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July 25, 2012

Dockets Management Branch  
Food and Drug Administration  
Room 1061  
5630 Fishers Lane  
Rockville MD 20852

The undersigned clinicians, researchers and health officials from fields that include Pain, Addiction, Primary Care, Internal Medicine, Anesthesiology, Psychiatry, Neurology, Emergency Medicine, Toxicology, Rheumatology, and Public Health submit this petition under Section 21 CFR 10.20 and 21 CFR 10.30 and other pertinent sections of the Federal Food, Drug and Cosmetic Act or any other statutory provision which authority has been delegated to the FDA Commissioner to regulate labeling of opioid analgesics.

At present, the FDA-approved indication for nearly all instant-release opioid analgesics is “moderate to severe pain”. For extended-release opioids, the indication is for “moderate to severe pain when a continuous, around-the clock analgesic is needed for an extended period of time.” These overly broad indications imply a determination by FDA that they are safe and effective for long-term use. As outlined below, an increasing body of medical literature suggests that long-term use of opioids may be neither safe nor effective for many patients, especially when prescribed in high doses.

Unfortunately, many clinicians are under the false impression that chronic opioid therapy (COT) is an evidence-based treatment for chronic non-cancer pain (CNCP) and that dose-related toxicities can be avoided by slow upward titration. These misperceptions lead to over-prescribing and high dose prescribing. By implementing the label changes proposed in this petition, FDA has an opportunity to reduce harm caused to chronic pain patients as well as societal harm caused by diversion of prescribed opioids. In addition, FDA will be able to reinforce adherence to dosing limits that have been recommended by the United States Centers for Disease Control<sup>1</sup>, the state of Washington<sup>2</sup> and the New York City Department of Health and Mental Hygiene<sup>3</sup>.

The Federal Food, Drug and Cosmetic Act established that a drug intended to treat a condition must be proven safe and effective for use as labeled.<sup>4</sup>The current label on opioid analgesics does not comply with this law. By taking the actions requested in this petition, FDA will be able to exercise its regulatory responsibility over opioid manufacturers by prohibiting the marketing of opioids for conditions in which their use has not been proven safe and effective.

SPECIFIC ACTIONS REQUESTED FOR CHANGES TO OPIOID ANALGESIC LABELS:

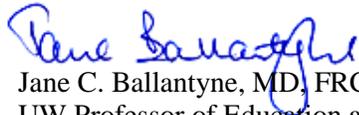
1. Strike the term “moderate” from the indication for non-cancer pain.
2. Add a maximum daily dose, equivalent to 100 milligrams of morphine for non-cancer pain.
3. Add a maximum duration of 90-days for continuous (daily) use for non-cancer pain.

STATEMENTS OF SCIENTIFIC BASIS FOR PETITION:

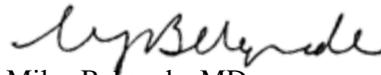
1. Over the past decade, a four-fold increase in prescribing of opioid analgesics has been associated with a four-fold increase in opioid related overdose deaths and a six-fold increase in individuals seeking treatment for addiction to opioid analgesics.<sup>5</sup>
2. Prescribing of opioids increased over the past 15 years in response to a campaign that minimized risks of long-term use for CNCP and exaggerated benefits.<sup>6,7,8</sup>
3. Long-term safety and effectiveness of managing CNCP with opioids has not been established.<sup>9</sup>
4. Recent surveys of CNCP patients receiving COT have shown that many continue to experience significant chronic pain and dysfunction.<sup>10,11</sup>
5. Recent surveys using DSM criteria found high rates of addiction in CNCP patients receiving COT.<sup>12,13</sup>
6. A large sample of medical and pharmacy claims records found that two-thirds of patients who took opioids on a daily basis for 90 days were still taking opioids five years later.<sup>14</sup>
7. Patients with mental health and substance abuse co-morbidities are more likely to receive COT than patients who lack these risk factors, a phenomenon referred to as *adverse selection*.<sup>15</sup>
8. Three large observational studies published in 2010 and 2011 found dose-related overdose risk in CNCP patients on COT.<sup>16,17,18</sup>
9. COT at high doses is associated with increased risk of overdose death<sup>18</sup>, emergency room visits<sup>19</sup> and fractures in the elderly<sup>20</sup>.

There is no environmental impact associated with this Citizen’s Petition and we wish to be excluded under 21 CFR Sec. 25.24.

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 petition which are unfavorable to the petition (21 CFR Sec.10.30b).



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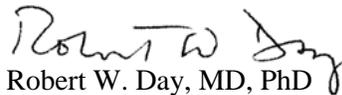
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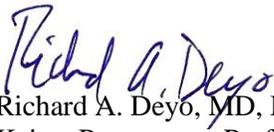
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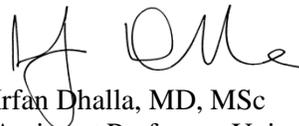
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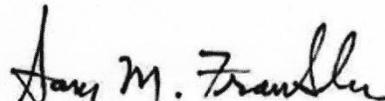
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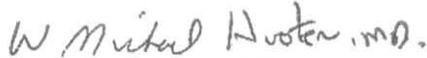
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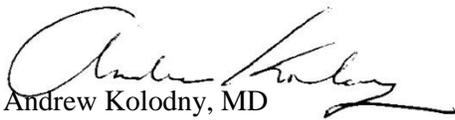
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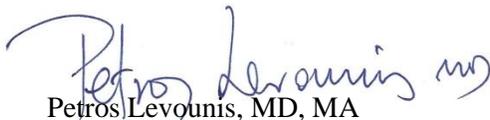
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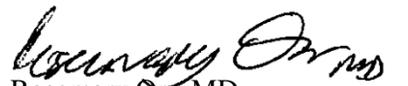
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