting from signals of abuse, misuse, overdose, and addiction.

   (8) A claims study to evaluate OxyContin (oxycodone hydrochloride) utilization patterns including opioid-tolerant utilization patterns before and after implementation of the REMS.

   (9) With respect to REMS goals, an assessment of the extent to which the elements to assure safe use are meeting the goals or whether the goals or such elements should be modified.

3. Survey Methodology:

   Submit for review the detailed plan that will be used to evaluate patients', prescribers' and pharmacists' understanding about the safe use of Oxycontin. The proposed plan **does not** need to be submitted for FDA review prior to approval of the REMS, however it should be submitted at least 90 days before the evaluation will be conducted. The submission should be coded "REMS Correspondence." The submission should include all methodology and instruments that will be used to evaluate the knowledge about the risks associated with and safe use of Oxycontin.

(1) We encourage you to recruit respondents using a multi-modal approach. For example, respondents could be recruited online, through physicians' offices, through pharmacies, managed care providers, or through consumer panels.

(2) Explain how often non-respondent follow-up or reminders will be completed, and the planned frequency.

(3) Explain how an incentive or honorarium will be offered, and the intended amount.

(4) Explain how any recruitment sites will be selected.

(5) Submit for review any recruitment advertisements.

(6) Define the sample size and confidence associated with that sample size.

(7) Define the expected number of people to be surveyed, and how the sample will be determined (selection criteria).

(8) Explain the inclusion criteria for patients, prescribers, pharmacists; that is, who is an eligible respondent. For example, patient respondents might be:

- Age 18 or older
- Currently taking Oxycontin or have taken in past 3 months
- Not currently participating in a clinical trial involving Oxycontin
- Not a healthcare provider

Submit any screener instruments, and describe if any quotas of sub-populations will be used.

(9) Explain how often surveys will be administered, and the intended frequency.

(10) Offer respondents multiple options for completing the survey. This is especially important for inclusion of the lower literacy population. For example, surveys could be completed online or through email, in writing or by mail, over the phone, and in person.

(11) Explain how surveyors will be trained.

(12) Explain controls used to compensate for the limitations or bias associated with the methodology.

(13) The sample should be demographically representative of the population who use the drug (patients), prescribe the drug (doctors), or dispense the drug (pharmacists).

(14) If possible and appropriate, sample should be diverse in terms of: age, race, ethnicity, sex, socio-economic status, education level, geographically.

(15) Submit for review the introductory text that will be used to inform respondents about the purpose of the survey.

(16) Potential respondents should be told that their answers will not affect their ability to receive or take (patients), prescribe (doctors), or dispense (pharmacists) the drug, and that their answers and personal information will be kept confidential and anonymous.

(17) Respondents should not be eligible for more than one wave of the survey.

(18) Results should be analyzed on an item-by-item or variable-by-variable basis. The data may be presented using descriptive statistics, such as sample size, mean, standard deviation, median, minimum and maximum (for continuous variables), and frequency distributions (for categorical variables).

(19) Data may be stratified by any relevant demographic variable, and presented in aggregate. Submit with your assessments all methodology and instruments that were utilized.

Regarding an assessment of patients' knowledge:

(20) The assessment is to evaluate the effectiveness of the REMS in achieving the goal by evaluating patients' knowledge of the serious risks associated with use of the drug; the assessment is not to evaluate consumer comprehension of the Medication Guide.

Other than when the patient received the Medication Guide at the time the prescription was filled/dispensed, respondents should not be offered an opportunity to read or see the Medication Guide, Package Insert, or any other related educational materials again prior to taking the survey.

(21) Submit for review the survey instruments (questionnaires and/or moderator's guide), including any background information on testing survey questions and correlation to the messages in the Medication Guide.

(22) The patient knowledge survey should include a section with questions asking about the specific risks or safety information conveyed in the Medication Guide to see if the patient not only understands the information, but knows what to do if they experience the event.

(23) Most of the risk-specific questions should be derived from information located in the "What is the Most Important Information I should know about Oxycontin?" section of the Medication Guide.

(24) The risk-specific questions should be non-biased, non-leading, multiple choice questions with the instruction to "select all that apply." Each question should have an "I don't know" answer option.

(25) The order of the multiple choice responses should be randomized on each survey.

(26) The order of the patient questions should be such that the risk-specific questions are asked first, followed by questions about receipt of the Medication Guide. Demographic questions should be collected last or as part of any screener questions.

(27) Respondents should not have the opportunity or ability to go back to previous questions in the survey.

(28) Explain if and when any education will be offered for incorrect responses.

(29) Include questions about receipt of the Medication Guide in the patient survey as a way to fulfill the obligation to report on the distribution of the Medication Guide.

(30) Just prior to the questions about receipt of the Medication Guide, include text that describes a Medication Guide. For example,

> Now we are going to ask you some questions about the Medication Guide you may have received with Oxycontin. The Medication Guide is a paper handout that contains important information about the risks associated with use of Oxycontin and how to use Oxycontin safely. Medication Guides always include the title "Medication Guide."

(31) Use the following (or similar) questions to assess receipt and use of the Medication Guide.

- Who gave you the Medication Guide for Oxycontin? (Select all that apply)
  - My doctor or someone in my doctor's office
  - My pharmacist or someone at the pharmacy
  - Someone else - please explain:_____
  - I did not get a Medication Guide for Oxycontin

- Did you read the Medication Guide?
  - All,
  - Most,
  - Some,
  - None

- Did you understand what you read in the Medication Guide?
  - All,

- Most,
- Some,
- None

- Did someone offer to explain to you the information in the Medication Guide?
  - Yes, my doctor or someone in my doctor's office
  - Yes, my pharmacist or someone at the pharmacy
  - Yes, someone else – please explain: _____
  - No

- Did you accept the offer? Yes or No

- Did you understand the explanation that was given to you?
  - All,
  - Most,
  - Some,
  - None

- Did or do you have any questions about the Medication Guide?
  - Yes (If Yes, list your question(s) below)
  - No

    _____

    Note: This is an open text field that should be grouped/coded by the sponsor prior to submitting to FDA.

Regarding an assessment of healthcare providers' (prescribers and/or pharmacists) knowledge:

(32) The assessment is to evaluate the effectiveness of the REMS in achieving the goal by evaluating healthcare providers' knowledge of: the serious risks associated with use of Oxycontin, how to properly prescribe or dispense Oxycontin, and how to how to properly monitor for the serious risks associated with the use of Oxycontin; the assessment is not to evaluate healthcare providers' comprehension of the educational materials.

Respondents should not be offered an opportunity to read or see any educational materials (prescribing information, communications, promotional materials, videos, etc.) again prior to taking the survey.

(33) Submit for review the survey instruments (questionnaires and/or moderator's guide), including any background information on testing survey questions and correlation to the messages in any educational materials.

(34) The healthcare provider knowledge survey should include a section with questions asking about the specific risks and safety information conveyed in the educational materials.

Questions should be non-biased, non-leading, multiple choice questions with the instruction to "select all that apply." Each question should have an "I don't know" answer option.

The order of the multiple choice responses should be randomized on each survey.

(35) The order of the survey questions should be such that the risk-specific questions are asked first, followed by questions about receipt of the educational materials. Demographic questions should be collected last or as part of any screener questions.

Respondents should not have the opportunity or ability to go back to previous questions in the survey.

Explain if and when any education will be offered for incorrect responses.

(36) Use the following (or similar) questions to assess receipt and use of the educational materials.

