DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

The Honorable Joseph R. Pitts
Chairman
Subcommittee on Health
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

SEP 26 2013

Dear Mr. Chairman:

Thank you for providing the opportunity for the Food and Drug Administration (FDA or the Agency) to testify at the June 14, 2013, hearing before the Subcommittee on Health, Committee on Energy and Commerce, entitled "Examining the Federal Government's Response to the Prescription Drug Abuse Crisis." This letter provides responses for the record to questions posed by you and one of the Committee Members, Congressman Bilirakis, which we received on July 10, 2013.

If you have further questions, please let us know.

Sincerely,

Sally Howard
Deputy Commissioner
Policy, Planning, and Legislation

cc: The Honorable Frank Pallone, Jr.
Ranking member

We have restated your questions below in bold, followed by our responses.

**The Honorable Joseph R. Pitts**

1. **FDA has taken a number of steps this year to encourage the development of abuse-deterrent opiates and to protect the public from being inundated with non-abuse-deterrent versions of those safer products once they have been introduced to the market. There remains the threat, however, that drug makers continue to seek approval of new opiate products that have no abuse-deterrent features. Last December, one such product was brought before an FDA advisory panel which voted 11 to 2 against approving the product, in part because it would have been readily crushable and abusable just as OxyContin used to be. An agency spokesperson at the meeting (Rappaport), however, expressed uncertainty whether the FDA is legally empowered to refuse to approve a new opiate drug product on the ground that it lacks abuse deterrent features.**

    a. **Has the agency, since last December, decided whether it has the legal authority to accept its own expert advisory panel recommendation and refuse to approve a new opiate drug product on the ground that it lacks abuse deterrent features considered necessary to the safety of the drug?**

FDA shares your concerns regarding prescription drug abuse, including the abuse of opioid analgesics. Your question references the December 7, 2012, meeting of the Anesthetic and Analgesic Drug Products Advisory Committee, which focused on a specific pending application. Under applicable statutory and regulatory provisions, we are generally prohibited from disclosing information about any pending new drug application (NDA).

FDA is strongly committed to finding ways to reduce abuse and misuse of opioid medications. As part of our ongoing mission to protect the public health, we often seek advice from advisory committees on a wide range of medical and technical issues. Advisory committees are comprised of outside experts with a broad range of expertise and different backgrounds. Advisory committee recommendations are not binding on the Agency; however, they are considered carefully. When considering whether to approve a proposed new opioid drug product, FDA must determine if the product meets the statutory approval standard, which is whether the product has been shown to be safe and effective. In addition, the Agency considers the known risks associated with the drug along with the potential benefits the drug will provide. While we consider the views of advisory committee members, ultimately FDA must review and evaluate the science and determine whether the product that is the subject of a given new drug application meets this approval standard.

**b. Is there a need for legislation to clarify that FDA has this authority?**

The Administration has taken no position on the need for legislation in this area.

**2. FDA provided guidance in January on the development and testing of new abuse-deterrent opiate drugs. However, my understanding is that it has so far chosen not to develop guidance on the requirements for approval of generic versions of abuse-deterrent drugs.**

**a. Why did the agency choose not to issue guidance on the development and testing of abuse-deterrent generic drugs?**

It is correct that FDA has not issued guidance on the development and testing of generic versions of drugs with abuse-deterrent properties. However, FDA is actively working on the scientific and regulatory issues surrounding the development and evaluation of abuse-deterrent generics, and we may address this topic in future guidance documents.

Providing guidance in this area needs to be a sequential process, beginning with guidance on the development of abuse-deterrent products by innovators. We understand the critical role generics play in our health care system and that the issues around the development of generics that are abuse-deterrent need to be addressed.

