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The FDA's Latest One-Two Punch to Combat Drug Shortages

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On October 31, 2013, the U.S. Food and Drug Administration ("FDA") unveiled its latest steps for preventing and resolving prescription drug shortages. First, the agency announced a proposed rule[1] requiring manufacturers of certain medically important prescription drug products, including biological drugs (e.g., vaccines), to notify the FDA if they intend to discontinue making a drug or learn of manufacturing problems that are likely to affect its supply. Second, the FDA's Drug Shortages Task Force (the "Task Force") submitted to Congress the agency's "Strategic Plan for Preserving and Mitigating Drug Shortages" (the "Strategic Plan").[2] The Strategic Plan identified two central goals for addressing drug shortages: improving the FDA's mitigation response to imminent or existing shortages, and implementing long-term strategies for the prevention of shortages by focusing on their root causes.[3] The proposed rule and Strategic Plan target a thorny area for a large swath of manufacturers of both generic and brand-name medications. We explore each in more detail below.

The Proposed Rule

In response to growing concerns about the impact of shortages of pharmaceuticals in the United States, on October 31, 2011, President Obama issued an Executive Order directing the FDA "to take steps that will help to prevent and reduce current and future disruptions in the supply of lifesaving medicines," including "requir[ing] drug manufacturers to provide adequate advance notice of manufacturing discontinuances that could lead to shortages of drugs that are life supporting or life sustaining, or that prevent debilitating disease."[4] The FDA responded to the President's directive by publishing an interim final rule ("IFR") on December 19, 2011, which amended the regulations implementing the postmarketing reporting provisions of the Federal, Food, Drug, and Cosmetic Act ("FD&C Act"); namely, to increase the scope of information that the FDA receives regarding discontinuances.[5] Specifically, the IFR broadened the term ''discontinuance'' and clarified the previously undefined term ''sole manufacturer" with respect to notification of discontinuance requirements.[6]

In July 2012, the President signed into law the Food and Drug Administration Safety and Innovation Act ("FDASIA").[7] Among other things, the FDASIA amended Section 506C of the

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[1] 78 Fed. Reg. 65904, 65921 (Nov. 4, 2013).

[2] *See* "Strategic Plan for Preserving and Mitigating Drug Shortages," http://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf.

[3] *See id.* at 4.

[4] *See* "Executive Order 13588 - Reducing Prescription Drug Shortages," http://www.whitehouse.gov/the-press-office/2011/10/31/executive-order-reducing-prescription-drug-shortages.

[5] 76 Fed. Reg. 78530, 78530 (Dec. 19, 2011).

[6] *See id.* at 78539-40.

[7] Pub. L. No. 112–144, 126 Stat. 993 (July 9, 2012).

FD&C Act to modify the requirements for reporting and addressing permanent discontinuances or interruptions in the manufacturing of life-saving drug products.[8] Now, with the November 4 proposed rule, the FDA seeks to implement the expanded early notification requirements in the FDASIA. The rule includes the following definitional and other substantive changes:

- Requiring any permanent discontinuance or any interruption in manufacturing that is likely to lead to a "significant" or "meaningful" disruption in the supply of a covered drug or biological product to be reported to the FDA.[9]
- Expanding the early notification requirements of Section 506C of the FD&C Act to apply to all biological products, including plasma-derived products and their recombinant analogs, vaccines, and in a more limited manner, to blood or blood components.[10]
    - Extending the notice requirements of the FD&C Act to all manufacturers of covered drugs and biological products, not only their "sole manufacturer."[11]
    - For the first time, requiring the FDA to issue a public noncompliance letter to a manufacturer who fails to provide sufficient warning of an impending drug shortage.[12]
    - Defining a "life supporting or life sustaining" drug product as one "essential to, or that yields information that is essential to, the restoration or continuation of a bodily function important to the continuation of human life."[13]
    - Defining the phrase "intended for use in the prevention or treatment of a debilitating disease or condition" in the FD&C Act, as amended by the FDASIA, to mean "a drug product intended for use in the prevention or treatment of a disease or condition associated with mortality or morbidity that has a substantial impact on day-to-day functioning."[14]

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[8] 21 U.S.C. §§ 356c(a); 356c(b).

[9] *See* 78 Fed. Reg. 65904, 65914 (2013). Under the rule, a "meaningful disruption" is defined to encompass any

> change in production that is reasonably likely to lead to a reduction in the supply of a drug by a manufacturer that is more than negligible and affects the ability of the manufacturer to fill orders or meet expected demand for its product, [but] does not include interruptions in manufacturing due to matters such as routine maintenance or insignificant changes in manufacturing so long as the manufacturer expects to resume operations in a short period of time.