- Prior to today, which of the following were you aware of or received with regard to Oxycontin? (Select all that apply)

Educational Material	Aware	Received
Full Prescribing Information	□	□
Medication Guide	□	□
Dear Healthcare Provider Letter	□	□
Healthcare Provider Training Guide: Prescribing OxyContin	□	□
Something else - please explain:	□	□
None of the above	□	□

- Did you read the Full Prescribing Information?
    - All,
    - Most,
    - Some,
    - None
    - I did not receive the Oxycontin Full Prescribing Information

- Did you read the Medication Guide?
    - All,
    - Most,
    - Some,
    - None
    - I did not receive the Oxycontin Medication Guide

- Did you read the Dear Healthcare Provider Letter?
    - All,
    - Most,
    - Some,
    - None
    - I did not receive the Oxycontin Dear Healthcare Provider Letter

- Did you read the Healthcare Provider Training Guide: Prescribing OxyContin?
    - All,
    - Most,
    - Some,
    - None
    - I did not receive the Training Educational Brochure for Oxycontin

- Do you have any questions about any of the educational materials related to Oxycontin?
    - Yes(If Yes, list your question(s) below
    - No

    _____

    Note: This is an open text field that should be grouped/coded by the sponsor prior to submitting to FDA.

G. General Comments:

Resubmission Requirements: Submit the revised Proposed REMS with appended materials and the REMS Supporting Document. Please provide a track changes and clean version of all revised materials and documents.

Format Request: Please submit your proposed REMS and other materials in WORD format. It makes review of these materials more efficient and it is easier for the web posting staff to make the document 508 compliant. It is preferable that the entire REMS and appended materials be a single WORD document.

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

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

ATTACHMENTS:
Appendix A: Amended REMS (changes tracked)
Appendix B: Amended REMS (clean)
Appendix C: Amended DHCP Letter (changes tracked)
Appendix D: Healthcare Provider Training Guide

36 pp withheld in full immed. after this page as (b)(4) Draft labeling.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

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/s/

LISA E BASHAM
03/18/2010
For Parinda Jani

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022272 **DISCIPLINE REVIEW LETTER**

Purdue Pharma LP
One Stamford Forum
Stamford, CT 06901-3431

Attention: Craig Landau, M.D.
CMO & VP Clinical, Medical & Regulatory Affairs

Dear Dr. Landau:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets.

We also refer to our December 30, 2009, Complete Response letter in which we informed you that our review of your amended REMS, submitted on December 22, 2009, would be deferred until the next cycle.

Our review of your December 22, 2009, REMS proposal is complete, and we have the following comments:

A. Goals

The goals are acceptable.

B. Medication Guide

The Medication Guide has been reviewed and has been found to be acceptable. No revisions are expected at this time.

C. Communication Plan:

In the REMS notification letter dated December 11, 2009, you were informed that a Medication Guide and Communication Plan would not be adequate to ensure adequate training of healthcare providers to address the labeled risks and to prevent the occurrence of serious adverse events associated with those risks. You were required to submit a Medication Guide, elements to assure safe use [specifically healthcare provider training under 505-1(f)(3)(A)], and a timetable for the submission of an assessment of the REMS to ensure that benefits of OxyContin outweigh the risks of abuse, misuse, overdose, and addiction. We are not requesting a communication plan; therefore we are requiring you to

remove this section of your submitted REMS. Letters can be sent out to targeted prescribers but will not be part of the REMS.

D. Elements to Assure Safe Use

1. REMS Template

   Move the following statement to Section B1b:

   Prescribers will be re-trained every two years

2. Healthcare Provider Training Guide

   a. The black box warning has been removed from the revised training guide yet similar information is provided in the Important Safety Information. Place the black box warning back into the guide with verbatim language from the label.

   b. We compared the table of contents in the September 18, 2009 submission and think that the order of content from the September version is better than was submitted December 21, 2009. Revise the current brochure to the follow the September 18, 2009 OxyContin Healthcare Provider Training Guide sequence.

   c. Include a purpose statement for the guide. The current guide reflects the goals of the REMS but does not clearly state a purpose for the guide. Example: The purpose of the Healthcare Provider Training Guide is to inform prescribers about important safety information about OxyContin to enable them to appropriately prescribe, dispense and counsel patients about the potential risk of misuse, abuse and addiction of OxyContin.

E. REMS Supporting Document

   a. Changes in REMS should be reflected in the Supporting Document.

   b. Assessments need to be consistent with those requested in the December 11, 2009. Example: It is not clear how you are going to conduct a claims study to evaluate OxyContin utilization patterns including opioid-tolerant utilization patterns before and after implementation of the REMS.

General Comments:

Resubmission Requirements: Submit the revised Proposed REMS with appended materials and the REMS Supporting Document. Please provide a track changes and clean version of all revised materials and documents.

Format Request: Please submit your proposed REMS and other materials in WORD format. It makes review of these materials more efficient and it is easier for the web posting staff to make the document 508 compliant. It is preferable that the entire REMS and appended materials be a single WORD document. If certain documents such as enrollment forms are only in PDF format, they may be submitted as such, but the preference is to include as many as possible be in a single WORD document.

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

Sincerely,

{See appended electronic signature page}

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

ATTACHMENTS:
Edited REMS Document

14 pp withheld in full immed. after this page as (b)(4) Draft Labeling.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

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/s/

PARINDA JANI
01/26/2010

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 022272 **REMS NOTIFICATON LETTER**

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

Attention: Craig Landau, M.D.
CMO & VP Clinical, Medical & Regulatory Affairs

Dear Dr. Landau:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for OxyContin (oxycodone hydrochloride) Controlled-Release Tablets.

We also refer to our complete response letter dated October 3, 2008, and to our letter dated June 17, 2009. In our letter dated October 3, 2008, we notified you that a Risk Evaluation and Mitigation Strategy (REMS) is required for OxyContin (oxycodone hydrochloride) to ensure that the benefits of the drug outweighed the risks of: 1) use in non-opioid-tolerant individuals; 2) abuse; and 3) overdose, both accidental and intentional. In our letter dated June 17, 2009, we indicated that your REMS must include a Medication Guide, a Communication Plan targeted to healthcare providers to support implementation of the elements of your REMS, and a timetable for submission of the assessments of the REMS.

As you know, we are considering what REMS elements should be implemented across the class of modified-release opioids to address the risks of abuse, misuse, overdose, and addiction. We intend to continue to approve new products in this class that meet the statutory and regulatory standards for approval with a REMS that provides at least as much protection as the risk management plans for already marketed products. Once we determine the necessary elements of the class-wide REMS, we will notify you in writing and you will be required to submit a modified REMS incorporating those elements.

We are in the process of reviewing your proposed REMS as described in your submission of November 17, 2009. Upon further consideration, we believe that the Medication Guide and Communication Plan will not be adequate to ensure adequate training of healthcare providers to address the labeled risks described above, and to prevent the occurrence of serious adverse events associated with those risks. Therefore, we have determined that the REMS for OxyContin (oxycodone hydrochloride) should contain an element to assure safe use, specifically healthcare provider training under 505-1(f)(3)(A), to ensure that the benefits of OxyContin (oxycodone hydrochloride) outweigh the risks described above.

Based on our current understanding of the risks of OxyContin (oxycodone hydrochloride), we have determined that the REMS must include a Medication Guide, elements to assure safe use, specifically training for healthcare providers as described under 505-1(f)(3)(A), and a timetable for the submission of assessments of the REMS.

