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ONE HUNDRED FOURTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE
2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6115
Majority (202) 225–2927
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July 7, 2015

Dr. Stephen Ostroff
Acting Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20903

Dear Dr. Ostroff:

Pursuant to Rules X and XI of the U.S. House of Representatives, the Committee on Energy and Commerce is seeking information concerning ongoing efforts by federal agencies, including the Food and Drug Administration (FDA), to combat the opioid abuse epidemic and more effectively incentivize the development and broadened use of evidence-based practices and treatments. To help the committee further understand this issue, the Subcommittee on Oversight and Investigations conducted a hearing on May 1, 2015 entitled, "What is the Federal Government Doing to Combat the Opioid Abuse Epidemic?" At the hearing, members of the subcommittee heard from a federal panel which included Douglas Throckmorton, M.D., Deputy Director of the Center for Drug Evaluation and Research at FDA.

Over the past several months, the committee has heard testimony on the nature, scope, and harmful effects of prescription drug and heroin abuse across the United States. From 1999 to 2013, the rate for drug poisoning deaths involving opioid analgesics, or pain medications, nearly quadrupled.[1] Deaths related to heroin, an illicit opioid, have also increased sharply since 2010, including a 39 percent increase between 2012 and 2013 and the mortality rate from heroin overdose increased each year from 2010 to 2013.[2] By 2009, drug overdose deaths outnumbered deaths due to motor vehicle crashes for the first time. Heroin and prescription opioid abuse can result in other health consequences, such as neonatal abstinence syndrome, increased risk of transmission of HIV and Hepatitis C, and bone fractures in older adults due to falls.[3]

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[1] Centers for Disease Control and Prevention. QuickStats: Rates of Deaths from Drug Poisoning and Drug Poisoning Involving Opioid Analgesics – United States, 1999-2013. MMWR Weekly. Retrieved from: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6401a10.htm.

[2] Hedegaard H, Chen LH, Warner M.; National Center for Health Statistics (NCHS). Drug-poisoning deaths involving heroin: States, 2000-2013. NCHS data brief, no190. Retrieved from: http://www.cdc.gov/nchs/data/databriefs/db190.pdf.

[3] Creanga AA, SabelJC, Ko JY, Wasserman CR, Shapiro-Medoza CK, Taylor P, Barfield W, et al. Maternal drug use and its effect on neonates: a population-based study in Washington State. Obstet Gynecol. 2012; 199(5):924-

In 2013, FDA adopted labeling changes affecting Extended Release and Long-Acting (ER/LA) opioid analgesics, requiring manufacturers to adopt the most restrictive language that can be found in drug labeling, a "black box" warning about their potential for abuse, the risk of fatal overdose, and a warning that maternal use of these products during pregnancy can result in neonatal opioid withdrawal syndrome.[4] At the time, similar requirements were not imposed on manufacturers of Immediate Release (IR) opioid analgesics. In addition, FDA's posted "Guide to Safe Use of Pain Medicine" states: "According to NIH, studies have shown that properly managed medical use of opioid analgesic compounds (taken exactly as prescribed) is safe, can manage pain effectively, and rarely causes addiction" and "pain medications are safe and effective when used as directed."[5] Experts have raised concerns with staff about the basis and effectiveness of these and other FDA labeling and risk-management strategies, and a recent review on opioid use for chronic pain by the Agency for Healthcare Research and Quality (AHRQ) found no evidence that risk mitigation strategies were effective.[6] Additionally, Democratic members of the Committee, led by Ranking Member Frank Pallone, recently wrote FDA to request that the agency ensure that all IR opioid formulations bear the same black box warning as ER/LA formulations.

To assist the committee in understanding FDA's policies regarding opioid medications, please provide the following documents and answer the subsequent questions by July 21, 2015:

1. Please identify the NIH source and provide the studies referenced that support the FDA's statement in the "Guide to Safe Use of Pain Medicine." Since the statement was made in 2009, does FDA have any updates or further clarifications on the statement?

2. Has FDA reviewed the AHRQ study? If so, how are the studies reflected in FDA policy?

3. Does the use of enriched enrollment exclude patients from clinical trials who might have a pre-existing low tolerance for any forms of opioids? What is FDA's justification for permitting enriched enrollment for clinical trials using opioids? Is there a concern that this practice underestimates the risk of abuse?

933.; Zibell JE, Hart-Mallory R, Barry J, Fan L, Flanigan C. Risk Factors for HCV infection among young adults in rural New York who inject prescription opioid analgesics. Am J Public Health. 2014 Nov;104(11):2226-32. Doi: 10.2105/AJPH.2014.302142. Epub 2014 Sep 11.; Mateu-Gelabert P1, Guarino H2, Jessel L2, Teper A2. Injection and sexual HIV/HCV risk behaviors associated with nonmedical use of prescription opioids among young adults in New York City. J Subst Abuse Treat. 2015 Jan;48(1):13-20. Doi: 10.1015/j.jsat.2014.07.002. Epub 2014 Jul 11.; Rolita L, Spegman A, Tang X, Cronstein BN. Greater number of narcotic analgesic prescriptions for osteoarthritis is associated with falls and fractures in elderly adults. J Am Geriatr Soc. 2013;61(3):335-340.; Miller M, Sturmer T, Azrael D, Levin R, Solomon DH. Opioid analgesics and the risk of fractures in older adults with arthritis. J Am Geriatr Soc. 2011;59(3):430-438.

[4] Letter from Dr. Janet Woodcock, Director, Center for Drug Evaluation and Research, Food and Drug Administration, to Dr. Andrew Kolodny, President, Physicians for Responsible Opioid Prescribing, Re: Docket No. FDA-2012-P-0818 (Sept. 10 2013).

[5] http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm095673.htm

[6] http://www.ahrq.gov/research/findings/evidence-based-reports/opoidstp.html

4. Please identify and provide the studies that FDA relied on in its decision to exempt manufacturers of immediate-release opioids from the black box warning required for extended release opioids.

5. What is FDA's policy on when an advisory panel is used to review Schedule II drugs?

6. Why did the FDA remove mandatory training for prescribing physicians for opioid drugs from its initial design of the Risk Evaluation and Mitigation Strategy (REMS) for opioid drugs?

7. Why did the FDA remove patient registries for opioid drugs from its initial design of REMS for opioid drugs?

8. How does the FDA evaluate the effectiveness of REMS for opioid drugs?

9. What evidence does FDA have showing that REMS for opioid drugs is effective?

10. In light of the national opioid abuse epidemic, how does FDA believe that risk mitigation strategies can be improved?

If you have any questions regarding this request, please contact Alan Slobodin, Sam Spector, or Brittany Havens with the majority committee staff at (202) 225-2927, or Una Lee with the minority committee staff at (202) 225-3641.

Sincerely,

Fred Upton
Chairman

Frank Pallone, Jr.
Ranking Member

Tim Murphy
Chairman
Subcommittee on Oversight
and Investigations

Diana DeGette
Ranking Member
Subcommittee on Oversight
and Investigations

Attachment