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November 20, 2008

Via Certified Mail-Return Receipt Requested

Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, RM 1061
Rockville, MD 20852

Citizen Petition

The undersigned, by and through counsel, submits this petition under 21 U.S.C. §§ 301-394 of the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act or any other statutory provision for which authority has been delegated to the Commissioner of Food and Drugs under 21 CFR 5.10 to request the Commissioner of Food and Drugs to revoke its approval of the current drug label / package insert for the prescription drug OxyContin, declare the OxyContin drug label / package insert misleading, and require the manufacturer of OxyContin (Purdue Pharma) to revise the label / package insert by removing the log scale graph contained in the label, disclosing dysphoria as an adverse experience and more prominently disclosing the adverse risks of euphoria and dysphoria from taking OxyContin.

I. Action Requested

1. Petitioner requests that the FDA compel Purdue Pharma to revise the

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FDA-2008-P-0618-0001

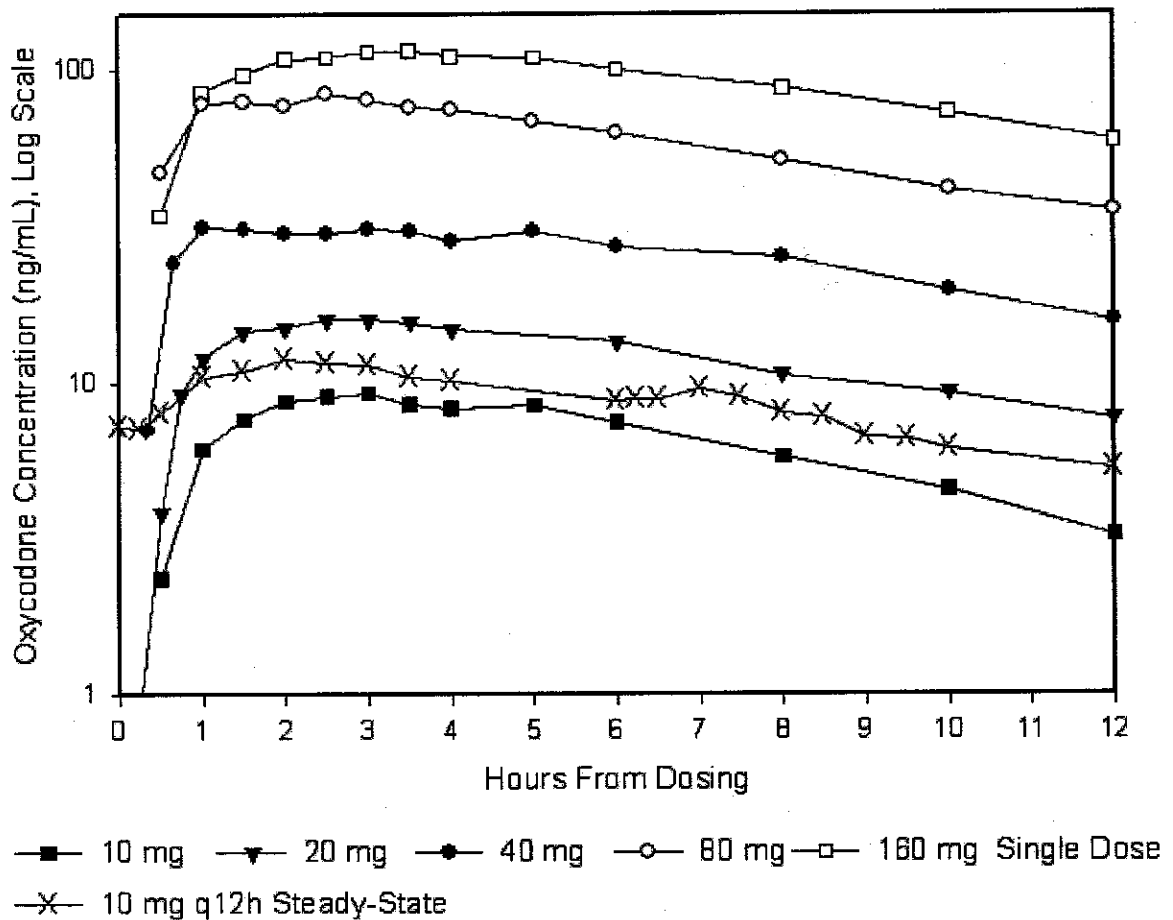
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label / package insert of OxyContin in three ways. First, by removing the misleading log scale graph from the package insert. The current drug label / package insert for the prescription drug OxyContin contains the following graph:

Plasma Oxycodone By Time



2. Petitioner requests that the FDA require that Purdue Pharma remove this graph from the OxyContin package insert.

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The following adverse experiences were reported in OxyContin[®]-treated patients with an incidence between 1% and 5%. In descending order of frequency they were anorexia, nervousness, insomnia, fever, confusion, diarrhea, abdominal pain, dyspepsia, rash, anxiety, euphoria, dyspnea, postural hypotension, chills, twitching, gastritis, abnormal dreams, thought abnormalities, and hiccups.