The Elements to Assure Safe Use must include, at a minimum, the following:

1) A plan to ensure that OxyContin (oxycodone hydrochloride) will only be prescribed by healthcare providers who have particular training under 505-1(f)(3)(A) about the information described below. At a minimum the plan shall require that:
   (a) Healthcare providers are trained about:
      (i) Proper patient selection
      (ii) Appropriate product dosing and administration
      (iii) General opioid use including information about opioid abuse and how to identify patients who are at risk for addiction
      (iv) The risks of abuse, misuse, overdose, and addiction from exposure to opioids, including OxyContin (oxycodone hydrochloride)
      (v) The risks of OxyContin (oxycodone hydrochloride) including:
         1. The risk of overdose caused by exposure to an essentially immediate-release form of oxycodone due to broken, chewed crushed or dissolved OxyContin (oxycodone hydrochloride)
         2. The risk of addiction from exposure to OxyContin (oxycodone hydrochloride)
         3. The risk of overdose with use of 60 mg dosages and above in non-opioid-tolerant individuals
      (vi) Information to counsel patients on the need to store opioid analgesics safely out of reach of children and household acquaintances
      (vii) The importance of providing each patient a Medication Guide with each prescription and instructing the patient to read it.

   (b) Healthcare providers will be retrained periodically, at a specified interval.

Information needed for assessment of the REMS may include but may not be limited to:

a. An evaluation of patients' understanding of the serious risks of OxyContin (oxycodone hydrochloride).
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24.
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance.
d. A report on the status of the training program for healthcare providers.
e. An evaluation of healthcare providers' awareness and understanding of the serious risks associated with OxyContin (oxycodone hydrochloride) (for example, through surveys of healthcare providers).

f. Specification of measures that would be taken to increase awareness if surveys of healthcare providers indicate that healthcare provider awareness is not adequate.
g. An analysis and summary of surveillance and monitoring activities for abuse, misuse and overdose, and any intervention taken resulting from signals of abuse, misuse and overdose.
h. A claims study to evaluate OxyContin (oxycodone hydrochloride) utilization patterns including opioid-tolerant utilization patterns before and after implementation of the REMS.
i. With respect to REMS goals, an assessment of the extent to which the elements to assure safe use are meeting the goals or whether the goals or such elements should be modified.

Each assessment must assess the extent to which the elements to assure safe use of your REMS are meeting the goals of your REMS and whether the goals or elements should be modified.

You should submit a revision to the proposed REMS and REMS supporting document included in your November 17, 2009, submission that contained the Medication Guide, Communication Plan, and the timetable for submission of assessments of the REMS described in our June 17, 2009, letter. You should remove the Communication Plan from your proposed REMS and include the elements to assure safe use for healthcare provider training as described above.

Updates to the REMS supporting document may be included in a new document that references the previous REMS supporting document submission for unchanged portions of the REMS, or updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted.

Prominently identify subsequent submissions related to the Proposed REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 022272
PROPOSED REMS-AMENDMENT

If you have any questions, call Lisa E. Basham, Regulatory Project Manager, at 301-796-1175.

Sincerely,

{See appended electronic signature page}

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

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/s/

SHARON H HERTZ
12/11/2009
Signing for Bob Rappaport, M.D.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22-272 **DISCIPLINE REVIEW LETTER**

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

Attention: Craig Landau, M.D.
CMO & VP Clinical, Medical & Regulatory Affairs

Dear Dr. Landau:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OxyContin (Oxycodone HCl Controlled-Release) Tablets.

Our initial review of your amended proposed Risk Evaluation and Mitigation Strategy (REMS), submitted on September 18, 2009, is complete, and we have identified the following deficiencies:

I. Goals

Goals should be:

a) to inform patients and providers about the potential for abuse, misuse, overdose, and addiction of OxyContin

b) to inform patients and providers about the safe use of OxyContin

II. Medication Guide

As you are aware, the Medication Guide is in the final stages of revision.

III. Communication Plan:

a) Information Letters (Healthcare Providers, Pharmacist and Professional Associations)

The sequence of the risk information within the letters minimizes the risks associated with OxyContin. For example, (b) (4) is presented before warnings related to respiratory depression and severe hypotension. See the attached revised letters

b) Guide for Healthcare Providers (HCP)

1. Present the purpose of the guide towards the front. The healthcare provider should be able to open the guide and see the sponsor's rationale for providing them with this particular resource.

2. Introduction section- explain that the REMS was created to educate prescribers about the potential risks associated with OxyContin which are reflected in the goals of the REMS. Follow this sentence with the goals.

3. The words in all caps can minimize the risk of other information provided. Despite being shown in the professional labeling in all caps this is promotion. Remove all caps (e.g., NOT, CONTRAINDICATED).

4. The boxed warning presented on page one of the HCP Guide is inconsistent with the current PI for OxyContin and could minimize the risks associated with OxyContin. Revise this section to be consistent with the PI.

5. The sequence of the risk information within the HCP Guide minimizes the risks being communicated and is inconsistent with the PI for OxyContin. For example, serious and common adverse effects are presented on page two of the HCP Guide, while warnings and precautions are presented on page three. Revise the sequence of the risk information within the HCP Guide to be consistent with the PI.

6. The HCP Guide fails to include material information regarding the REMS risks associated with OxyContin. For example, the HCP Guide presents risk information related to use, misuse, accidental overdose, and addiction but omits the following statement from the PI:

   - With parenteral abuse, the tablet excipients can result in death, local tissue necrosis, infection, pulmonary granulomas, and increased risk of endocarditis and valvular heart injury. Parenteral drug abuse is commonly associated with transmission of infectious diseases, such as hepatitis and HIV.

   - Revise the HCP Guide to present REMS specific risk and material information.

IV. Patient and provider surveys

Please submit for review a detailed plan to evaluate patients' and healthcare providers' understanding about the risks associated with and safe use of OxyContin. This information does not need to be submitted for FDA review prior to approval of your REMS, however it should be submitted at least 90 days before you plan to conduct the evaluation. The submission should be coded "REMS Correspondence." The submission should include all methodology and survey instruments that will be used to evaluate the

patients' and healthcare providers' understanding about the risks associated with and safe use of OxyContin. This should include, but not be limited to:

- Sample size and confidence associated with that sample size
- How the sample will be determined (selection criteria)
- The expected number of patients/healthcare providers to be surveyed
- How the participants will be recruited
- How and how often the surveys will be administered
- Explain controls used to minimize bias
- Explain controls used to compensate for the limitations associated with the methodology
- The survey instruments (questionnaires and/or moderator's guide).
- Any background information on testing survey questions and correlation to the messages in the Medication Guide.

General Comments:

Resubmission Requirements: Submit the revised Proposed REMS with appended materials and the REMS Supporting Document. Please provide a track changes and clean version of all revised materials and documents.

Format Request: Please submit your proposed REMS and other materials in WORD format. It makes review of these materials more efficient and it is easier for the web posting staff to make the document 508 compliant. It is preferable that the entire REMS and appended materials be a single WORD document. If certain documents such as enrollment forms are only in PDF format, they may be submitted as such, but the preference is to include as many as possible be in a single WORD document.

The proposed REMS materials present claims such as, "OxyContin and other opioid analgesics", "as with all opioid agents", and "Like morphine and other opioids used for analgesia." The proposed claims minimize the risks associated with OxyContin therapy. Eliminate this language.

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 Lisa Basham, Regulatory Project Manager, at (301) 796-1175.

Sincerely,

{See appended electronic signature page}

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

ATTACHMENTS:
Edited REMS document, Prescriber Letter, Pharmacist Letter, and Association Information Letter

34 pp withheld in full immed. after this page as (b)(4) Draft labeling.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

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/s/

LISA E BASHAM
11/06/2009
Signing for Parinda Jani

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022272 **DISCIPLINE REVIEW LETTER**

Purdue Pharma L.P.
One Stamford Forum
Stamford, CT

Attention: Craig Landau, M.D.
CMO & VP Clinical, Medical & Regulatory Affairs

Dear Dr. Landau:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OxyContin (Controlled-Release) Tablets.

