

February 1, 2005

Documents Management Branch, Food and Drug Administration, Department of Health  
and Human Services, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857

## Citizen Petition

The undersigned submits this petition under Section 505b of the Federal Food, Drug and Cosmetic Act to request the Commissioner of Food and Drugs to temporarily revoke and/or permanently amend the FDA actions identified below.

### FDA Actions Taken:

- 1) Title 21 CFR 314.105 Approval of (NDA) 020553 OxyContin  
12/12/95
- 2) Title 21 CFR 314.105 Approval of (NDA)021044 Palladone  
9/24/04
- 3) Title 21 CFR 314.70 Approval of Supplemental New Drug  
Applications providing for labeling changes of (NDA) 020553  
11-20-03 (1-15-02, 7-18-01, 7-25-97, 6-21-96)

### Actions Requested by Petitioner:

- 1) Temporary recall of approval of OxyContin (and generic equivalents)  
and removal from market until chemically reformulated by  
manufacturer(s) to drug of minimal abuse potential.
- 2) Temporary recall of approval of Palladone and removal from market  
until chemically reformulated by manufacturer to drug of minimal  
abuse potential.
- 3) Label changes limiting indications for OxyContin (and generic  
equivalents) to severe chronic pain from documented peripheral tissue  
disease processes.
- 4) Label changes limiting indications for Palladone to severe chronic  
pain from documented peripheral tissue disease processes.

## **I. Statement of Grounds – Overview**

Numerous reports from across the country of death and addiction caused by OxyContin clearly document a national problem of escalating opioid abuse, diversion, and inappropriate physician prescribing.

- A recent University of Michigan study conducted for the National Institute on Drug Abuse found that despite a 17% overall decrease in illicit drug use among teens over the past four years, there has been a 49% increase in OxyContin abuse. 1.9 million individuals have used OxyContin for non-medical purposes at least once in their lifetime [Ref. #2] and non-medical use by people 12 or older rose from 399,000 in the year 2000 to 2.8 million in the year 2003. Between 1997 and 2002, there was a 400% increase in the medical use of oxycodone. During that same period of time, there was a 300% increase in abuse of oxycodone as recorded by DAWN data [Ref. #3].
- In the year 2000, the OxyContin problem had been located primarily in Maine, Pennsylvania, Kentucky, Virginia, West Virginia, and Alabama. By 2001, it was a major and emerging problem in South Carolina, Florida, Tennessee, Montana, Louisiana, Texas, and Washington State [Ref.#1]. By 2004, the OxyContin abuse problem had affected multiple other states. Parts of Canada now have severe OxyContin problems (Nova Scotia and Ontario).
- An April 2002 report from the DEA implicated OxyContin as the direct cause or main contributing factor in 146 deaths and a likely contributor in an additional 318 deaths. The DEA based its findings on a survey of state medical examiners using autopsy data. A total of 949 reports were received, half of which involved OxyContin. More current figures seem to be unavailable but the death rate since 2002 continues to escalate.
- Non-medical use of prescription painkillers now comprises 30% of emergency room visits. The Department of Justice reports 20,000 prescription painkiller emergency room visits in 2002 alone.
- OxyContin death and addiction is not limited to those taking it for non-medical uses. Since Purdue Pharma's 1997 launch of OxyContin

into the moderate pain market and due to the company's aggressive and untruthful marketing campaign, increasing numbers of patients legally prescribed OxyContin have suffered tragic devastation of their lives and/or death (reports and stories of such patients can be found at [www.oxyconned.org](http://www.oxyconned.org) ).

- On October 25, 2004 John Walters, White House anti-drug czar, announced in Missouri that the National Synthetic Drugs Action Plan is in response to the increased abuse of methamphetamines, Ecstasy and OxyContin.
- In an opinion issued on January 5, 2004 Judge Sidney Stein, federal judge in New York, ruled that the representations made by Purdue to the government concerning the effectiveness of OxyContin for chronic pain sufferers were fraudulent and misleading and that the patents issued to Purdue were therefore invalid. In particular, Judge Stein ruled that Purdue had misled the government by claiming that they had conducted clinical studies demonstrating OxyContin's unique pain-relieving qualities when **no such studies existed**.
- In March, 2004 Lester Crawford, Acting Commissioner of the FDA, stated “ *As beneficiaries of the world's premiere health system, Americans should not have to endure preventable medical errors and adverse events related to medical products...Americans deserve better than settling for serious health consequences that can't be spotted until many years after a product has been on the market.* ”

**It is near the one-year anniversary of the General Accounting Office report on OxyContin abuse and the Florida Hearings before the U.S. House of Representatives Subcommittee on Criminal Justice, Drug Policy and Human Resources, at the latter of which, Robert Meyer, M.D. outlined a number of laudable FDA actions to prevent prescription drug abuse. As documented above, however, these efforts have fallen short, as the incidence of addiction and death from OxyContin has continued to escalate. Clear evidence of the severity of these adverse events has been known for more than five years, and the time is thus overdue to implement the more stringent measures requested in this petition. If it is appropriate to reevaluate the Cox-2 inhibitor pain medications, there is certainly a need for the FDA to**

reexamine regulation of the much more powerful and dangerous sustained-release opioids.