4. Petitioner requests that the FDA order Purdue Pharma to disclose dysphoria as an additional adverse experience in the above paragraph.

5. Third, Petitioner requests that the FDA order Purdue Pharma to add the following language to the black box warnings in the OxyContin label/package insert:

OxyContin blood plasma levels peak and trough at levels similar to immediate release opioids of similar mg. strengths. There is no clinical evidence that OxyContin causes less euphoria and dysphoria than immediate release opioids and Purdue Pharma has received reports of euphoria associated with the use of OxyContin. OxyContin tablets are subject to abuse, misuse and diversion.

II. Statement of Grounds

A. Purdue's Admission and Criminal Guilty Plea.

6. On December 12, 1995, FDA approved OxyContin for sale in the United States.

7. On May 10, 2007, Purdue Fredrick and three of Purdue's top executives pleaded guilty in federal court to criminal charges that they misled doctors and patients when they claimed that OxyContin was less likely to be abused than traditional narcotics.

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8. The three Purdue executives who pleaded guilty were Michael Friedman-president, Howard R. Udell-top legal officer and Dr. Paul D. Goldenheimer-former medical director.

9. Purdue pleaded guilty to felony misbranding a drug with the intent to defraud or mislead in violation of Title 21, United States Code, Sections 331(a) and 333(a)(2).

10. Purdue pleaded guilty because it was in fact guilty of these crimes.

11. As part of the guilty plea, Purdue agreed that neither it nor any of its associated entities would make any public statements contradicting the statement of facts set forth in the Agreed Statement of Facts that was attached to the plea agreement.

12. The guilty pleas of Purdue and its executives were freely and voluntarily made.

13. Purdue and its executives pleaded guilty because they were guilty of the crimes to which they entered guilty pleas.

14. In connection with the guilty plea, Purdue and its three executives agreed that the facts identified in an Agreed Statement of Facts were true.

15. Beginning on or about December 12, 1995, and continuing until on or about June 30, 2001, certain Purdue supervisors and employees, **with the intent to defraud or mislead**, marketed and promoted OxyContin as less addictive, less subject to

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abuse and diversion, and less likely to cause tolerance and withdrawal than other pain medications, as follows:

- a. Trained Purdue sales representatives and told some health care providers that it was more difficult to extract the oxycodone from an OxyContin tablet for the purpose of intravenous abuse, although Purdue's own study showed that a drug abuser could extract approximately 68% of the oxycodone from a single 10 mg OxyContin tablet by crushing the tablet, stirring it in water, and drawing the solution through cotton into a syringe;
- b. Told Purdue sales representatives they could tell health care providers that OxyContin potentially creates less chance for addiction than immediate-release opioids;
- c. Sponsored training that taught Purdue sales supervisors that OxyContin had fewer "peak and trough" blood level effects than immediate-release opioids resulting in less euphoria and less potential for abuse than short-acting opioids;
- d. Told certain health care providers that patients could stop therapy abruptly without experiencing withdrawal symptoms and that patients who took OxyContin would not develop tolerance to the drug; and

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e. Told certain health care providers that OxyContin did not cause a “buzz” or euphoria, caused less euphoria, had less addiction potential, had less abuse potential, was less likely to be diverted than immediate-release opioids, and could be used to “weed out” addicts and drug seekers.

16. In implementing this scheme to defraud and mislead healthcare providers, Purdue supervisors and employees were following a company decision and policy to market OxyContin based on misperceptions about the drug in the minds of physicians.

17. In connection with its guilty plea, Purdue entered into a Corporate Integrity Agreement (“CIA”) with the Office of Inspector General of the Department of Health and Human Services. See <http://www.oig.hhs.gov/fraud/cia/docs/CIAPurdue.pdf>.