Our review of the proposed carton and container labels is complete, and we have identified the following deficiencies:

1. The 10 mg, 15 mg, 20 mg, 30 mg, and 40 mg statements of strength are presented in a pastel color that matches the color of the respective tablet strength. Although the strength is outlined in black, the pastel colors are not prominent and make it difficult to clearly distinguish the differences between the colors. Make the colors bolder/deeper so that they are more easily distinguished from one another. Additionally, increase the size of the strength presentation.

2. Increase the prominence of the "Swallow tablets whole. Do not cut, ..." statement on the side panel of the container label.

3. The labels do not have a Medication Guide statement. We recommend the following language dependent upon whether the Medication Guide accompanies the product or is enclosed in the bottle/carton:

    a. "Dispense the enclosed Medication Guide to each patient." or

    b. "Dispense the accompanying Medication Guide to each patient."

4. Container Label 60 mg Strength Only
Both the 60 mg strength and the tablet picture are presented in red. This red color is also used in the triangular box on the 80 mg label. Using the same red color prominently on the labels for both strengths minimizes the differentiation between the two strengths. We recommend you use a different color for the triangular box on the 80 mg label. Ensure

that this color is not used on any of the other container labels in order to better differentiate all of the strengths.

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 Lisa Basham, Regulatory Project Manager, at (301) 796-1175.

Sincerely,

{See appended electronic signature page}

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

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/s/

PARINDA JANI
10/16/2009

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022272

PDUFA GOAL DATE EXTENSION

Purdue Pharma LP
One Stamford Forum
Stamford, CT 06901-3431

SEP 30 2009

Attention: Craig Landau, M.D.
CMO & VP Clinical, Medical & Regulatory Affairs

Dear Dr. Landau:

Please refer to your November 29, 2007, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OxyContin (Oxycodone Hydrochloride Controlled-Release Tablets).

On September 18, 2009, we received your September 18, 2009, major amendment to this application. The receipt date is within three months of the user fee goal date. Therefore, we are extending the goal date by three months to provide time for a full review of the submission. The extended user fee goal date is December 30, 2009.

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

Sincerely yours,

Parinda Jani

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

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/s/

PARINDA JANI
09/30/2009

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22-272 **DISCIPLINE REVIEW LETTER**

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

Attention: Craig Landau, M.D.
CMO & VP Clinical, Medical & Regulatory Affairs

Dear Dr. Landau:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OxyContin (Oxycodone HCl Controlled-Release) Tablets.

Our initial review of your proposed Risk Evaluation and Mitigation Strategy (REMS) is complete, and we have identified the following deficiencies:

I. Medication Guide

See attached REMS document with track changes.

II. Communication Plan:

Revise the Communication Plan as follows:

Add: In accordance with the United States Federal Food, Drug, and Cosmetic ACT (FDCA) 505-1(e)(3), Purdue Pharma L.P. will execute a communication plan to Health-Care Professionals (HCPs) to support implementation of OxyContin REMS for the first year following approval of the NDA for OxyContin.

Healthcare Professional Information Letter

1. The HCP Information letter should be written in such a manner that important safety information is readily available to the healthcare professionals.

    a. Bring important safety information to the top of the letter.

    b. Clearly identify the risks associated with the misuse or abuse of the drug in the proposed letter.

    c. Follow the goals in organizing the information provided. Begin with prescribing and dispensing information. Go on to briefly outline how the

product should be stored and disposed of. Then discuss how prescribing, dispensing, storage and proper disposal, contribute to the reduction in potential medical errors and nonmedical use. Patient counseling information should be provided further into the letter.

2. The information provided in the letter should be consistent with the label.
   The proposed letter boxed warning states that OxyContin 60 mg, 80 mg, and 160 mg Tablet, or a single dose greater than 40 mg, **ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY**. The proposed label states that OxyContin 60 mg and 80 mg, or doses greater than 40 mg **ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY**. Determine the correct doses available and place this corrected information in both the labeling and REMS.

3. Remove the following promotional reference- from the letter:

   (b) (4)

4. Refer the prescriber to the full prescribing information for details about important safety information.

5. On Page 8 & 9 of the REMS Supporting Document, you state that the Dear Prescriber and Pharmacy Letter will be updated annually and sent to prescribers, as described above. Submit the letter to FDA for review after any updates are made. Submit a timeline describing the duration of the letter's dissemination from the time of launch.

6. The totality of the presentation within the Prescriber and Pharmacist information letters minimizes the REMS risks associated with OxyContin. The letters present the goals of the REMS program but omit specific risks related to "use, misuse, overdose, and addiction" and material information from the prescribing information (PI) on appropriate prescribing, dispensing, use, storage, and disposal of OxyContin. For example, the REMS related risk omissions include but are not limited to omission of the following statement:

   Patients should be instructed against use by individuals other than the patient, for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death.

7. Revise the letters to present ALL the REMS-specific risk information and material information related to those risks **within the running text of the letter**.

8. The contraindications provided in the proposed letter are not complete. Refer to the label.
   Page two of the letter presents the statement, *"OxyContin **is not indicated** for patients with . . ."* under the header, *"Contraindications for OxyContin."*

This claim minimizes the risk being communicated by failing to clearly state that it is "contraindicated." We note that the phrase "is not indicated for . . ." is used only within the INDICATIONS AND USAGE section of the PI to describe types of pain for which the drug is not indicated.

9. Remove the box and present the information in bullet format.

10. Provide the definition of opioid-tolerant patient; not just tolerant to respiratory depressant effects of opioids.

Prescribing OxyContin: A Healthcare Professional Guide

1. The healthcare professional guide describes information already found in the full Prescribing Information. The new guide will need to be reduced in size. There are too many pages. The information is displayed as if it were the PI.

2. You state that there will not be an Element to Assure Safe Use; therefore, a REMS based-program name is not necessary. Delete all references to a program name.

3. Page two of the proposed guide includes the following claim, (b) (4) (emphasis added). This is an inadequate presentation of the indication for the drug. Specifically, the PI states, "*OxyContin Tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain* ***when a continuous, around-the-clock analgesic is needed for an extended period of time***."

4. Page two of the proposed guide includes the following claim, (b) (4) (emphasis added) The claim, ". . . , (b) (4) " is promotional in tone and suggest that the (b) (4) is a benefit of the drug, and a voluntary action by Purdue.

Pharmacy Information Letter

1. Remove this promotional reference from the letter: (b) (4)

2. The totality of the presentation within the Prescriber and Pharmacist information letters minimizes the REMS risks associated with OxyContin. The letters present the goals of the REMS program but omit specific risks related to "use, misuse, overdose, and addiction" and material information from the prescribing information (PI) on appropriate prescribing, dispensing, use, storage, and disposal of OxyContin. For example, the REMS related risk omissions include but are not limited to omission of the following statement:

Patients should be instructed against use by individuals other than the patient, for whom it was prescribed, as such inappropriate use may have severe medical consequences, including death.

3. Revise the letters to present ALL the REMS-specific risk information and material information related to those risks **within the running text of the letter.**

4. The information provided in the letter should be consistent with the label.
   The proposed letter boxed warning states that OxyContin 60 mg, 80 mg, and 160 mg Tablet, or a single dose greater than 40 mg, **ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY**. The proposed label states that OxyContin 60 mg and 80 mg, or doses greater than 40 mg ARE FOR USE IN OPIOID-TOLERANT PATIENTS ONLY. Determine the correct doses available and place this correct information in both the labeling and REMS.

5. The contraindications provided in the proposed letter are not complete. Refer to the label.
   Page two of each letter presents the statement, *"OxyContin **is not indicated** for patients with . . ."* under the header, *"Contraindications for OxyContin"*. This claim minimizes the risk being communicated by failing to clearly state that it is "contraindicated." We note that the phrase "is not indicated for . . ." is used only within the INDICATIONS AND USAGE section of the PI to describe types of pain for which the drug is not indicated.