## II. STATEMENT OF GROUNDS – SPECIFICS FOR REQUESTS #1 and #2

- In the current formulations of OxyContin and Palladone, full doses of oxycodone and hydromorphone can be easily converted from sustained to one-time immediate release. Ingestion of this immediate release form of the drug can be fatal or lead to opiate addiction. Large numbers of accidental overdoses of patients legally prescribed OxyContin have also been documented. ([www.oxyconned.org](http://www.oxyconned.org)).
- OxyContin (and soon Palladone) are easily available through Internet pharmacies. Legislation such as the Ryan Haight Act, co-sponsored by Senator Feinstein of California addresses this problem; however, the U.S. government is currently unable to regulate foreign online pharmacies. Unless OxyContin and Palladone are reformulated as abuse resistant, the current dangerously potent formulations will continue to be easily accessible.
- Randomized, double blind studies comparing OxyContin given every 12 hours with immediate-release oxycodone given four times daily demonstrated comparable efficacy and safety in chronic back pain [Ref. #4] and cancer pain [Ref. #5,6]. Compared with sustained release hydromorphone immediate release hydromorphone demonstrated **no difference** in efficacy and safety in cancer patients [Ref. #7,8]. Chou and colleagues in a recent review of the medical literature concluded that there is insufficient evidence to conclude that sustained release opioids have any better efficacy or safety than immediate release opioids [Ref.#9].
- Despite the wide publicity of the rapidly growing OxyContin problem since 2000, OxyContin sales have grown from about \$1.2 billion in 2000 to about \$1.9 billion in 2004 (IMS Health)----in spite of the lack of any scientific evidence that this is a better drug than what is available with other preparations.

- State Attorney General of Pennsylvania Jerry Pappert accurately stated that Purdue Pharma is not living up to its public commitment to reformulate OxyContin. He stated “We were told in April 2001 that they were aggressively researching adding anti-abuse ingredients to OxyContin, which would make the drug non-effective if a tablet was crushed and then snorted or taken intravenously by an abuser. The drug was expected to be ready in about three years. It is now (more than) three years later, and Purdue Pharma is currently stating in press reports that the drug development is 10 to 12 years away. They are working on a timetable that is financially best for them.” Pain Therapeutics Inc. (South San Francisco) has already received regulatory clearance to initiate clinical studies in the U.S. with Remoxy, a long-acting version of oral oxycodone that incorporates several abuse-deterrent properties. Additionally, a number of recent patent applications are pending, based on the strategy of combining an opioid with a chemical irritant that would be active when the drug is snorted, chewed or administered intravenously, but not when taken as prescribed, ie, swallowed whole [Ref.# 10-14]. Purdue Pharma’s claims that it will take 10-12 years to develop a less abuseable form of OxyContin are thus clearly inaccurate.
  
- By 2001, the increasingly widespread pain and suffering associated with the diversion of OxyContin abuse led some communities to formulate a national petition to recall Oxycontin [Attachment B] [www.recalloxycontinnow.org](http://www.recalloxycontinnow.org) . The underlying thesis of the petition was that the harm brought by the widespread availability of OxyContin on the market-place was simply greater than the benefits of the drug; that there were equally effective opioids available for treatment of severe pain, some of which posed less abuse potential; and that nothing short of a recall could begin to address the problem. The petition was introduced in California in late 2004. Currently over 8,000 individuals have signed the petition online or in person, further support for the position of this FDA Citizen Petition (signatures available upon request).

**At the February 2004 Florida hearing before the Subcommittee on Criminal Justice, Drug Policy and Human Resources, chairman Mark Souder emphasized the need for a regulatory plan that balances the**

competing concerns of those suffering from chronic pain and those whose lives have been devastated by OxyContin. The above documentation establishes both the unacceptable (and unnecessary) danger inherent in the current chemical formulation of OxyContin and the equivalent effectiveness of other preparations. This petition's request for temporary recall of OxyContin (and generic equivalents) and Palladone until chemically reformulated by the manufacturer therefore would not compromise treatment of pain patients, would actually increase patient safety and is necessary if the single largest impetus for abuse of the drugs is to be eliminated.