**b. How is the agency assuring that generic versions of abuse-deterrent drugs have the same abuse-deterrence features as the innovator products they would substitute for?**

FDA has been working internally on the scientific and regulatory issues surrounding development and evaluation of abuse-deterrent generics. In addition, FDA will be presenting at an upcoming meeting focused on issues concerning development and evaluation of abuse-deterrent generics. The public meeting, "Abuse Deterrent Formulation Science Meeting on the FDA Draft Guidance," has been organized by Cross Company Abuse Liability Consortium and will be held on September 30-October 1, 2013.[1]

FDA may also address this topic in future guidance documents.

**c. How does the agency intend to publicize the requirements for abuse-deterrent generic drugs so that generic drug makers can design and test their products accordingly and the public can have confidence that appropriate standards are being applied?**

FDA may address this topic in future guidance documents.

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[1] See *www.adfsciencemeeting.com*

3. **As you are aware, DEA's current strategy of attempting to curb prescription drug abuse is what they call a "chokepoint" approach, in which they are targeting prescription drug wholesalers and chain pharmacies with enforcement actions to restrict the amount of controlled substances being provided to patients. I am hearing that this is causing significant problems for patients with chronic pain to access their critical pain medications. What is your agency doing to ensure that patients continue to have access to critical pain medications? If people who use these medications legitimately are having problems accessing them, to whom should they report the information?**

   Under the Controlled Substances Act (CSA), the authority for quota-setting for controlled substances is vested with the Drug Enforcement Agency (DEA), not FDA. However, FDA provides DEA with information to aid in the process. FDA determines annual estimates of medical need for the drugs listed in Schedule II of the CSA.

   The estimates of medical needs for each Schedule II active pharmaceutical substance are provided to DEA to assist them in setting manufacturing and production quotas. The estimates of medical need for each substance are derived from previous years' sales data. In addition to projecting estimates, FDA also provides information it has received that relates to newly approved drug products on the market as well as discontinued drug products that are no longer available. In this way, DEA will have current, up-to-date information to assist them in setting the appropriate quotas for each substance.

   If FDA is informed about a possible shortage of a drug, FDA informs DEA so that DEA can revise the quota, if appropriate. If patients are experiencing difficulty obtaining their prescribed medications because of a shortage of the drug, FDA's Drug Shortage Staff (DSS) may be contacted at drugshortages@fda.hhs.gov. DSS will provide information about how to obtain the drug if it is available and, if there is a shortage, will work to address it with the manufacturer.

   In addition, individuals can contact the Board of Pharmacy in their state to report problems accessing medications.

4. **How is interagency development of REMS for controlled substances coordinated? For example, how is DEA brought in to ensure that a REMS will not conflict with DEA's regulations? Does FDA consult with SAMHSA and/or the HHS-Office of Civil Rights on REMS compliance with HIPAA and other privacy laws regarding information about controlled substances? Finally, how is it ensured that controlled substance REMS do not put pharmacists in the untenable position where compliance with a REMS would require violating state controlled substance or state pharmacy laws?**

   FDA has and will continue to consult with other agencies as needed to ensure that a Risk Evaluation Mitigation Strategy (REMS) will not conflict with other Federal

laws, such as the CSA. For example, the Substance Abuse and Mental Health Services Administration (SAMHSA) participated in reviewing the syllabus for the prescriber education programs under the REMS for extended-release and long-acting (ER/LA) opioids. As part of the Office of National Drug Control Policy (ONDCP), National Drug Control Strategy, FDA and SAMHSA have been working together with other Federal partners to explore mandatory prescriber education.

FDA strives to craft REMS in a way that is specific enough to ensure that the benefits of a drug outweigh its risks, but general enough to avoid conflict with state pharmacy or other laws.

**The Honorable Gus Bilirakis**

1. **What changes can we make to our prescription drug laws to make it harder for people to improperly obtain and abuse prescription drugs?**

Combating opioid misuse, abuse, and addiction has long been a priority for the FDA. As a scientific and public health regulatory agency, FDA's approach to regulation of prescription opioids must be grounded in science; specifically we must bring to bear the best available knowledge and understanding concerning both the treatment of pain and the potential adverse consequences of opioid use.