6. Remove the box and present the information in bullet format.

7. Provide the definition of opioid-tolerant patient; not just tolerant to respiratory depressant effects of opioids.

3. Timetable for Submission of Assessment

Present the Timetable for Submission of Assessment as follows: Purdue Pharma L.P. will submit REMS Assessments to FDA every 6 months from the date of the approval of the REMS for the first year and annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Purdue Pharma L.P. will submit each assessment so that it will be received by the FDA on or before the due date.

4. Supporting Document

Details of the surveys, including methodology and sampling were not provided and must be provided to FDA prior to implementation

General Comments:

- REMS do not address diversion. Remove the word “diversion”; “misuse” can be used
- Delete all reference to a REMS *program*
- Insert all references in the Healthcare Professional Guide
- Submit letter to be sent to Physician and Other Healthcare Professional Associations.
- The proposed REMS materials present claims such as, (b) (4) , and (b) (4) The proposed claims minimize the risks associated with OxyContin therapy. Eliminate the language.

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 Lisa Basham, Regulatory Project Manager, at (301) 796-1175.

Sincerely,

{See appended electronic signature page}

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

6 pp withheld in full immed. after this page as (b)(4) Draft Labeling.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22272	ORIG-1	PURDUE PHARMA INC	OXYCONTIN

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/s/

PARINDA JANI
09/11/2009

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

INFORMATION REQUEST LETTER

NDA 22-272

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

Attention: Beth Connelly
Assistant Director, Regulatory Affairs

Dear Ms. Connelly:

Please refer to your new drug application (NDA), dated November 27, 2007, received November 29, 2007, submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets.

We also refer to our complete response letter dated October 3, 2008, and to our letter dated December 4, 2008, requesting that you not submit a Risk Evaluation and Mitigation Strategy (REMS) proposal until the Agency has notified you in writing about the elements necessary for a REMS across the class of modified-release opioids to address the risks of abuse and overdose and use in non-opioid tolerant individuals. We also refer to your March 30, 2009, resubmission in response to our October 3, 2008, complete response letter.

As you know, we are considering what REMS elements should be implemented across the class of modified-release opioids to address the risks of abuse, misuse, overdose, and addiction. We intend to continue to approve new products in this class that meet the statutory and regulatory standards for approval with a REMS that provides at least as much protection as the risk management plans for already marketed products. Once we determine the necessary elements of the class-wide REMS, we will notify you in writing and you will be required to submit a modified REMS incorporating those elements.

Your proposed REMS must include the following:

The Agency has determined that, until the class-wide REMS program is established, the following REMS program will be required for OxyContin:

> **Medication Guide**: As one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that OxyContin poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of OxyContin. FDA has determined that OxyContin is a product that has serious risks (relative to benefits) of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use OxyContin. FDA has also determined that OxyContin is a product for which patient labeling could help prevent serious adverse

events. Under 21 CFR Part 208 and in accordance with 505-1, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed OxyContin.

Communication Plan: We have determined that a communication plan targeted to healthcare providers who are likely to prescribe OxyContin will support implementation of the elements of your REMS during the first three years after product launch. The communication plan must provide for the dissemination of information about the risks of OxyContin.

The communication plan must include, at a minimum, the following:

1. Educational materials for prescribers that address at least the following:

    a) Proper patient selection
    b) Appropriate product dosing and administration
    c) General opioid use including information about opioid abuse and how to identify patients who are at risk for addiction
    d) The risks of abuse, misuse, overdose, and addiction from exposure to opioids, including OxyContin
    e) The risks of OxyContin including:
        (1) The risk of overdose caused by exposure to an essentially immediate-release form of oxycodone due to breaking, chewing, crushing or dissolving OxyContin
        (2) The risk of overdose due to prescribing OxyContin at doses of 60 mg or greater to opioid non-tolerant patients
    f) Information to counsel patients on the need to store opioid analgesics safely out of reach of children and household acquaintances
    g) The importance of providing each patient a Medication Guide with each prescription and instructing the patient to read it.

2. A description of the audience for the communication plan, stating specifically the types and specialties of healthcare providers to which the communication plan will be directed as well as the professional medical associations and societies. These should include: the American Medical Association, American Pain Society, American Academy of Pain Medicine, American Academy of Family Physicians, American Academy of Physical Medicine and Rehabilitation, American Society of Anesthesiologists, American Osteopathic Association, American Academy of Neurology, and the American College of Rheumatology.

3. A schedule for when and how the plan's materials are to be distributed to healthcare providers and medical associations.

Timetable for Submission of Assessments: The proposed REMS must include a timetable for submission of assessments of the REMS that shall be no less frequent than by 6 months, 1 year, and annually thereafter after the REMS is initially approved. You should specify the reporting interval (dates) that each assessment will cover and the planned date of submission to the FDA of the assessment. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission,

the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. For example, the reporting interval covered by an assessment that is to be submitted by July 31st should conclude no earlier than June 1st.

Your proposed REMS submission should include two parts: a "proposed REMS" and a "REMS supporting document." Attached is a template for the proposed REMS that you should complete with concise, specific information (see Appendix A). Include information in the template that is specific to your proposed REMS for OxyContin. Additionally, all relevant proposed REMS materials including educational and communication materials should be appended to the proposed REMS. Once FDA finds the content acceptable and determines that the application can be approved, we will include these documents as an attachment to the approval letter that includes the REMS. The REMS, once approved, will create enforceable obligations.

The REMS supporting document should be a document explaining the rationale for each of the elements included in the proposed REMS (see Appendix B).

The REMS assessment plan should include but may not be limited to:

1. An evaluation of patients' understanding of the serious risks of OxyContin.

2. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24.

3. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance.

4. An evaluation of healthcare providers' awareness and understanding of the serious risks associated with OxyContin (for example, through surveys of healthcare providers).

5. Specification of measures that would be taken to increase awareness if surveys of healthcare providers indicate that healthcare provider awareness is not adequate.

6. An analysis and summary of surveillance and monitoring activities for abuse, misuse, overdose, and addiction and any intervention taken resulting from signals of abuse, misuse, overdose, and addiction.

Before we can continue our evaluation of this NDA 22-272, you will need to submit the proposed REMS.

Prominently identify the proposed REMS submission with the following wording in bold capital letters at the top of the first page of the submission:

NDA 22-272 PROPOSED REMS

Prominently identify subsequent submissions related to the proposed REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 22-272 PROPOSED REMS-AMENDMENT

If you do not submit electronically, please send 5 copies of your REMS-related submissions.

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

Sincerely,

{See appended electronic signature page}

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

Attachment

Appendix A: REMS Template

If you are not proposing to include one of the listed elements, include a statement that the element is not necessary.

Application number TRADE NAME (DRUG NAME)

Class of Product as per label

Applicant name
Address
Contact Information

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S):

List the goals and objectives of the REMS.

II. REMS ELEMENTS:

A. Medication Guide or PPI

If a Medication Guide is included in the proposed REMS, include the following:

A Medication Guide will be dispensed with each [drug name] prescription. [Describe in detail how you will comply with 21 CFR 208.24.]

B. Communication Plan

If a Communication Plan is included in the proposed REMS, include the following:

[Applicant] will implement a communication plan to healthcare providers to support implementation of this REMS.

List elements of communication plan. Include a description of the intended audience, including the types and specialties of healthcare providers to which the materials will be directed. Include a schedule for when and how materials will be distributed. Append the printed material and web shots to the REMS Document.

