

Client Alert

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FDA Issues Draft Guidance on Drug-Shortage Reporting

On February 21, 2012, the U.S. Food and Drug Administration (“FDA” or “the Agency”) made available a new draft guidance document titled “Notification to FDA of Issues that May Result in a Prescription Drug or Biological Product Shortage.”¹ The draft guidance aims to address the Agency’s significant concerns about the increased incidence of drug shortages in the U.S. and the consequent impact on public health. To that end, the document provides guidance to industry regarding mandatory and voluntary notifications to FDA for prescription drug and biological product shortages.

Mandatory Notification

Under Section 506C of the Federal Food, Drug, and Cosmetic Act (“FDCA” or “the Act”), a “sole manufacturer” of a drug approved under Section 505(b) or 505(j) of the Act must notify FDA at least six months prior to discontinuing manufacture of the drug product, if the drug is “life-supporting, life-sustaining, or intended for use in the prevention of a debilitating disease or condition.” The goal of mandatory notification under the FDCA is to enable the Agency to help manufacturers prevent or mitigate some drug shortages.

FDA originally interpreted Section 506C to apply only to permanent manufacturing discontinuances; however, such discontinuances account for only a small portion of drug shortages in the U.S. Moreover, mandatory notification does not apply to biological products. To address these concerns, and in response to President Obama’s Executive Order 13588 regarding prescription drug shortages,² the Agency published an Interim Final Rule (“IFR”) amending its regulations that implement Section 506C.³ The IFR expands the circumstances for which mandatory notification is required and clarifies who must notify the Agency of a discontinuance. Because the goal of Section 506C is to reduce or mitigate drug shortages, thereby minimizing disruptions in patient access to certain drug products, the draft guidance encourages over-inclusiveness when determining whether mandatory notification under Section 506C applies to a given situation.

Who is Responsible for Mandatory Notification

In the IFR, FDA defined the term “sole manufacturer,” as used in Section 506C, to mean “an applicant

¹ Guidance for Industry: Notification to FDA of Issues that May Result in a Prescription Drug or Biological Product Shortage; Draft Guidance (FDA, HHS Feb. 2012), available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM292426.pdf>.

² Executive Order 13588, Reducing Prescription Drug Shortages (Oct. 31, 2011), available at <http://www.gpo.gov/fdsys/pkg/DCPD-201100808/pdf/DCPD-201100808.pdf>.

³ Applications for Food and Drug Administration Approval To Market a New Drug; Revision of Postmarketing Reporting Requirements—Discontinuance; Interim Final Rule; Request for Comments; 76 Fed. Reg. 78530 (Dec. 19, 2011).

that is the only entity currently manufacturing a drug product of a specific strength, dosage form, or route of administration for sale in the United States, whether the product is manufactured by the applicant or for the applicant under contract with one or more different entities.” According to the draft guidance, the definition establishes the following:

- “Sole manufacturer” means the only applicant currently supplying the U.S. market with the drug product. It does not mean the sole holder of an approved new drug application or abbreviated new drug application. A manufacturer should therefore use commercial data or other methods to determine whether it is the only entity currently manufacturing the product for sale in the U.S.
- The specific strength, dosage form and route of administration are critical in determining “sole manufacturer” status.
- The application holder of the drug product bears the responsibility for reporting a discontinuance to the Agency — even if the application holder contracts the manufacture of the product to another entity.

What Products are Subject to Mandatory Notification

Mandatory notification applies to drugs that are “life-supporting, life-sustaining, or intended for use in the prevention of a debilitating disease or condition.” Based on FDA’s interpretation of these terms, the draft guidance advises that a drug product is subject to Section 506C if it “is used to treat or prevent a serious disease or medical condition.”

What Information Should be Reported to FDA

FDA’s original interpretation of Section 506C as applying only to permanent discontinuances is no longer valid. The IFR revised the meaning of “discontinuance” to include all interruptions in manufacturing, whether temporary or permanent, that could lead to a disruption in supply of the product. All permanent discontinuances clearly satisfy this standard. As to temporary interruptions in manufacturing and supply, the draft guidance provides examples of circumstances that warrant mandatory notification (e.g., delay in acquiring API or inactive ingredients, equipment failure or routine manufacturing shutdowns, any of which lead or could lead to an interruption in manufacturing or supply).

When and How to Notify FDA

Under Section 506C, mandatory notification must occur at least six months prior to the manufacturing discontinuance. The six-month period may be shortened only if the manufacturer submits a written certification of “good cause” and the Agency affirmatively allows a reduction in the notification period for an established “good cause” reason. The draft guidance recognizes an exception to this requirement where a manufacturer is unable to notify FDA at least six months before a temporary discontinuance because it was unforeseen. In such circumstances, the manufacturer must notify FDA as soon as possible after it knows that a discontinuance will occur.

FDA encourages manufacturers to make mandatory notifications by telephone or email. Certifications of good cause must continue to be submitted according to procedures established by 21 C.F.R. § 314.91.

Voluntary Notification

FDA strongly encourages voluntary notification of issues that could lead to a shortage of any prescription drug or biological product. Voluntary notification is encouraged even when the manufacturer is not a sole manufacturer of the drug or biological product at issue. According to the draft guidance, the following

issues should be voluntarily reported if they reasonably could be expected to lead to a potential shortage or disruption in supply:

- Product quality problems;
- Interruptions or other adjustments in manufacturing that temporarily halt production and may adversely affect market supply;
- Delays in acquiring critical raw materials or components;
- Loss of suppliers of raw materials or components;
- Transfer of manufacturing to an alternate facility;
- Loss of a production line or production capacity;
- Any production problems that occur during or after manufacturing that could result in supply disruptions;
- Import delays;
- Unexpected increases in demand;
- Product discontinuances, even if not by a sole manufacturer; and
- Any other circumstances that may result in a shortage or potential disruption in supply.

As with mandatory notification, FDA encourages manufacturers to be over-inclusive when determining whether to make a voluntary notification. The draft guidance advises that voluntary notification should be made as soon as the manufacturer becomes aware of an issue that may result in a product shortage. Like mandatory notifications, voluntary notification should be made to FDA electronically or by telephone.

What FDA Does With Information Reported

The draft guidance provides an overview of what FDA does with the information it receives through mandatory and voluntary notifications. Most importantly, FDA works with the manufacturer with the goal of preventing a product shortage. Specific actions that the Agency might take include:

- Expediting review of manufacturer submissions;
- Identifying additional sources of supply or alternate manufacturers;
- Finding new or additional sources of raw material(s);
- Consulting with and advising sponsors on resolution of manufacturing or quality issues; and
- In rare instances, exercising regulatory discretion for the temporary importation of a non-U.S. product.

In addition, FDA uses the information it receives through mandatory and voluntary notifications to inform the public about actual product shortages.

Additional Considerations for Manufacturers

Finally, the draft guidance identifies other actions that manufacturers can take that may help prevent product shortages. These actions include maintaining compliance with current good manufacturing practices and making contingency plans for responding to situations that could lead to a shortage.

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