

United States Senate

WASHINGTON, DC 20510

September 18, 2015

The Honorable Stephen Ostroff, Acting Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Acting Commissioner Ostroff:

We write to express our dismay over the FDA's recent approval of the opioid prescription painkiller OxyContin for use by children as young as 11 years old and to request additional information about this troubling decision.

The country is in the midst of an opioid abuse crisis, with more than 2 million Americans aged 12 or older abusing or dependent on opioids.¹ Approximately 38,000 people die each year from drug overdoses — more than 100 per day² — and opioids play a large role in this tragedy.³ Opioid overdoses, once almost always due to heroin use, are now increasingly due to abuse of prescription painkillers like OxyContin.⁴

Children, whose brains are not yet fully developed, are especially vulnerable to drug dependency and abuse.⁵ In 2012, an estimated 2.4 million adolescents aged 12 to 17 reported using an illicit drug in the previous month.⁶ Illicit drug use negatively impacts adolescent behavior, as well as physical and mental development.⁷ Moreover, substance-abusing adolescents are more likely to engage in substance abuse or become substance-dependent as adults.⁸

We recognize that, in serious cases, children may need appropriately approved and prescribed narcotics. But an increase in the availability of opioids like OxyContin to children — and the potential for abuse — poses a serious U.S. public-health issue.⁹

¹ Substance Abuse and Mental Health Services Administration, *Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings*, NSDUH Series H-46, HHS Publication No. (SMA) 13-4795.

² CDC Press Release: Opioids drive continued increase in drug overdose deaths. February 20, 2013. Total drug overdose numbers: 38,329 in 2010; 60% of these related to prescription drugs including opioid pain medications.

³ <http://www.cdc.gov/drugoverdose/epidemic/index.html>.

⁴ *Unintentional Drug Poisoning in the United States*, National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, July 2010.

⁵ <https://www.nlm.nih.gov/medlineplus/drugsandyoungpeople.html>.

⁶ http://www.samhsa.gov/data/sites/default/files/report_1967/ShortReport-1967.pdf (citing Center for Behavioral Health Statistics and Quality. (2013). Behavioral health barometer: United States, 2013 (HHS Publication No. SMA 13-4796)).

⁷ *Id.* (citing Toumbourou, J., Stockwell, T., Neighbors, C., Marlatt, G., Sturge, J., & Rehm, J. (2007). Interventions to reduce harm associated with adolescent substance use. *The Lancet*, 369 (9570), 1391–1401).

⁸ *Id.* (citing Center for Behavioral Health Statistics and Quality (2014, July 17). The TEDS Report: Age of substance use initiation among treatment admissions aged 18 to 30. Rockville, MD: Substance Abuse and Mental Health Services Administration).

⁹ *Id.* (citing Levy, S. (2014). Adolescent substance use. *Pediatric Annals*, 43(10), 406–407. doi:10.3928/00904481-20140924-06).

Despite the obvious and alarming concerns about the potential for abuse by pre-teens and teenagers, the FDA approved the pediatric prescription use of OxyContin without the benefit of an independent Advisory Committee review. The FDA eschewed such a review despite its own regulations mandating one when a matter is of significant public interest, highly controversial, or requires a special type of expertise. The question whether the FDA should approve for children the indication of a powerful, dependency-inducing opioid patently implicated each of those factors.

Furthermore, while the FDA has publicly explained that it required OxyContin's manufacturer to evaluate its safety and metabolization in pediatric patients, the FDA apparently did not seek any information about the potential for addiction and abuse by children. That is disconcerting.