C. Elements To Assure Safe Use

If one or more Elements to Ensure Safe Use are included in the proposed REMS, include the following:
List elements to assure safe use of Section 505-1(f)(3)(A-F) included in this REMS. Elements to assure safe use may, to mitigate a specific serious risk listed in the labeling, require that:

A. Healthcare providers who prescribe [drug name] have particular training or experience, or are specially certified. Append any enrollment forms and relevant attestations/certifications to the REMS;

B. Pharmacies, practitioners, or healthcare settings that dispense [drug name] are specially certified. Append any enrollment forms and relevant attestations/certifications to the REMS;

C. [Drug name] may be dispensed to patients only in certain healthcare settings (e.g., hospitals);

D. [Drug name] may be dispensed to patients with documentation of safe-use conditions;

E. Each patient using [drug name] is subject to certain monitoring. Append specified procedures to the REMS; or

F. Each patient using [drug name] be enrolled in a registry. Append any enrollment forms and other related materials to the REMS Document.

D. Implementation System

If an Implementation System is included in the proposed REMS, include the following:

Describe the implementation system to monitor and evaluate implementation for, and work to improve implementation of, Elements to Assure Safe Use (B),(C), and (D), listed above .

E. Timetable for Submission of Assessments

For products approved under an NDA or BLA, specify the timetable for submission of assessments of the REMS. The timetable for submission of assessments shall be no less frequent than by 18 months, 3 years, and in the 7th year after the REMS is initially approved. You should specify the reporting interval (dates) that each assessment will cover and the planned date of submission to the FDA of the assessment. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. For example, the reporting interval covered by an assessment that is to be submitted by July 31st should conclude no earlier than June 1st.

Appendix B: supporting document

This REMS Supporting Document should include the following listed sections 1 through 6. If you are not proposing to include one of the listed elements, the REMS Supporting Document should simply state that the element is not necessary. Include in section 4 the reason you believe each of the potential elements you are proposing to include in the REMS is necessary to ensure that the benefits of the drug outweigh the risks.

1. Table of Contents
2. Background
3. Goals
4. Supporting Information on Proposed REMS Elements
    a. Additional Potential Elements
        i. Medication Guide
        ii. Patient Package Insert
        iii. Communication Plan
    b. Elements to Assure Safe Use, including a statement of how the elements to assure safe use will mitigate the observed safety risk
    c. Implementation System
    d. Timetable for Assessment of the REMS (for products approved under an NDA or BLA)
5. REMS Assessment Plan (for products approved under a NDA or BLA)
6. Other Relevant Information

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/s/

Bob Rappaport

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 22-272

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

Attention: Craig Landau, M.D.
CMO & VP Clinical, Medical & Regulatory Affairs

Dear Dr. Landau:

We acknowledge receipt on March 31, 2009, of your March 30, 2009, resubmission to your new drug application for OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets.

We consider this a complete, Class 2 response to our October 3, 2008, action letter. Therefore, the user fee goal date is September 30, 2009.

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

Sincerely,

{See appended electronic signature page}

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

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/s/

Lisa Basham

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-272

Purdue Pharma LP
One Stamford Forum
Stamford, CT 06901-3431

Attention: Craig J. Landau, MD
CMO & VP Clinical, Medical & Regulatory Affairs

Dear Dr. Landau:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Reformulated OxyContin (oxycodone hydrochloride) Controlled-Release Tablets.

We also refer to the meeting between representatives of your firm and the FDA on January 21, 2009. The purpose of the meeting was to discuss your response to our October 3, 2008, Complete Response Letter to NDA 22,272.

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

If you have any questions, please call me at 301-796-1175.

Sincerely,

{See appended electronic signature page}

Lisa Basham, MS
Regulatory Project Manager
Division of Anesthesia, Analgesia and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

SPONSOR MEETING AGENDA

MEETING DATE/TIME: January 21, 2009/3 PM
LOCATION: White Oak Campus
10903 New Hampshire Ave
Bldg 22, Room 1315
Silver Spring, MD 20903
APPLICATION: NDA 22-272 (reformulated OxyContin)
STATUS OF APPLICATION: Complete Response Issued October 3, 2008
PRODUCT: Reformulated OxyContin (oxycodone hydrochloride) Controlled-Release Tablets
INDICATION: Management of moderate to severe pain when a continuous, around-the-clock analgesic is needed for an extended period of time.
SPONSOR: Purdue Pharma LP
TYPE OF MEETING: Type A
MEETING CHAIR: Sharon Hertz, MD, Division of Anesthesia, Analgesia and Rheumatology Products (DAARP)
MEETING RECORDER: Lisa Basham, Regulatory Project Manager

FDA Attendees	Title
Bob A. Rappaport, MD	Director, DAARP
Sharon Hertz, MD	Deputy Director, DAARP
Rob Shibuya, MD	Clinical Team Leader
Jin Chen, MD	Medical Officer
Suresh Doddapaneni, PhD	Deputy Director; Division of Clinical Pharmacology 2, Office of Clinical Pharmacology
Sayed (Sam) Al Habet, RPh., Ph.D.	Clinical Pharmacologist/Reviewer
Craig Bertha, PhD	Chemistry Reviewer
Michael Klein, PhD	Director, Controlled Substance Staff (CSS)
Silvia Calderon, PhD	Team Leader, CSS
Mary Willy, PhD	Acting Team Leader, Risk Management Analyst, DRISK, Office of Surveillance and Epidemiology (OSE)
Jeanne Perla, PhD	Risk Management Analyst, DRISK, OSE
Igor Cerny, MD	Medical Officer
Afrouz Nayernama	Pharmacist, OSE
Lisa Basham, MS	Regulatory Project Manager
Attendees	**Title**
John Stewart	President, Purdue Pharma LP (PPLP)
Craig Landau, MD	Chief Medical Officer, VP Clinical, Med. & Reg. Affairs, PPLP
Anthony Santopolo, MD	Vice President, Regulatory Affairs, PPLP
Brianne Weingarten	Executive Director, Alliance Management, PPLP
Stephen Harris, MD	Executive Medical Director, PPLP
Judy Lee, PhD	Senior Director, Analytics/Preformulation, PPLP
Jennifer Giordano	Sr. Research Scientist Analytics, PPLP
Salvadore Colucci	Director, Phase 1, Biostatistics
Edward J. Cone, PhD	Scientific Advisor, Pinney Associates; Director Chronic Pain Treatment Programs, Johns Hopkins Bayview Medical Center
Robert Bianchi	VP & Chief of Scientific & Technical Affairs, Prescription Drug Research Center
Peter R. Mathers	Kleinfeld, Kaplan & Becker, LLP
Russell Gasdia	Vice President, Sales and Marketing for Purdue
Edward M. Sellers, MD, PhD	President & CEO, Decision Line Clinical Research

Background:
Purdue Pharma LP submitted a New Drug Application on November 27, 2007 for a new formulation of OxyContin purported to possess abuse-deterrent characteristics. The application received priority review status. An Advisory Committee meeting was held on May 5, 2008, to discuss the validity of the methods used to evaluate the potential abuse-deterrent characteristics of this formulation, the results of those studies, and the possible impact of the formulation changes on abuse. On October 3, 2008, the Division issued a Complete Response letter to the applicant. The deficiencies in the letter included the need for additional and more robust evaluation of the formulation in vitro, reanalysis or exclusion of plasma samples from bioequivalence study 6770-407 due to sample and testing integrity issues, and the need for a Risk Evaluation and Mitigation Strategy. The sponsor submitted a request on October 30, 2008, for a Type A post-action meeting. The meeting request was granted and scheduled for January 21, 2009. The minutes from that meeting follow.

Meeting Minutes:
Note: The sponsor's questions are presented below in italicized text, followed by our responses, provided to the sponsor on January 16, 2009, in bolded text. On the morning of the meeting, PPLP provided comment/clarification for the items they wished to discuss during the meeting. This is presented in boxed and italicized text. Discussion during the meeting is presented in normal text.

