



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

The Honorable Fred Upton
Chairman
Committee on Energy and Commerce
House of Representatives
Washington, D.C. 20515-6115

APR 16 2013

Dear Mr. Chairman:

Thank you for your letter of March 5, 2013, cosigned by Senator Tom Coburn, expressing concern regarding the marketing of non-abuse-deterrent generic versions of innovator extended-release opioid drug products that have been withdrawn from the market and replaced with new, potentially abuse-deterrent formulations. We appreciate your continued interest in this important topic. The Food and Drug Administration (FDA or the Agency) shares your concern about the public health imperative to address inappropriate use of opioids.

You specifically ask whether FDA is “prepared, under its existing authority, to prevent the marketing of non-abuse-deterrent versions of innovator products that have been withdrawn from the market and replaced with abuse-deterrent formulations.” As we have noted previously, if FDA determines that a formulation of an extended-release opioid drug product has abuse-deterrent properties, the Agency has authority under the Federal Food, Drug, and Cosmetic Act (FD&C Act) to require generic versions of the product to have abuse-deterrent properties also. In addition, we believe that we would 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.

Today, the FDA announced that Purdue Pharma L.P.’s original formulation of OxyContin was withdrawn from the market for reasons of safety or effectiveness. FDA has concluded that although the original OxyContin has the same therapeutic benefits as reformulated OxyContin, original OxyContin poses an increased potential for abuse by non-oral routes of administration (injecting and snorting) compared to reformulated OxyContin. The benefits of original OxyContin no longer outweigh its risks. Thus, the original formulation of OxyContin will be removed from the list of approved drugs published in the FDA Orange Book, and as a result, the Agency will not accept or approve any abbreviated new drug applications (generics) that rely upon the approval of the original formulation.

In addition, today FDA approved labeling for reformulated OxyContin, stating that it possesses physicochemical properties that are expected to: (1) make abuse via injection difficult, and (2) reduce abuse via the intranasal route. This is the first opioid product for which FDA has approved labeling that includes statements regarding abuse-deterrence.

Regarding the remaining questions in your letter, we have restated your questions below in bold, followed by our responses.

1. What advice has FDA provided to date to Abbreviated New Drug Application applicants regarding the type and extent of data which will be required to establish that a generic product has comparable abuse-deterrent features to an abuse-deterrent innovator product?

FDA reviews every application on its merits, based on applicable scientific and regulatory standards and encourages an ongoing dialogue with manufacturers as they consider developing one of these products.

FDA is actively working on these issues in connection with certain products, but we are not permitted to disclose the existence of pending applications or any confidential communications with sponsors of pending applications, unless that information has otherwise been made public.

We continue to actively encourage the development of abuse-deterrent formulations of opioids and believe that these products have promise to help reduce prescription drug abuse and impact public health.

2. What are FDA's criteria for deciding whether to provide public advice on a specific category of testing requirements applicable to a large number of products both pending and in development?

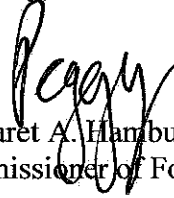
FDA's good guidance practices regulation (21 *Code of Federal Regulations* (CFR) Section 10.115) provides that the Agency generally should use guidance documents (rather than other forms of communication) to communicate new or different regulatory expectations that are not readily apparent from the statute or regulations to a broad public audience for the first time. For example, when FDA develops standards for testing requirements for generic versions of specific drugs, the Agency publishes guidance. (See *Guidance for Industry Bioequivalence Recommendations for Specific Products*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072872.pdf>.) These documents are intended to provide advice to sponsors regarding the recommended studies and how they should be designed.

3. Are offices within FDA which are developing policies on abuse-deterrent formulations coordinating with each other so those policies are consistently understood and applied, particularly when it comes to the question of how generic products could demonstrate that they have abuse-deterrent features comparable to the innovator?

Yes. FDA coordinates work on potentially abuse-deterrent formulations of extended-release opioids across the offices involved in the development of policies on abuse-deterrence. For example, within FDA's Center for Drug Evaluation and Research, personnel from the Office of Generic Drugs are working closely with personnel from the Office of New Drugs and other relevant offices in the development and application of FDA's policies on these issues. We also have internal work groups comprised of staff from throughout the Agency, which meet regularly to coordinate FDA's scientific reviews, policy development, and other activities related to inappropriate use and abuse of opioids.

Thank you, again, for contacting FDA concerning this important topic. Please let us know if you have further questions. We have also provided this response to Senator Coburn.

Sincerely,

A handwritten signature in black ink, appearing to read "Peggy", written over the printed name of Margaret A. Hamburg.

Margaret A. Hamburg, M.D.
Commissioner of Food and Drugs