18. The CIA requires Purdue to self-report violation of FDA labeling requirements.

19. Despite its guilty plea, Purdue continues to misbrand OxyContin, as explained below, and has not self reported FDA labeling requirements to the Officer of Inspector General as required by the CIA.

B. Purdue’s Over-promotion of OxyContin.

1. Doctor Focus Groups used to shape false marketing plan.

20. The active ingredient in OxyContin is oxycodone, which is an opiate.

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21. Before Purdue's launch of OxyContin in 1996, Purdue conducted doctor focus group studies in order to evaluate how doctors would react to and use the drug in the treatment of their patients.

22. The doctor focus groups showed that when doctors understood that OxyContin was a strong opioid, they would be reluctant to prescribe it because of concerns over physical dependence and addiction.

23. The terms "physical dependence" and "addiction" are generally used interchangeably by doctors and the general public. Consistent with this general practice, the terms do not have separate meaning in this petition.

24. Purdue's doctor focus groups educated Purdue to the fact that many doctors mistakenly believed that oxycodone, the active ingredient of OxyContin, was weaker than morphine. In reality, at equal mg. strength oxycodone is twice as potent as morphine.

25. In order to overcome physicians' concerns about the addiction risks of OxyContin, Purdue developed a marketing plan to over-promote OxyContin and misrepresent to physicians that the risk of addiction with OxyContin was less than immediate release opioids.

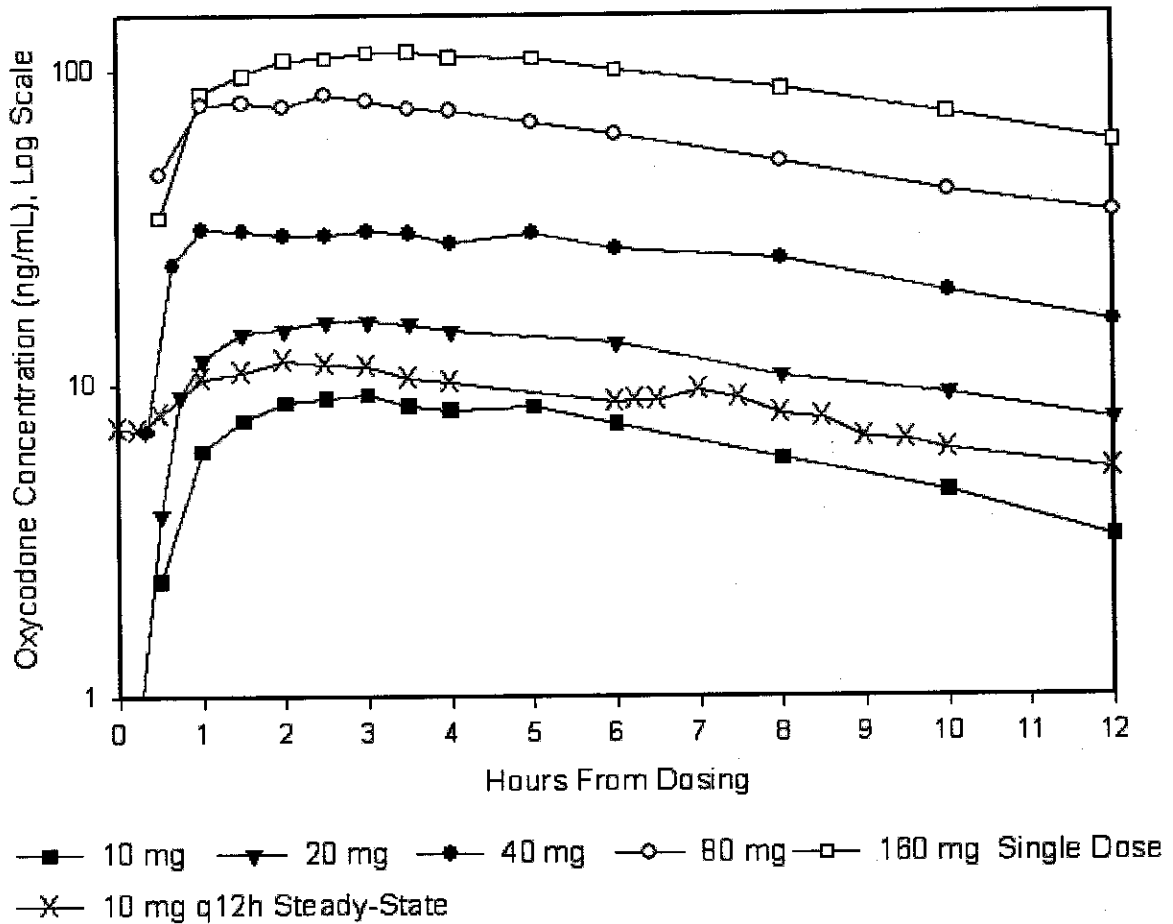
2. Misleading use of log scale graph.