The sponsor began the meeting with a brief overview of their current thoughts on the product. They believe that the product is safe when used appropriately in the intended patient population and that there is no way of prospectively knowing how this formulation change will impact abuse. They stated that their research on abuse methods shows that initially crushing the current OxyContin product is the most prevalent precursor to medication errors and abuse, both often leading to tragedy. Their intention was to create a product for which the controlled-release mechanism is harder to defeat. They continued that, at the May Advisory Committee meeting, they learned the following:

- Having two forms of OxyContin on the market at the same time would be problematic.
- Including information about the (b) (4) properties in the label could lead prescribers and patients to a false sense of security.
- The previous in vitro data submitted in support of the original application (reformulated) were inadequate.
- The impact of the formulation change on abuse cannot be prospectively predicted or quantified.

After receiving the Complete Response letter from the Agency, the sponsor met with several groups to discuss their approach to evaluating the product characteristics. Based upon these communications, they developed a testing battery, conducted and QA'd by a third party, that they feel is exhaustive. They stated that, with every method, there is a demonstrated improvement over the older formulation, i.e., the reformulated product cannot be rendered immediate-release. In addition, they continued, the poly-oxide excipient renders the product more difficult to insufflate, inject, etc. They summarized that, since the impact of the

formulation change on abuse cannot be prospectively predicted or quantified, they plan to remain completely silent on the formulation change.

In the resubmission, the sponsor plans to submit data to support the approval of the 60- and 80-mg tablets and to provide bioequivalence data on the lower strengths. They will include data from their full in-vitro testing program. They are currently planning more studies, including an in vivo chewing PK study and a drug liking study in opioid-experienced abusers, and proposed submitting the data from these studies as a Phase 4 Commitment.

Dr. Rappaport stated that the sponsor's approach sounds promising and expressed his hope that the sponsor will provide the kind of quality data necessary to fully understand the characteristics of this new product. He continued that the Agency is fully supportive of efforts to develop products that are an incremental improvement over the current formulation, as it may protect a subset of abusers, e.g., teenagers, as well as protect against some medication errors. Dr. Rappaport apologized in advance for not being able to comment in full about the REMS requirements at this time. He stated that the Agency is currently discussing how to approach the development of a program that will be effective without placing insurmountable burdens on stakeholders. The sponsor inquired whether the pending status of the REMS discussions would hold up approval of this application. Dr. Rappaport responded that this issue is currently being discussed within the Agency.

FDA CRL Recommendation #1:

Question 1. Purdue does not intend to simultaneously distribute both formulations (current product and reformulated product) under the same trade name. As previously expressed to FDA, our plan is to cease shipping the original formulation as soon as all tablet strengths (10-80 mg) of the reformulated product have been approved and are available for shipping. Purdue intends to keep the trade name OxyContin for the reformulated product and does not intend to launch the reformulated product until all of its tablet strengths (10-80 mg) are approved and available for shipping. Based upon our ability to maintain low levels (2-3 weeks) of original formulation inventory at the wholesaler level, we expect the transition from original formulation OCR to reformulated OCR at the individual patient level to occur within approximately 6-8 weeks of shipping.
Does the Division agree with this proposed plan?

FDA Response:

The proposed plan may be acceptable. Provide clarification regarding the duration of time that the two formulations will be available concurrently.

It is acceptable to keep the trade name Oxycontin for the reformulated product.

Purdue-provided clarification prior to meeting:

> *Purdue clarification:*
> *Our goal is to replace the current formulation with the new formulation as seamlessly and silently as possible, in as rapid a time frame as possible. We will do this in a manner designed to minimize confusion and disruption to physicians, pharmacists, and most importantly patients. Once we begin shipping of the new formulation from our manufacturing facility, we will no longer be shipping the current version to wholesalers. Therefore, from that point forward the only formulation the wholesalers can obtain from Purdue, and distribute to pharmacies, is the new formulation.*

DISCUSSION:
Dr. Hertz asked how long the change-over to the new formulation is likely to take. The sponsor responded that their intention is to replace the current product with the new product as quickly as possible. A limiting factor is whether they are able to obtain allocation from DEA of enough drug substance to build up enough inventory of the new product to make the switch outright. The current DEA allocation is based on the current formulation. With a binary switch from current product to new product, they expect that, within the first week, 95% of the material available for distribution would be the new product. They anticipate that it would take about 30 days for the product to be switched over at the pharmacy level. In summary, it would take several weeks for most inventory to be fully switched over to the new product.

FDA CRL Recommendation #2:

Question 2. We intend to respond in full to CRL Recommendation #2. Section 9b and Appendix II describe the design and rationale for an in vitro testing battery that we believe addresses all recommendations made by the FDA. Does the proposed battery of in vitro testing adequately address these recommendations? If not, please clarify.

FDA Response:

The proposed in vitro testing plan seems to be adequate as far as the analytical approach described (Please see additional comments in the responses below.)

NO DISCUSSION NECESSARY

Question 3. In response to Recommendation #2a, all experiments associated with new OCR will be performed by a third party vendor, and to the extent feasible, will be conducted under blinded conditions. Quality assurance review of all experiments will be conducted by a third party. Does the Agency agree that this plan is sufficient to address the request made in Recommendation #2a? If not, please clarify.

FDA Response:

Yes. Please identify the third party vendor.

NO DISCUSSION NECESSARY

Question 4. In response to Recommendation #2b Purdue has convened an expert panel (Appendix I) experienced in the intentional extraction of oxycodone from OxyContin for abuse - to determine the methods for testing that would most likely replicate the methods encountered once the product is marketed. Input gathered on testing methods and was then used to design appropriate testing protocols. The protocols have undergone a validation procedure to ensure they are conducted in a reproducible and meaningful manner. Does the Agency agree that this approach addresses the request made in Recommendation 2b? If not, please clarify.

FDA Response:

Yes.

NO DISCUSSION NECESSARY

Question 5. In response to CRL Recommendation #2c Purdue has convened experts on extraction techniques to assess the design of the extraction protocols and the resultant data upon completion of the studies (Appendix I). Does the Agency agree that this approach addresses the request made in Recommendation 2c? If not, please clarify.

FDA Response:

Yes.

NO DISCUSSION NECESSARY

Question 6. In response to CRL Recommendation #2d new OCR will be crushed via different methods to understand the maximum expected range of minimum particle sizes achievable by chewing OCR tablets. Dissolution performance of the formulation matrix will then be assessed across all particle sizes achieved. Release of oxycodone API kinetics will be assessed in a time, solvent and temperature dependent manner. Purdue will also generate pharmacokinetic simulations from which "worst case scenario" in vivo oxycodone exposures can be estimated based on oxycodone release kinetics obtained in vitro (see below and Appendix II). Does the Agency agree that our proposed in vitro approach is sufficient to answer the concern raised about API release when tablets are chewed? If not, please clarify.

FDA Response:

Address the possibility that abusers may chew the matrix after (b) (4) and the consequences thereof.

The value of the pharmacokinetic simulations that you are proposing to generate, as mentioned in your question to address the concern raised about API release when tablets are chewed, is unclear. In the absence of representative in vivo data, simulations based on in vitro release kinetics alone is unlikely to add significant strength to these data.

Purdue-provided clarification prior to meeting:

Purdue clarification:
Chewing the current OxyContin quickly and easily results in the immediate release of the entire oxycodone content in seconds. In vitro testing demonstrates that in every manipulation scenario, API release is slower from new OCR than from OxyContin. Our data demonstrate that insults that exceed the physical and chemical effects of chewing new OCR result in slower oxycodone release than when current OxyContin is chewed. This conclusion can be reached without the results of the chewing PK study.

DISCUSSION:
Dr. Doddapaneni stated that an in vivo chewing study is not required. He clarified that pharmacokinetic simulations cannot be developed without some representative in vivo data to support them. Therefore, if a simulation was to be used to support in vitro data, then an in vivo study would be needed to support generation of the pharmacokinetic simulations themselves.

