DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
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STATEMENT

OF

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FOOD AND DRUG ADMINISTRATION

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

CAUCUS ON INTERNATIONAL NARCOTICS CONTROL

UNITED STATES SENATE

"IMPROVING MANAGEMENT OF THE CONTROLLED SUBSTANCES QUOTA PROCESS"

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INTRODUCTION

Chairman Grassley, Chairman Feinstein, and Members of the Caucus, I am Captain Valerie Jensen, Associate Director of the Drug Shortages Staff (DSS) in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to speak with you today. I'd like to share with you some information about the issue of drug shortages in general, before addressing the more specific issue of controlled substance shortages and what FDA is doing to improve our response to these and other drug shortages.

Drug shortages pose a significant public health threat, affecting individual patients from across the United States, including patients who are in need of drugs to treat life-threatening diseases such as cancer, serious infections, and malnutrition. The number of new drug shortages in the United States rose steadily between 2005, when FDA began tracking 60 new shortages, and the all-time high in 2011, when 251 new shortages were reported. After a series of interventions, including an Executive Order on reducing prescription drug shortages issued by the President in 2011 and enactment of the Food and Drug Administration Safety and Innovation Act (FDASIA), and FDA outreach to a variety of stakeholders, including our work with the pharmaceutical community, the number of new drug shortages declined significantly in 2012 to 117, fell even further to 44 in 2013, and remained steady in 2014, with 44 new shortages occurring. However, there continues to be new shortages occurring in 2015, as well as older shortages that have persisted. Currently, FDA is tracking and working to resolve over 70 shortages that began in 2014 and prior years, which is a decrease from the 97 ongoing shortages tracked at the end of 2013.

The focus of today's hearing is not solely drug shortages; however, it is important to understand the basic causes of these shortages. While increases in demand for a given drug can sometimes challenge the drug supply, drug shortages are usually preceded by a production disruption, which can be either a permanent product discontinuation or temporary interruption in manufacturing. Once a manufacturer experiences a discontinuance or interruption in manufacturing, a shortage may occur, if other manufacturers cannot increase production quickly enough to make up the loss. These production disruptions can be triggered by several factors, including factors within the control of manufacturers, such as a decision to permanently discontinue production of a drug because the product is no longer profitable. Production disruptions can also be caused by factors outside of the manufacturer's control, such as natural disasters or the unavailability of raw materials or needed materials for drug manufacturing. Most often, however, production disruptions leading to shortages are the result of failures within manufacturing facilities that result in failures of product or facility quality.

While manufacturers have a central role in ensuring that drugs are manufactured to a consistently high quality, FDA and other stakeholders have important roles to play in addressing drug shortages in the United States. When FDA is aware of a potential, imminent, or ongoing shortage, the Agency offers to work with the affected manufacturer to find ways to prevent or mitigate the shortage and lessen a shortage's impact on patients. With early and timely notification by manufacturers, FDA helped prevent 195 shortages in 2011, 282 shortages in 2012, 170 shortages in 2013, and 101 shortages in 2014. These numbers illustrate the value of FDA's receiving early notification of potential drug shortages. On July 9, 2012, Congress provided FDA with new authorities as part of FDASIA. Section 1001 of FDASIA broadened the scope of early notification provisions previously in place by requiring all manufacturers of all

covered prescription drugs (approved or unapproved) to notify FDA at least six months in advance or as soon as practicable of a permanent discontinuance or interruption in manufacturing that is likely to lead to a meaningful disruption in the U.S. supply of the drug. The current rate of notifications per month continues to be over double the rate observed prior to FDASIA.

Once notified of a pending shortage, FDA's staff has a variety of tools to help prevent or mitigate shortages. Our FDA staff, led by DSS, begins by verifying that an actual shortage exists or may occur. FDA uses the FDASIA definition of a shortage, which is when the demand or projected demand for the drug within the United States exceeds the supply of the drug. Before concluding that a shortage exists, FDA applies a standard process that involves a careful review by our shortage staff of data from multiple sources, which can include IMS Health market research; product manufacturers; internal FDA databases; reports from prescribers, patients, pharmacies, and other stakeholders about supply disruptions; the American Society of Health-System Pharmacists, which also maintains drug shortage listings; and other Federal agencies, such as the Drug Enforcement Administration (DEA), the Centers for Disease Control and Prevention (CDC), and the National Institutes of Health (NIH). Steps that DSS may take to verify the presence or potential for a shortage include:

- Using a market research database to collect initial information to determine whether or not the current supply of product across manufacturers is stable.

- Contacting product manufacturer(s) to collect up-to-date inventory information, rate of demand (units/month), manufacturing schedules, and any changes in ordering patterns. Although manufacturers are generally not required to provide this information to FDA, voluntarily sharing this information greatly facilitates the management of shortages.

- Evaluating product inventory in the distribution chain to the extent possible. This information can help predict how quickly a shortage may develop (if at all).

When the shortage staff determines that a shortage either exists or is likely to occur, shortage staff members lead or coordinate the efforts to mitigate, and whenever possible, prevent the shortage.

FDA can and does take a variety of actions to mitigate or prevent shortages. For example:

- Identify the extent of the shortfall and determine if other manufacturers are willing and able to increase production to make up the gap.
- Expedite FDA inspections and reviews of submissions from manufacturers attempting to restore production.
- Expedite FDA inspections and reviews of submissions from manufacturers interested in starting new production or increasing existing production of products in shortage.
- Exercise temporary enforcement discretion for new sources of medically necessary drugs.
- Work with the manufacturer to ensure adequate investigation into the root cause of the quality problem.
- Explore risk-mitigation measures for products initially not meeting established standards to allow them to be used safely.