26. The lynchpin of Purdue's over-promotion of OxyContin was the following "log scale" graph contained in the drug's label/ package insert:

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Plasma Oxycodone By Time



27. From the time of its initial labeling approval until the present the OxyContin label has included this log scale graph of blood concentration over time depicting each dosage strength of OxyContin pills.

28. When used for legitimate purposes, a logarithmic scale allows the presentation of data that covers a large range of values.

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29. Putting the OxyContin blood plasma graph in log scale rather than mean scale flattened the curves and caused the graph to depict lower peaks and higher troughs.

30. The use of logarithmic scale rather than mean scale flattened the blood plasma curves in the graph in the OxyContin package insert. Purdue's marketing of OxyContin emphasizes the smooth sustained blood plasma as depicted in the log scale graph.

31. The OxyContin package insert identified that the graph was in "log scale" in typeset that was "exceedingly small".

32. In addition, many physicians are not trained in the intricacies of graph scales and do not understand the affect of depicting the graph in log scale.

33. Purdue did not educate and train its sales force on the affect of depicting the graph in log scale. As a result, the Purdue sales force had and still has misperceptions about the oxycodone delivery system in OxyContin.

34. Purdue trained its sales force to emphasize the smooth and sustained blood plasma levels as depicted in the OxyContin label's log scale graph.

35. Purdue also trained its sales force that differences in blood plasma peaks and valleys with OxyContin were not as great as in immediate release opioids at similar mg. strengths. In order to support this claim, Purdue used graphs that depicted OxyContin blood plasma levels in log scale and immediate release opioid blood plasma levels in mean scale. Such a presentation was very misleading.

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36. Peaks and valleys of blood plasma levels of addictive drugs such as OxyContin have a direct connection to euphoria and sedation and, as a result, the addictive potential of the drug.

37. The log scale graph in the OxyContin label graphically suggests less potential for euphoria and sedation and, therefore, less potential for addiction.

3. After the FDA approved the OxyContin label Purdue obtained information that the log scale graph in the OxyContin label is misleading.

38. No later than November 2007, Purdue obtained information that physicians did not recognize the fact that the use of log scale in the OxyContin label's graph flattened the blood plasma curves. Purdue also learned that physicians interpret the graph as suggesting less potential for euphoria and sedation and, therefore, less potential for addiction.

39. In August 2008 Purdue obtained information that members of its current sales force, including a former district manager, did not understand the significance of the use of log scale in the OxyContin label's graph. Purdue also learned at this time that its district managers did not train sales reps on the difference between log scale and mean scale.

40. Purdue also obtained information in August 2008 that as a result of the misleading log scale graph, members of its current sales force incorrectly believe and

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communicate to physicians that at comparable dosage levels, OxyContin has lower peak blood plasma levels than short-acting opioids.

41. As a result of the facts alleged above, Purdue has knowledge that the current OxyContin package is misbranded within the meaning of 21 U.S.C. §§ 331 and 352 in violation of FDA regulations.

42. Purdue did not self-report the ongoing misbranding of OxyContin pursuant to the CIA.

4. Misleading claim of smooth, sustained release of oxycodone.

43. Since the launch of OxyContin in 1996, the Purdue sales force has marketed OxyContin as providing a smooth and sustained release of oxycodone over a twelve hour period due to the unique delivery system in OxyContin.

44. Purdue's claim of a smooth and sustained delivery system was supported by the log scale graph contained in the OxyContin package insert.

45. Purdue promoted OxyContin as—unlike immediate release opioids—not having peaks and valleys of blood plasma due to the smooth and sustained delivery system as depicted in the log scale graph.

46. There is a direct correlation between blood plasma peaks and valleys and the risk of addiction from an opiate painkiller. This is because blood plasma peaks can cause euphoria and blood plasma valleys can cause dysphoria. The cycle of euphoric and dysphoric peaks and valleys can lead to addiction.