### **III. STATEMENT OF GROUNDS – SPECIFICS FOR REQUEST #3 and #4**

- Only two years after introducing OxyContin for the treatment of cancer-related and other severe pain, Purdue Pharma was allowed to extend its indications to moderate pain situations. At about the same time, the more potent 80 mg. And 160 mg. (1999) tablets were introduced. As a result of this expansion and Purdue Pharma's aggressive marketing, two-thirds of all OxyContin prescriptions are now for non-severe, non-cancer pain, and OxyContin is the most frequently prescribed narcotic type pain medication. That the opportunities for, and actual incidence of, OxyContin diversion and abuse have grown exponentially during this time period is not a coincidence.
- In spite of concerns expressed by DEA officials (Wall Street Journal, 9/27/04), the FDA recently approved similar indications for the use of Palladone, a drug acknowledged to be even more potent than OxyContin.
- The Risk Management Plan (RMP) for Palladone (notably omitted for OxyContin), which mandates Purdue Pharma's monitoring and reporting of adverse events related to the drug, really represents no improvement vis-à-vis a preventative effect on the OxyContin/Palladone problem. The RMP will only reinforce, in an after-the-fact manner, perspectives that are already well known, and depends for its impact on the fallacious premise that Palladone is appropriate for moderate pain. Having intervention strategies in place

“in case these things (abuse, addiction, death) occur” is analogous to closing the barn door after the horse is out.

- “Educational” OxyContin label changes have been made with FDA approval on five occasions, the 7/18/01 change notably acknowledging the issue of misuse and abuse of the drug. Although well intentioned, none of these changes has reduced the scope of the problem (as previously documented in this petition it has worsened significantly). This is because they do not address its root cause – failure to limit OxyContin use to severe, intractable pain from documented peripheral tissue disease processes.
- When Purdue Pharma was allowed to broaden the indications for OxyContin, the way was paved for the legitimate (prescribing) use of the drug in a large population of patients based on symptomatology only. Unlike severe, cancer-related pain, “moderate” pain can be treated as a “disease unto itself” without essential attention being paid to the underlying cause (diagnosis). This is akin to using narcotic type pain medications – known to be effective – to treat chronic cough without establishing the source of the cough (pneumonia, tuberculosis, lung cancer etc.) [Attachments C & D].
- It is well recognized that pain may be centrally (brain) mediated only and originate from a number of psychophysiologic entities not involving true tissue damage. Appropriate management of this no less real type of pain involves the use of many modalities other than narcotic drugs, which can actually have adverse effects on brain chemistry.

**Based on the above, there is no question that under current FDA prescribing regulations the harm produced by OxyContin considerably outweighs the benefits, and that continuing the current indication guidelines for OxyContin and Palladone will aggravate the societal devastation they have produced. These regulations also run contrary to both the stated mission of the FDA and several fundamental tenets of medical diagnosis and therapy. There is an urgent need for the FDA to rescind the current therapeutic parameters for OxyContin and Palladone, and to revert to “severe pain attributable to medically**

documented tissue disease processes” as the only indication for their use.

#### **IV. Concluding Statements**

**This petition has provided evidence that there is a national problem of crisis proportions involving inappropriate prescribing, diversion and abuse of the drug OxyContin, and that a similar situation will occur with Palladone in proportion to its prescribing and availability. It has established that the FDA allowing liberalization of the original indications for use of the drug(s) and the continued existence of a hazardous chemical formulation have enhanced both the availability and inherent dangers of OxyContin. The petition has demonstrated that there is insufficient scientific evidence that sustained release opioids offer the improved efficacy over immediate release forms to justify the increased risk. It has shown that previous/current efforts by the FDA to address the problem have been unsuccessful and that the situation is worsening. It has pointed out that allowing use of OxyContin and Palladone for “moderate” pain indications violates several basic and important principles of medical diagnosis and therapy, as well as the FDA’s responsibility to its citizens. Finally, the petition demonstrates that the more restrictive regulations requested, while perhaps logistically and politically challenging, are warranted both from an historical and scientific standpoint and it calls upon the FDA to exercise bold and responsible action that will prevent many future tragedies.**

## **Attachments**

- A. NATIONAL PETITION TO RECALL OXYCONTIN**  
Lee Coalition for Health
  
- B. COMMENTARY ON THE PITFALLS OF OPIOIDS FOR  
CHRONIC NON-MALIGNANT PAIN OF CENTRAL ORIGIN**  
Stephen G. Gelfand, M.D.
  
- C. OXYCONTIN RISKS AND THE FDA**  
Stephen G. Gelfand, M.D.

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12. ENDO PHARMACEUTICALS INC (Goldberg, M, Galer BS, Kao H) Abuse resistant pharmaceutical composition containing capsaicin. WO-02094254 (2002)
13. Sackler R: Pharmaceutical formulation containing irritant. US-20030068370 (2003)
14. THE GENERAL HOSPITAL CORPORATION (Woolf CJ): Compositions and methods for preventing abuse of orally administered medications. WO-03092676 (2003)

**Claim for Categorical Exclusion of Environmental Impact  
Assessment**

For Citizen Petition submitted by  
Barbara Van Rooyan

To the best of my knowledge and understanding the agency actions requested in this citizen petition qualify for exclusion of an environmental assessment.

Requests 1) and 2) qualify for exclusion under Section 25.31 (a) and (d).  
Requests 3) and 4) qualify for exclusion under Section 25.31 (a) and (h) as specified in 25.20 (f)