When a shortage is unavoidable, even with all steps being taken to mitigate it, FDA posts the shortage in the online Drug Shortage Database on the FDA website to inform the public of the shortfall, and includes the reasons reported by the manufacturers for the shortage as well as the estimated duration, if known. The information in the database is updated daily, and manufacturers are asked to provide regular updates. FDA closely monitors drug shortage situations, including the supply of and demand for a product, and moves the shortage to the Resolved section of the database, once supplies are meeting all demand.

Controlled Substance Shortages

The processes outlined above are used for all drugs, including controlled substances. It is important to note that shortages of controlled substances, including Schedule II controlled substances that are subject to DEA-established quotas limiting the amounts that can be produced, are normally caused by the same factors as non-controlled substances. These factors mainly involve quality problems with the manufacturer, such as a sterility failure or production line breakdown, or specific drugs experiencing quality failures, such as contamination with glass, metal, or other foreign particles. The last time a manufacturer reported a shortage that was related to a DEA-established quota was in 2011, and since that time, all shortages of controlled substances have been reported to be caused by other factors, including quality failures, manufacturing delays, discontinuations, and raw material problems, and were not related to DEA or the established quota. After FDA receives a notification of a discontinuation or interruption under section 506C, FDASIA requires FDA to determine whether the notification relates to a controlled substance subject to quota under section 306 of the Controlled Substances Act. We then coordinate with DEA, as appropriate, on a response. For example, FDA may work with

DEA to enable a manufacturer to increase its allotted quota, if this step would help avoid a shortage of the product.

In September 2014, CDER revised its Manual of Policies and Procedures, or MaPP, to clarify FDA's process of addressing shortages of controlled substances. According to the revised MaPP, when FDA's DSS determines that a potential or actual shortage involves a request for an adjustment in applicable quotas made by an Active Pharmaceutical Ingredient (API) or final dosage manufacturer of a Schedule II product, we will:

1. Determine if we have a notification related to a DEA allocation.

2. Request that the manufacturer tell us when they officially submitted their quota request to DEA—if the shortage notification is related to a DEA quota allocation—the outcome of that request, and the expected month of the product shortage, if the quota increase was not granted.

3. Review and update, if needed, the product listing on our Drug Shortage Database.

4. Contact DEA to provide information about the potential or actual shortage and the current market impact, if the quota request is partially granted by DEA.

5. Contact DEA to communicate the need for quota modifications, when DSS determines the increased quota is needed to address a shortage.

6. Submit a formal request for quota increase to DEA, if the manufacturer has not done so already.

7. Post the denial letter(s) on the Drug Shortage website, when a request for additional quota to mitigate an actual or potential shortage (either by the manufacturer or the Agency) is denied.

Since FDASIA was enacted, there have not been any shortages of controlled substances reported to be due to quota allocations. FDA will follow the process outlined in our MaPP, if there are any quota-related shortages or potential shortages reported in the future by manufacturers.

To help streamline and improve communications, FDA and DEA have developed a Memorandum of Understanding (MOU).[1] The MOU sets forth steps and procedures for more consistent and efficient exchange and tracking of information between the two agencies.

Next Steps

Going forward, there is important additional work needed to mitigate the factors that lead to shortages of all kinds. In October 2013, FDA released a Strategic Plan[2] (the Plan), called for in FDASIA, both to improve FDA's response to potential, imminent, or existing shortages and to advance longer-term approaches for addressing the underlying causes of shortages to prevent supply disruptions from occurring in the first place. We are actively working on implementing the actions identified in the Plan. For example, the Plan suggests that FDA improve data and

[1] MOU 225-15-011 is available at *http://www.fda.gov/AboutFDA/PartnershipsCollaborations/MemorandaofUnderstandingMOUs/DomesticMOUs/ucm440091.htm*

[2] FDA's "Strategic Plan for Preventing and Mitigating Drug Shortages" is available at *http://www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf*.

response tracking. In line with this suggestion, and GAO's suggestion in a February 2014 report on drug shortages,[3] we have created a dedicated data system that focuses solely on collecting data related to shortages—a system that integrates data from the other general data systems and is designed to improve tracking efficiency. This new drug data system will enable FDA to more efficiently track and assess issues relating to drug shortages, including enhancing our tracking of time from notification of shortage to resolution. The Plan also suggests that FDA enhance public communications about drug shortages. To address this suggestion, we have updated our online Drug Shortage Database on the FDA website[4] to improve functionality and allow users to sort by different therapeutic categories. Also, we have recently launched a drug shortages mobile app to improve access to information, by allowing users to search or browse for drug information and report suspected drug shortages or supply issues to FDA.

CONCLUSION

Drug shortages remain a significant public health issue in the United States, and addressing them is a top priority for FDA. By collaborating with external stakeholders, and by exercising regulatory flexibility in appropriate cases, FDA has had a substantial positive impact on drug shortages.

[3] "Drug Shortages: Public Health Threat Continues, Despite Efforts to Help Ensure Product Availability." Available at *http://www.gao.gov/assets/670/660785.pdf.*

[4] FDA Drug Shortage Website is available at *http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm.*

It is extremely important that FDA and DEA have good coordination and communication when there is an impending shortage of a controlled substance, whether or not it is reported to be related to quota. FDA has processes in place to govern how we communicate about potential shortages with DEA, informed by FDASIA mandates and our own Strategic Plan for Preventing and Mitigating Drug Shortages. FDA and DEA worked closely together to finalize our MOU to further streamline our communications, and we look forward to continued collaboration with DEA to further our shared mission of serving the American public.

Thank you, again, for having me here today. I am happy to answer any questions you may have.