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 Minority (202) 225-3641

May 27, 2015

The Honorable Stephen Ostroff, M.D. 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 examining the Food and Drug Administration's (FDA) policies and practices regarding the use and publication of untitled letters, including whether such policies and practices are consistently fair, effective, and efficient in gaining compliance.

In the event of a violation of the Federal Food, Drug, and Cosmetic Act, FDA may give individuals and firms an opportunity to take voluntary and prompt action to correct the violation before the FDA initiates an enforcement action. FDA will issue either a warning letter or an untitled letter to individuals or firms notifying them of such violations to allow them to voluntarily comply with the law. Warning letters are used for violations that may lead to enforcement action if not promptly and adequately corrected. Untitled letters request correction of violations that do not meet the threshold of regulatory significance for a warning letter. Further, unlike warning letters, untitled letters do not include a statement that FDA will advise other federal agencies of the issuance of the letter so that they may take this information into account when considering the awarding of contracts.

While every FDA center that issues untitled letters has posted some of these letters, each center has its own policy on which letters get posted. For example, the FDA's Center for Drug Evaluation and Research (CDER) only posts untitled letters related to advertising and promotional labeling, the FDA's Center for Food Safety and Nutrition (CFSAN) posts untitled letters related to violations from manufacturing controls or labeling that do not meet the threshold of regulatory significance for a Warning Letter, or that are issued to Internet websites (cyber letters), while the FDA's Center for Veterinary Medicine (CVM) posts all untitled letters

² FDA RPM 4-2-1.

¹ FDA Regulatory Procedures Manual (RPM), Chapter 4: Advisory Actions (March 2009)

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issued by the Center, but not those issued by the field offices. Other centers have still different policies.

FDA's recent handling of an untitled letter illustrates questions raised about the issuance and posting of such letters. In this instance, an FDA inspection of a firm resulted in a No Action Indicated classification; an FDA Form 483, which lists inspection observations that may indicate an FDA-regulated product is in violation of FDA requirements, was not issued. More than a year later, the firm received an untitled letter from FDA asserting a violation based on information collected during the inspection. FDA also sent the untitled letters to the firm's related distributors. The violation alleged by FDA was based on the agency's conclusion that the firm's product should also be regulated as a drug, not just as a biologic, because the firm's manufacturing process did not meet a certain criterion. The letters did not mention how the information collected during the inspection supported the basis for FDA's conclusion. Three business days after sending the untitled letters, FDA publicly released the letters on its website, a rapid posting in comparison to other similar instances.³

By 12:55 p.m. on the day of the letters' release, the business press had published an article about the untitled letters. At one point on the same day, the stock price for the firm's shares declined 70 percent before recovering some of its losses for a net loss of 36 percent in share price in one day. A shareholder lawsuit was filed against the firm related to the untitled letter and is still in litigation. The FDA Regulatory Procedures Manual explicitly aims to limit the economic impact of an untitled letter by noting that unlike a warning letter an untitled letter does not include a statement that about notifying other federal agencies, yet FDA posted the untitled letters during the trading session that were likely to affect the markets and before the firm was able to engage with FDA about its concerns and take corrective action.

Policies and practices surrounding untitled letters would address not just the timing of their release, but whether sufficient details are included about the basis for FDA's conclusion of a violation and the adequacy of notice of a violation. Again, in this instance it is not clear that FDA's practices are consistently fair, effective, or efficient. For several weeks, the firm sought details from FDA about the basis for the violation. After about 90 days, FDA issued a second letter to the firm including reasons for its conclusion. More than a year after the issuance of the second letter, FDA published a draft guidance governing the firm's product and the basis for FDA's conclusion. The draft guidance used similar language and reasoning as the FDA's second letter to the firm and provided a case-study example that matched the firm's situation, and seemed to be based on the firm's case. This raises questions about whether the FDA center was using an untitled letter to advance new policies or interpretations without providing adequate prior notice to the firm and other manufacturers in this product category.

This case study represents some of the broader concerns about the FDA's untitled letter practices. Committee staff has heard generalized concerns from individuals involved with different FDA-regulated industries about FDA's decentralized, inconsistent practices with

³ For example, a few weeks later the same FDA center sent another firm an untitled letter, and did not post the letter until almost a month after its issuance to this firm. By that time, this other firm was able to announce that it had reached agreement with the FDA on a regulatory pathway for its product.

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untitled letters. Some of the inconsistencies involve the publicizing of untitled letters. In some cases, FDA will quickly post the letter on its website. In other cases, committee staff has heard of complaints about Freedom-of-Information-Act requesters making multiple attempts to get copies of untitled letters that FDA has decided not to make public. Other concerns have been raised about the need for FDA to be more thoughtful about the consequences from the impact of both disclosure and timing of untitled letters on FDA-regulated companies, in which FDA purports to seek compliance as opposed to punishment of the firm.

To assist the committee's examination, we request that FDA provide a briefing to committee staff. In preparation for this briefing, please respond in writing to the following by June 10, 2015:

- Do FDA centers use different criteria for issuing untitled letters? If yes, please identify
 and explain the criteria used by each center, and the rationale for FDA centers using
 different criteria. If no, please identify and explain the criteria used by all the FDA
 centers.
- 2. Please identify and explain the criteria used by each FDA center for posting or not posting an untitled letter, and how many days after the untitled letter is sent to the firm until the letter posted on the FDA website. Please also explain why FDA does not have consistent policies and practices among its centers for publishing untitled letters.
- 3. Do any of the FDA centers use the number of Freedom of Information Act (FOIA) requests to FDA for untitled letters sent to a named firm as a basis for posting an untitled letter? If yes, what is the numerical threshold of FOIA requests used, and why does the FDA center have this practice?
- 4. Regarding the FDA's posting on its website of untitled letters that are sent to publicly traded firms, could FDA's practice be modified to schedule the posting at times after the trading session has closed, i.e., after 4:00 p.m.? If not, why not?
- 5. What is FDA's objective in sending untitled letters alleging violations found by a center (not the inspector) of which the firm was not notified during an inspection classified as No-Action-Indicated with no FDA Form 483 and not given an opportunity to correct and/or respond? How is this approach more efficient in gaining a firm's compliance than providing prior notice before issuing (or at least some reasonable period of time before posting) and giving the firm an opportunity to take corrective action? What evidence does FDA have that supports the superior efficiency of this approach?
- 6. Do any of the FDA centers use untitled letters as a way to announce new regulatory approaches or policies? What due process or other legal considerations apply, if any, to untitled letters that state a firm is in violation based on a new application by FDA of regulatory standards without prior notice to regulated industry?
- 7. How is FDA's approach more efficient than providing prior notice to the firm of the violation and the factual basis in support of FDA's conclusion of violation?

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- 8. Does FDA have any awareness of the economic and legal sensitivities associated with posting untitled letters sent to publicly traded companies? How does FDA account for these sensitivities in its policies and practices in posting untitled letters?
- 9. For each FDA center, what are examples of the "relatively minor violations" (per an FDA task force) that are the basis for untitled letters issued as a result of inspection?

If you have any questions regarding this request, please contact Alan Slobodin with the committee staff at (202) 225-2927.

Sincerely,

Tim Murphy Chairman

Tim Muzzh

Subcommittee on Oversight and Investigations

Cc:

The Honorable Fred Upton, Chairman

The Honorable Frank Pallone, Jr., Ranking Member

The Honorable Diana DeGette, Ranking Member Subcommittee on Oversight and Investigations