DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022272 **NDA APPROVAL**

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) dated, received November 29, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets.

We acknowledge receipt of your submissions dated November 30, and December 19, 20 and 21, 2007, January 14, February 8, 12, 14 (2), and 15 (2), March 7, 10, 14, 18, 25 (2), and 27, April 11 (2) and 23, May 7, August 20, September 26, October 30, November 11 and 20, and December 5, 8, and 10, 2008, and March 30, May 18, June 2, 10, and 16, July 13 and 24, August 7, September 18, October 6 and 9, and November 4, 6, 17, 19, and 23, December 16 and 22 2009, and February 5, and 24, March 11, 25, 26, and 31, and April 2, 2010.

The February 5, 2010, submission constituted a complete response to our December 30, 2009, action letter.

This new drug application provides for the use of OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, and 80 mg, for treatment of moderate-to-severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format submitted on March 31, 2010.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please resubmit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling text for the package insert and Medication Guide. For administrative purposes, please designate this submission, "**SPL for approved NDA 022272**."

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your March 31, 2010, submission containing final printed carton and container labels.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

POSTMARKETING REQUIREMENTS UNDER 505(o)

As you were informed in our December 30, 2009, Complete Response Letter, FDA has determined that you are required to conduct postmarketing studies of OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets to assess the known serious risks of OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets, in particular, whether the changes made to the OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets formulation that are the subject of this application and which are intended to deter misuse and abuse actually result in a decrease in the risks of misuse and abuse, and their consequences.

Specifically, we have determined that you are required, pursuant to section 505(o)(3) of the FDCA, to conduct epidemiological studies to address whether the changes made to the OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets formulation that are the subject of this application result in a decrease in misuse and abuse, and their consequences: addiction, overdose, and death.

We acknowledge receipt of your proposal, included in your February 5, 2010, resubmission to this application, that contains brief descriptions of possible postmarketing studies to fulfill this requirement. Because of design and methodology challenges, we continue to be concerned that the proposed studies will not successfully capture the necessary information that will allow us to assess the impact, if any, attributable to the change in the OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets formulation. Therefore, we will continue discussion of your postmarketing study proposals at an advisory committee meeting in the fall of 2010 on the design and methodology of the proposed studies.

For the study to be conducted first, you must submit the final protocol and the timetable for completion of the study by January 31, 2011. Likewise, for the study to be conducted last, you must submit the final protocol and timetable for completion of the study by March 1, 2011.

Submit future correspondences regarding your proposal(s) to address this requirement to your IND, with a cross-reference letter to this NDA. Prominently identify the submission(s) with the following wording in bold capital letters at the top of the first page of the submission:

- **REQUIRED POSTMARKETING CORRESPONDENCE UNDER 505(o)**

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)).

Pursuant to 505-1(f)(1), we have determined that OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets can be approved only if elements necessary to assure safe use are required as part of a REMS to mitigate the risks of abuse, misuse, and overdose, and addiction, as well as the risk of use of doses greater than 60 mg of OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets in non-opioid tolerant individuals, listed in the labeling. The elements to assure safe use will ensure that OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets will only be prescribed by healthcare providers who have particular training under 505-1(f)(3)(A) and will mitigate the aforementioned risks through informing and training healthcare providers about the potential risks and the safe use of OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets.

Your proposed REMS, submitted on April 2, 2010, and appended to this letter, is approved. The REMS consists of a Medication Guide, elements to assure safe use, and a timetable for submission of assessments of the REMS.

As you know, we are considering what REMS elements should be implemented for a number of opioid products, including modified-release opioids to address the risks of: 1) use in non-opioid-tolerant individuals and 2) abuse, misuse, overdose, and addiction. As discussed, once that determination is made, we will notify you in writing and you will be required to submit a modified REMS incorporating those elements.

The REMS assessment plan should include but is not limited to the following:

1. An evaluation of patients' understanding of the serious risks of OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets.

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 including the number of Dear Healthcare Professional letters mailed to each specialty identified in the

5. An evaluation of healthcare providers' awareness and understanding of the serious risks associated with OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets (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. An analysis to evaluate OxyContin (Oxycodone Hydrochloride Controlled-Release) Tablets utilization patterns including use in non-opioid tolerant patients.

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.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(A), an assessment of the extent to which the elements to assure safe use are meeting the goal or goals to mitigate a specific serious risk listed in the labeling of the drug, or whether the goal or goals or such elements should be modified.

Assessments of an approved REMS must also include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in Section 505-1(g)(2)(A) of FDCA.

Prominently identify any submission containing the REMS assessment or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission:

N 022272 REMS ASSESSMENT

NEW SUPPLEMENT FOR N 022272
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)

REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

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

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

EXPIRATION DATING PERIOD

An expiration dating period of 24 months is granted to the 10, 15, 20, 30, 40, 60, and 80 mg OxyContin tablets in HDPE bottle packaging configurations, stored at 25°C (77°F); excursions permitted between 15°-30°C (59°-86°F).

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

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