DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-553/S-060

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

Attention: Beth Connelly
Assistant Director, US Regulatory Affairs

Dear Ms. Connelly:

Please refer to your supplemental new drug application dated December 13, 2007, received December 14, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for OxyContin (oxycodone hydrochloride Controlled-Release) Tablets.

This "Changes Being Effected" supplemental new drug application provides for changes to the **Boxed Warning, PHARMACOKINETICS AND METABOLISM, WARNINGS, PRECAUTIONS, and DOSAGE AND ADMINISTRATION** sections of the package insert.

We have completed our review of this application and it is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert).

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 20-553/S-0060."

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A)).

Since OxyContin was approved on December 12, 1995, we have become aware of data in supplement 60 which suggest a major role for the isozyme, CYP3A4, in the metabolism of oxycodone. Given the role of CYP3A4 isozyme in the metabolism of oxycodone, drug-drug interaction with CYP3A4

inhibitors, such as ketoconazole, may result in unexpected inhibition of the metabolism of oxycodone, raising its blood levels and resulting in serious risk associated with opioid side effects including respiratory depression. Therefore, we consider this information to be "new safety information" as defined in FDAAA.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify an unexpected serious risk associated with the CYP3A4 drug-drug interaction from coadministration of ketoconazole and oxycodone.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA has not yet been established and is not sufficient to identify this unexpected serious risk.

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to identify this unexpected serious risk.

Therefore, based on appropriate scientific data, we have determined that you are required to conduct the following:

1539-1. An *in vivo* drug metabolism/drug interaction trial in normal volunteers to assess the effect of ketoconazole on the metabolism of oxycodone and its known metabolites.

The timetable you submitted on September 2, 2009, states that you will conduct this trial according to the following timetable:

Final Protocol Submission:	September 11, 2009
Trial Completion Date:	February 26, 2010
Final Report Submission:	June 30, 2011

See *Guidance for Industry: In Vivo Drug Metabolism/Drug Interaction Studies – Study Design, Data Analysis, and Recommendations for Dosing and Labeling* for additional details on the design and conduct of the trial.

Submit the protocol to your IND 29,038, with a cross-reference letter to NDA 20-553. Submit all final report(s) to your NDA 20-553. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate:

- **REQUIRED POSTMARKETING PROTOCOL UNDER 505(o)**
- **REQUIRED POSTMARKETING FINAL REPORT UNDER 505(o)**
- **REQUIRED POSTMARKETING CORRESPONDENCE UNDER 505(o)**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

HEALTH CARE PROFESSIONAL LETTER

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

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

Enclosure

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20553	SUPPL-60	PURDUE PHARMA LP	OXYCONTIN (OXYCODONE HCL) CR TABS

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

/s/

BOB A RAPPAPORT
09/02/2009