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47. Purdue marketed OxyContin as not having the blood plasma peaks and valleys that are characteristic of immediate release opioids. This suggested to physicians that OxyContin was less addictive than immediate release opioids.

48. Purdue sales representatives reinforced the graphic suggestion that the OxyContin was less addictive than immediate release opioids by directly making this claim. Purdue sales representatives made this claim because Purdue trained the representatives to make it.

49. In reality, at similar mg. strengths OxyContin has the same peak and valley blood plasma levels as immediate release opioids.

50. From 1996 to the present Purdue sales representatives mistakenly believed that OxyContin had lower peaks and higher valleys than immediate release opioids.

**5. Purdue's decision to maintain
misperceptions about OxyContin.**

51. In May 1997, Purdue's owner and top executives discussed by email physicians' perceptions about OxyContin.

52. During these discussions a Purdue executive recognized that many health care professionals had the misperception that oxycodone, which is the active ingredient in OxyContin, was weaker than morphine.

53. The same Purdue executive also recognized that the misperception about the strength of OxyContin was factored into Purdue's marketing and promotion of the drug.

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54. Another Purdue executive stated that "we are well aware of the view, held by many physicians, that oxycodone is weaker than morphine" and that this personality of oxycodone is an integral part of the personality of OxyContin.

55. The same Purdue executive stated that it would be dangerous to tamper with this personality to make physicians think oxycodone is stronger or equal to morphine and that he did not plan to try to change the personality of OxyContin so that the company could continue to focus on expanding the non-malignant pain usage.

56. Purdue executives also recognized in this email string that the misperceptions about OxyContin were an integral part of the company's marketing of the drug.

57. Despite invitations to disagree, not a single Purdue executive disagreed with the company's decision to promote OxyContin based on a misperception about the strength of the drug.

58. Because of this decision, certain Purdue supervisors and employees stated that while they were well aware of the incorrect view held by many physicians that oxycodone was weaker than morphine, they did not want to do anything "to make physicians think that oxycodone was stronger or equal to morphine" or to "take any steps in the form of promotional materials, symposia, clinicals, publications, conventions, or communications with the field force that would affect the unique position that OxyContin ha[d] in many physicians mind (sic)."

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59. As a result of this decision, no action was ever taken to address the misperception that many physicians had about OxyContin and its active ingredient.

6. Purdue's monetary compensation to FDA officer who approved OxyContin.

60. The FDA medical officer who approved OxyContin was Curtis Wright, M.D.

61. Within a short time of the FDA's approval of OxyContin Purdue hired Dr. Wright into the company's risk management department.

62. Dr. Wright had no prior experience in risk management.

63. Over the course of the next several years, Purdue paid Curtis Wright millions of dollars in salary and bonuses.

64. Purdue's hiring and compensation of Curtis Wright casts a cloud of suspicion over the entire approval of OxyContin, including the approval of the logarithmic scale graph in the drug's label.

7. Failure to identify dysphoria as adverse experiences of OxyContin.

65. Early preliminary drafts of the OxyContin label identified euphoria and dysphoria as frequent adverse experiences of OxyContin.

66. The final draft submitted to FDA and approved by FDA changed euphoria to a rare adverse experience and deleted dysphoria as an adverse experience. The current disclosure is as follows:

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The following adverse experiences were reported in OxyContin[®]-treated patients with an incidence between 1% and 5%. In descending order of frequency they were anorexia, nervousness, insomnia, fever, confusion, diarrhea, abdominal pain, dyspepsia, rash, anxiety, euphoria, dyspnea, postural hypotension, chills, twitching, gastritis, abnormal dreams, thought abnormalities, and hiccups.

67. Yet Purdue identifies dysphoria as an adverse experience in the label of its other product that contains oxycodone, Oxy IR:

Other adverse reactions include euphoria, dysphoria, constipation, skin rash, and pruritus.

68. As previously discussed, Purdue obtained information no later than November 2007 that physicians place significance on the adverse experiences of euphoria and dysphoria when evaluating the addictive potential of a drug.

69. Euphoria and dysphoria are potential adverse experiences of OxyContin and this information should be disclosed in the OxyContin label/ package insert.

III. Environmental Impact

70. Petitioner claims categorical exclusion under §§25.30, 25.31, 25.32, 25.33, or §25.34 of this chapter.

IV. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are

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unfavorable to the petition. The undersigned is willing to meet with the FDA to discuss the matters contained in this petition.

Signature: _____


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Attorney for and on behalf of Patricia Gwen Kiser

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