Accordingly, we respectfully ask that you provide responses to the following questions and document-production requests:

1. Please explain the basis for the FDA's decision to forego an Advisory Committee on the question of pediatric indication for OxyContin, including an explanation why the standing Pediatric Advisory Committee was not asked to review the matter. If there are any associated memoranda and correspondence that may assist us in better understanding the FDA decision, please provide them.
2. Please identify any studies the FDA required OxyContin's manufacturer to conduct before approving the pediatric indication, including identifying the conditions or diseases that were the subject of the studies. Please also identify any factors besides safety and metabolization in pediatric patients that the FDA required OxyContin's manufacturer to evaluate before the FDA approved the pediatric indication.
3. Please explain whether, and if so, how the FDA considered the issues of abuse or addiction by children prescribed OxyContin before the FDA approved the new pediatric indication. If there are any associated memoranda and correspondence that may assist us in understanding how FDA considered these issues, please provide them. If the FDA didn't consider such issues, why not?
4. Is it the FDA's position that the current "black box" warning for OxyContin is adequate for pediatric use, and that there is no need for specific mention of addiction risks in younger patients, even though, as referenced above, children are especially vulnerable to drug dependency and abuse? If so, please explain why.
5. In connection with the approval of the pediatric indication for OxyContin, the FDA explained: "Similar to adults, OxyContin is approved for use in [certain pediatric] patients to manage pain severe enough to require daily, around-the-clock, long-term opioid treatment for which alternative treatment options are inadequate."¹⁰ Under that standard, could a severely broken bone or another acute injury qualify for pediatric OxyContin use, as opposed to a chronic condition like cancer? In this regard, please

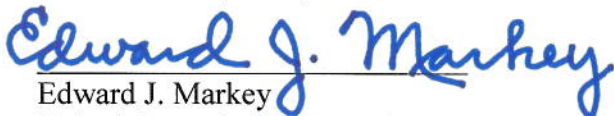
¹⁰ <http://www.fda.gov/drugs/newsevents/ucm456973.htm>.

identify the types — including specific examples — of medical conditions for which pediatric use of OxyContin is indicated, as well as those for which it is not.

6. The FDA has stated that “[t]he care of pediatric patients treated with an opioid analgesic has to be properly coordinated by a health care team experienced in opioid treatment.”¹¹ Please describe how you plan to ensure that patients treated with these medications are managed by experienced care teams, and what efforts are underway to educate providers regarding the pediatric-specific risks associated with use of these opioid treatments and the appropriate protocols for managing both the initiation and termination of use.
7. Please identify the information that physicians prescribing OxyContin under the new pediatric indication are required to provide to parents of children receiving the drug, including information about potential abuse or dependency. If the FDA did not require physicians to provide such information to parents of children being prescribed OxyContin, please explain why not.
8. Please explain how the FDA will be tracking abuse or dependency caused by pediatric use of OxyContin. For example, will the FDA be using its adverse-reporting database or post-market studies? Will it be working with other agencies like the Centers for Disease Control to track abuse or changes in patterns of use among the pediatric population? If not, please explain why not.

Thank you for your assistance and your cooperation in responding to these requests. Please respond no later than October 16, 2015. Should you have any questions, please have your staff contact Andrew Cohen at 202-224-2742.

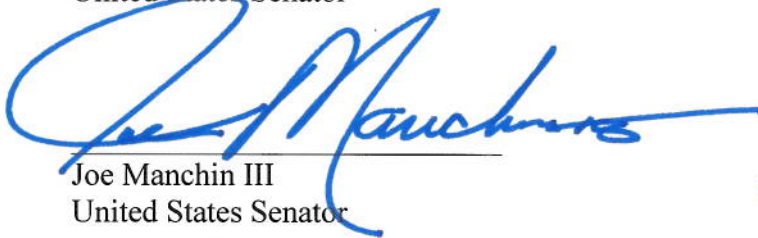
Sincerely,



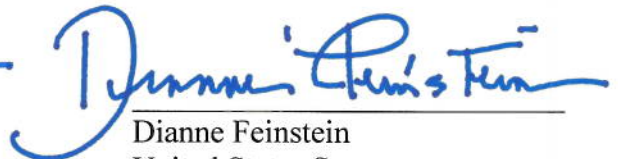
Edward J. Markey
United States Senator



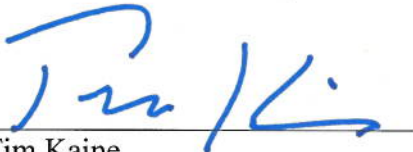
Kelly Ayotte
United States Senator



Joe Manchin III
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¹¹ *Id.*

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Jeanne Shaheen
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