



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

January 8, 2013

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

Dear Chairman Upton:

Thank you for your letter cosigned by Senator Tom Coburn, expressing concerns about non-tamper-resistant versions of extended-release opioids coming onto the market. Secretary Sebelius has asked the Food and Drug Administration (FDA or the Agency) to respond to you directly. You indicate that the availability of such products would be a significant setback in the battle against prescription drug abuse, and you pose several questions concerning the Department of Health and Human Services' (HHS) and the FDA's authority to refuse to approve or to remove non-tamper-resistant versions of extended-release opioids if a tamper-resistant version is on the market. Please note that, in this context, FDA uses the term "abuse-deterrent" and not "tamper-resistant." "Tamper-resistant" is used to refer to retail packaging requirements for certain cosmetic and over-the-counter drug products, and using the same term in this context could create confusion about its meaning.

Please be assured that HHS and FDA share your concerns, and those of your constituents, regarding prescription drug abuse, including the abuse of opioid analgesics. HHS and FDA are committed to finding ways to reduce abuse and misuse of these medications. As part of our ongoing mission to protect public health, FDA has concluded that if FDA determines that a formulation of a product significantly deters abuse, we have legal authority, under the drug approval and drug safety provisions of the Federal Food, Drug, and Cosmetic Act, to require generic versions of that product to have abuse-deterrent formulations as well.

The development and continued improvement of opioid analgesics formulated to deter abuse is one important tool in the effort, and FDA has undertaken several initiatives in this regard.

First, when the applicable statutory and regulatory requirements are satisfied, FDA grants Fast Track and Priority Review status to applications for potentially abuse-deterrent formulations of prescription opioid products to encourage the development and to speed the approval process of such products.

Second, as required by Section 1122 of the Food and Drug Administration Safety and Innovation Act (FDASIA, Public Law 112-144), FDA will be issuing guidance for industry on the development and evaluation of these products very soon.

Third, FDA is actively evaluating the available data on and analyses of opioid formulations designed to deter abuse in an effort to determine whether they do, or can be expected to, lead to a meaningful reduction in abuse and the adverse events associated with abuse.

Fourth, as discussed below, FDA is actively reviewing whether it can and should seek to remove or refuse to approve opioid drug products not formulated to deter abuse in certain circumstances.

I am pleased to provide responses to your specific questions below.

- 1. Assuming the Food and Drug Administration (FDA or Agency) was convinced that the innovator product was tamper resistant, what authority does the Agency have to prevent the marketing of these non-tamper-resistant generic versions, or remove them from market, should they jeopardize the public health?**

FDA scientific staff is reviewing recently submitted data to determine whether new formulations for certain products actually deter abuse. As previously noted, if FDA determines that the new formulations significantly deter abuse, we have concluded that FDA has legal authority, under the drug approval and drug safety provisions of the Federal Food, Drug, and Cosmetic Act, to require generic versions of those products to have abuse-deterrent formulations as well.

- 2. Section 505(e) of the Federal Food, Drug, and Cosmetic Act provides that the Secretary may suspend the approval of an application if she finds an “imminent hazard to the public health.” Please provide us examples of how this authority has been utilized. If FDA concluded that an innovator product was tamper resistant but the generic versions were not, are there any circumstances under which this imminent hazard authority could be applied to the situation?**

Section 505(e) of the Federal Food, Drug, and Cosmetic Act (the Act) authorizes the Secretary to withdraw the approval of a drug under certain circumstances after providing the applicant with notice and an opportunity for a hearing. As you note, the Secretary may also immediately suspend an approval without first providing the applicant with notice and opportunity for a hearing if the Secretary determines “that there is an imminent hazard to the public health,” although in that case, the Secretary must still provide the applicant with prompt notice of the action and the opportunity for an expedited hearing. It is my understanding that the imminent hazard authority has only been used once, in July 1977, to suspend all new drug approvals for phenformin hydrochloride, a drug used to treat diabetes.

- 3. Pursuant to section 1122 of the Food and Drug Administration Safety and Innovation Act (Public Law 112-144), FDA must promulgate guidance on the development of abuse-deterrent products by January 9, 2013. Please provide an update on the status of this guidance, whether FDA will comply with the statutory mandate and how this guidance will address the evidentiary standard to show tamper resistance and the release of these non-tamper-resistant opioids if FDA found that the innovator product was tamper resistant.**

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FDA is working diligently to complete the draft guidance by the January 9, 2013 deadline established by Section 1122 of FDASIA. Once it is published, FDA plans to solicit comments and discussion at a public forum. FDA is not able to comment on the substance of a draft guidance document before it is published.

Thank you, again, for contacting HHS concerning these important issues. Please contact us if you have further thoughts or concerns. We have also provided this response to Senator Coburn.

Sincerely,


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