See id. at 65921-22. A "significant disruption" is similarly, but separately, defined with respect to the supply of blood or blood components. *See id.*

[10] *See id.* at 65906.

[11] *Compare* 78 Fed. Reg. 65904, 65908 (2013) *with* 21 C.F.R. 314.81(b)(3)(iii)(a) (requiring notice of discontinuance from "the sole manufacturer of an approved drug product . . . ").

[12] *See* 78 Fed. Reg. 65904, 65922 (2013) ("[The] FDA will make the letter and the applicant's response to the letter public, unless, after review of the applicant's response, FDA determines that the applicant had a reasonable basis for not notifying FDA . . . .").

[13] *See id.* at 65921.

[14] *See id.*

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The Strategic Plan

The FDASIA directed the FDA to "establish a task force to develop and implement a strategic plan for enhancing the Secretary's response to preventing and mitigating drug shortages."[15] The Task Force released its Strategic Plan to deal with drug shortages on October 31.

The Strategic Plan details the FDA's current efforts to prevent and mitigate drug shortages, emphasizing the need for early notification of production disruptions from manufacturers.[16] To strengthen its mitigation response (i.e., goal #1), the Task Force recommended that the FDA develop and/or streamline internal processes for managing and tracking data relating to drug supply shortages and disruptions in production, improve communications with the public regarding actual or potential shortages, and more closely collaborate with drug manufacturers and other pharmaceutical industry stakeholders to anticipate and prevent production problems that can disrupt drug supplies.[17]

Effective long-term prevention strategies (i.e., goal #2), the Task Force wrote, "must [] recognize the importance of addressing the underlying causes of shortages, including sustaining manufacturing quality."[18] The Task Force noted that "shortages cannot be resolved until one or more manufacturers commit to fill in for lost production" and, accordingly, proposed developing ways for the FDA and industry stakeholders to give "more positive incentives" to ensuring and prioritizing manufacturing quality.[19] Another recommendation was that drug makers could explore building redundant manufacturing capacity, holding spare capacity, or increasing inventory levels to lower the risks of shortages — manufacturing practices the FDA admits it may neither require nor regulate. Thus, the Task Force told Congress that the FDA cannot legislate away the problem of shortages but that, practically speaking, "[s]uccess in addressing drug shortages requires a collective effort by all stakeholders — manufacturers, federal partners, researchers, professional organizations, and patients."[20]

Concluding thoughts

Despite the significant public health threat posed by shortages of drugs and biologics, the Task Force was forced to confront the reality that typically "cost [is] the major factor in purchasing decisions," not the ability of manufacturers to offer innovative manufacturing processes and technologies:

> Within the limits set by disclosure law, FDA makes certain information publicly available about the historical ability of manufacturers to produce quality products. . . . Nevertheless, numerous comments to the *Federal Register* notice suggested that buyers (e.g., hospitals, health maintenance

[15] *See* 21 U.S.C. § 356d(a)(1)(A).

[16] *See* Strategic Plan at 12.

[17] *See id.* at 18-19. While vague - almost certainly by design - the Task Force pointed out that, "[w]here justified, FDA may exercise regulatory flexibility to prevent or mitigate a shortage." *See id.* at 19.

[18] *See id.* at 20.

[19] *See id.* at 21; 22; 38. The FDA claims it is "currently considering an incentive program which would recognize manufacturers who help address a shortage." *See* "FDA Acts to Prevent More Drug Shortages," http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM373003.pdf.

[20] *See id.* at 21.

> organizations, group purchasing organizations, and others) do not consider or value this potentially important information. This decoupling of quality considerations from purchasing decisions makes cost the major factor in purchasing decisions, most likely intensifying price competition, leading manufacturers to focus more on reducing costs than on maintaining quality, and potentially contributing to shortages.[21]

The Task Force envisioned "[a]n effort by buyers to use publicly available information to take quality into account when making drug purchasing decisions";[22] however, it stopped short of offering any market-based approach or incentive for prioritizing manufacturing quality and/or "recoupling" it with product price.

The extent to which the FDA's November 4 proposed rule, if implemented in its current form, would further stem drug shortages ultimately remains to be seen. The rule's 60-day public comment period closes on January 3, 2014.

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[21] *See id.* at 22.
[22] *See id.*