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Question 9. The original NDA from Purdue provided extensive toxicological data regarding the effects of the polyethylene oxide (PEO) matrix of new OCR. The scientific literature has characterized the pathobiological effects of intravenous and intradermal injection as well as insufflation of PEO. At this time we are not planning to reproduce these experiments for new OCR. Does the FDA agree with this position?

FDA Response:

Yes, we agree with your position. Toxicology studies related to inappropriate use of the product or components of the product are not required for approval.

NO DISCUSSION NECESSARY

FDA CRL Recommendation #3:

For our Resubmission, Purdue will formally repeat the primary pharmacokinetic analyses following exclusion of all pharmacokinetic data from subjects 5040, 5041, 5042, 5043, 5044, and 5046. The results of this reanalysis will be provided as an addendum to the original OTR1005 Clinical Study Report. This addendum will include revised versions of the tables and figures in Sections 12 and 14 that present the summary pharmacokinetic data and the results of the statistical analysis. Does the Division agree that the proposed response is appropriate to fully address this issue?

FDA Response:

Yes, your proposed response is appropriate.

NO DISCUSSION NECESSARY

FDA CRL Recommendation #4:

In FDA's correspondence dated December 4th 2008, Purdue was instructed not to submit a REMS proposal until the Agency has determined the necessary contents for drugs within the class of modified-release opioid analgesics. This request supersedes FDA's previous request for such a proposal included as Recommendation #4 of the Complete Response Letter. For this reason and despite considerable progress made to date on developing REMS content suitable for this class of medications, we do not plan to include REMS material within the resubmission for NDA 22-272.

FDA Response:

Details regarding the REMS for modified-release opioids are still under discussion within the Agency. You will be informed as to the requirements for the REMS when the information is available.

DISCUSSION:

The sponsor stated that they are still running their current RiskMAP program with no changes. Dr. Rappaport assured the sponsor that we will provide information regarding REMS requirements when we are able to.

FDA CRL Recommendation #5:

Purdue intends to submit the data for the 60 mg and 80 mg tablets as part of its Resubmission so that all tablet strengths of the new formulation may be approved and be made available simultaneously to prescribers and patients as expeditiously as possible. Does the Division agree with this plan?

FDA Response:

Your proposal to include additional data to establish the bioequivalence of the new formulation to the current formulation at the 60- and 80-mg tablet strengths in the resubmission of NDA 22-272 is acceptable.

However, clarify if bioequivalence was established under both fasted and fed conditions (as was done for the 10- and 40-mg strengths); or, if bioequivalence was established under fasted conditions, whether the food effect information obtained for the lower strengths of the new formulation applies to the 60- and 80-mg strengths.

NO DISCUSSION NECESSARY

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/s/

Lisa Basham

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-272

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

Attention: Anthony C. Santopolo, MD
Vice President, Regulatory Affairs

Please refer to your new drug application (NDA) dated November 29, 2007, received November 29, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OxyContin (Oxycodone Hydrochloride Controlled-Release Tablets), 10, 15, 20, 30, and 40 mg.

We refer to our complete response to your application dated October 3, 2008. In that letter, we indicated that we had completed the review of your application, as amended, and determined that we cannot approve the application in its present form. One of the reasons for the complete response was that it would be necessary for you to submit a proposed Risk Evaluation and Mitigation Strategy (REMS) in accordance with section 505-1 of the Federal Food, Drug, and Cosmetic Act.

In the complete response letter we provided a detailed description of the required elements of your proposed REMS. Although a REMS will still be necessary for your product, we are considering what REMS elements should be implemented across the class of modified-release opioids to address the risks of abuse and overdose and use in non-opioid tolerant individuals. Therefore, we request that you do not submit a REMS until we have determined the contents of the necessary program for this class of products. Once that determination is made we will notify you in writing.

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

Sincerely,

{See appended electronic signature page}

Bob Rappaport, MD
Director
Division of Anesthesia, Analgesia and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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Bob Rappaport

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-272

DISCIPLINE REVIEW LETTER

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

Attention: Patricia R. Mayer, Ph.D.,
Senior Director, U.S. Regulatory Affairs

Dear Dr. Mayer:

Please refer to your November 29, 2007, new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for OxyContin® (oxycodone hydrochloride) Controlled-Release Tablets, 10mg, 15mg, 20mg, 30mg and 40 mg.

We also refer to your submission dated December 19, 2007.

Our review of the Chemistry, Manufacturing and Controls section of your submission is complete, and we have identified the following deficiencies:

1. Revise your release and stability specifications proposed for each strength such that they are consistent with the recommendations regarding regulatory acceptance criteria specific to the United States (see ICH Q6A). The regulatory acceptance criteria are the same from release throughout shelf life. However, you may propose tighter in-house criteria to be applied at release but these do not have to be a part of the application. You may also indicate in the specifications which tests are not performed during stability testing (e.g., identity).

2. Revise the various drug product specifications to either replace the identity test by HPLC retention time with a specific test, or add a complementary non-specific identification test with acceptance criterion.

3. Revise the system suitability requirements for the HPLC method (b) (4) for drug product degradants to reflect the system suitability requirements supported by and proposed in the method validation study report, provided in P.5.3, for that method.

4. The following preliminary labeling comments pertain to the package insert proposed.

   a. Provide confirmation that the polyethylene glycol that is included in the 10, 15, 20, 30, and 40 mg strengths is the [redacted (b) (4)], as is stated in the DESCRIPTION section of the package insert.

   b. Provide the data and information or reference to the submissions to NDA 20-553 that provided these to support your added description of the AcroContin® delivery system to the DESCRIPTION section of the package insert.

5. Comments regarding your proposed dissolution testing regulatory acceptance criteria (i.e., those applied on stability) may be forthcoming, depending on our determination that you have provided appropriate bioavailability data to validate those acceptance criteria ranges that are larger than [redacted (b) (4)]% of the labeled content (i.e., 4 hour).

6. Comments on the proposed expiration dating period may be forthcoming pending our evaluation of your statistical analysis of the long term stability data.

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 Lisa E. Basham, Regulatory Project Manager, at 301-796-1175.

Sincerely,

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

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/s/

Lisa Basham
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For Parinda Jani

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Rockville, MD 20857

FILING COMMUNICATION

NDA 22-272

Purdue Pharma LP
One Stamford Forum
Stamford, CT 06901-3431

Attention: Patricia Mayer, PhD
Senior Director, US Regulatory Affairs

Dear Dr. Mayer:

Please refer to your new drug application (NDA) dated November 29, 2007, received November 29, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for OxyContin® (oxycodone hydrochloride) Controlled-Release Tablets, 10 mg, 15 mg, 20 mg, 30 mg, and 40 mg.

We also refer to your submissions dated November 30, December 19, 20, and 21, 2007, and January 14, 2008.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Priority**. Therefore, the user fee goal date is May 29, 2008.

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

> The submitted Risk Management Plan will need to be updated for consistency with that of NDA 20-553/ (b) (4) The timeliness and acceptability of this updated RMP submission may affect the approvability of this application.

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

We also request that you submit the following information:

1. Provide statistical analysis of the stability and dissolution test data in SAS format during early stage of the review cycle.

2. Identify the packaging components that are supplied by [redacted] (b) (4), holder of DMF [redacted] (b) (4).

3. Provide the master batch (blank) records for the lowest (10 mg) and highest (40 mg) tablets.

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/oc/datacouncil/spl.html. 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, call Lisa Basham, Regulatory Project Manager, at (301) 796-1175.

Sincerely,

{See appended electronic signature page}

Bob Rappaport, MD
Director
Division of Anesthesia, Analgesia and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

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/s/

Parinda Jani
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for Bob Rappaport, M.D.