Over the last decade or so, under its existing authorities within the FD&C Act, FDA has worked to pursue a targeted, science-based, multi-pronged approach that addresses misuse, abuse, and addiction at critical points in the development of an opioid product and in its use throughout the health care system.

We would like to highlight three areas of recent activity within a broader comprehensive approach:

Abuse-deterrent formulations: FDA is committed to finding ways to reduce abuse and misuse of opioid medications. As part of our ongoing mission to protect public health, FDA has concluded that if the Agency determines that a formulation of an extended-release opioid drug product has abuse-deterrent properties, the Agency has authority under the FD&C Act to require generic versions of the product to have abuse-deterrent properties also. In addition, we have the authority to refrain from approving non-abuse-deterrent formulations of that drug and to initiate procedures to withdraw non-abuse-deterrent versions already on the market.

FDA recently made a determination regarding a drug reformulated with the intention of deterring misuse and abuse: OxyContin ER (oxycodone hydrochloride). After an extensive, science-based review, on April 16, 2013, FDA approved product labeling describing reformulated OxyContin's properties that are expected to make abuse via injection difficult and to reduce abuse via the intranasal (snorting) route. The Agency also concluded that the benefits of the earlier formulation that lacks abuse-deterrent properties no longer outweigh its risks, and that the earlier formulation of OxyContin

was withdrawn from the market for reasons of safety or effectiveness. That determination precludes approval of generic versions of the earlier formulation of OxyContin.

This decision was the subject of extensive consideration by FDA experts over the course of many months. FDA's decision took into account the totality of the evidence for OxyContin.

Improving appropriate use of opioids through prescriber education: It is critically important to improve prescribers' knowledge about the best uses of opioids, including knowing when these products should be used and by which patients. Thus, prescriber education is an important element of FDA's REMS for ER/LA opioids. Under the ER/LA opioid REMS, manufacturers are required to ensure that prescriber training programs—offered by accredited continuing education providers—are made available for all U.S.-licensed prescribers, using a syllabus developed by FDA with input from many stakeholders. As a part of our assessment of this REMS, these courses will be audited to ensure that they are unbiased and accurate. The first of these voluntary prescriber training programs was rolled out on March 1, 2013.

While voluntary training is an important public health measure, a new law requiring mandatory training would go even further to help ensure the safe use of opioid drugs. That is why the Administration stated in *Epidemic: Responding to American's Prescription Drug Abuse Crisis*[2] that it will work with Congress to amend Federal law to require practitioners who request DEA registration to prescribe controlled substances to be trained on responsible opioid prescribing practices as a precondition of registering and receiving their license to prescribe a controlled substance.

Improving the availability of products to treat abuse and overdose: FDA has been working with many stakeholders to explore the best ways to treat overdoses of opioids, including overdoses of FDA-approved opioid medications. Each year, prescription opioid medications are involved in over 15,000 deaths. Naloxone is an injectable medication that is the standard treatment to rapidly reverse the overdose of either prescription (e.g., oxycodone) or illicit (e.g., heroin) opioids. Naloxone is most commonly used by trained medical personnel in emergency departments and on ambulances. There is a growing interest by prescribers, patients, and advocates in exploring the broader uses of naloxone, including its use in non-medical settings such as nursing homes and hospices.

FDA, working with other parts of the Federal Government, is looking at new ways of giving naloxone that are potentially easier and do not require needles or syringes. The goal of this work is to expand the availability of naloxone in the places patients might overdose, and make it easier to administer to save lives. For example, FDA can grant priority review to products that involve new ways of delivering naloxone, such as using autoinjectors or intranasally, that would be easier to use in non-medical settings.

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[2] *http://www.whitehouse.gov/sites/default/files/ondcp/policy-and-research/rx_abuse_plan.pdf*