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Oral Remarks
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My name is Gabrielle Cosel; I manage drug safety initiatives at the Pew Charitable Trusts – an independent, nonpartisan research and policy organization dedicated to serving the public.

Thank you for the opportunity to speak today about the Generic Drug User Fee Program and its importance to public health. Patients rely on generic medicines every day, from chemotherapy to antibiotics; they are essential to our health care system. Not only do patients need access to these drugs, they need them to be safe and of good quality.

The first, landmark Generic Drug User Fee agreement supported both access to, and quality of, generic medications. To support access, the agreement included metrics to hasten the review of generic drug applications, as well as new staff to conduct reviews. To support quality and safety, the agreement provided resources – and a mandate – for FDA to conduct more frequent inspections of overseas drug manufacturing facilities.

Importance of foreign plant inspections

The geography and complexity of our drug supply has changed significantly over the past several decades; our drugs and their ingredients are increasingly sourced from foreign countries, creating an oversight challenge for both industry and the FDA.

Insufficient oversight increases the risk that substandard drugs enter the drug supply and harm patients. Perhaps the most well-known example of this occurred in 2008, when dozens of adverse events in the U.S., including some deaths, were linked to an adulterant in heparin, a widely used blood thinner. The drug was manufactured by a U.S. company that was sourcing active and precursor ingredients from a complex upstream supply chain in China.[1] Investigations revealed that somewhere in that supply chain, the correct active ingredient was replaced by a substance with toxic effects known as over-sulfated chondroitin sulfate (OSCS), which standard tests then in use were unable to detect.[2]

Adulterated heparin exposed a number of significant supply-chain management problems on the part of the manufacturer and the FDA. The U.S. manufacturer began receiving heparin from a new Chinese plant in 2004, but did not conduct its own audit of that plant until 2007, relying instead on an earlier assessment by a different company.[3] FDA approved the plant as a supplier without conducting a pre-approval inspection,[4] in part because the agency confused the plant with another site in its database. When FDA finally inspected the plant after the adverse events occurred, its inspectors found a number of manufacturing quality issues, including poor control of incoming raw materials.[5]

One of FDA's most important tools for ensuring the safety of drugs sold in the United States – whether they are made domestically or abroad – is the inspection of factories to verify compliance with good manufacturing practice (GMP) standards. The volume of drugs destined for the U.S. market makes it impossible to test samples of all products before they reach patients. While FDA inspections alone cannot guarantee quality, the expectation of inspection is a critical driver of compliance.

Despite our increasing reliance on overseas production plants, the FDA has historically inspected foreign plants much less frequently than those in the United States – about every 9 years on average, compared with every 2 to 3 years domestically.[6] But the FDA's inspection program is now changing as a result of GDUFA and additional supply chain provisions in the Food and Drug Administration Safety and Innovation Act of 2012. FDASIA's Title VII placed all manufacturing plants, whether foreign or domestic, on a single risk-based inspection schedule. Meanwhile, the GDUFA agreement provided FDA with additional funds to inspect foreign generic drug facilities, and established a goal for FDA to reach inspectional parity between foreign and domestic plants by fiscal year 2017.

In FY 2014, FDA conducted 993 total inspections of foreign human drug establishments and 1,869 inspections of domestic human drug establishments. But sub-counts of GMP surveillance inspections were much more similar: FDA conducted 780 GMP inspections of domestic drug plants, and 757 GMP inspections of foreign plants.[7] In prior years these numbers were farther apart – in FY 2013 FDA conducted 967 domestic GMP inspections and 604 foreign GMP inspections.[8] In FY 2012, the numbers were 1,134 and 588 respectively.[9]

GDUFA and drug shortages

It is important to note that there is a range of manufacturing quality in all countries. There are well-run plants in emerging economies doing high quality manufacturing. There are also U.S. facilities with significant quality problems. For example, many of the drug shortages the U.S. is grappling with today have been linked with sterile production problems at domestic finished-dose plants.

When these plants are faced with a need to quickly move production to another line, or update production equipment, they often need to get FDA approval. GDUFA helps provide FDA with the resources and staff to allow them to expedite applications and inspect plants to ameliorate shortage situations.

Drug shortages continue to plague the U.S. healthcare system. While new drug shortages have begun to decline thanks in part to the work of the FDA, a legacy of ongoing drug shortages persists. In 2012, the U.S. experienced over 450 shortages, according to the Government Accountability Office.[10]

Shortages can be disastrous to patients, interrupting or delaying their treatment, or forcing use of second or third choice medicines that may be less effective or have worse side effects. Drug shortages also affect the healthcare providers who must devote staff and resources to identifying new sources of supply, rationing existing supplies, and communicating contingency plans throughout the health-system.

Conclusion

In conclusion, we strongly support the continuation of the GDUFA program. Funding to support timely review of generic drug applications will help ensure patient access to safe and high-quality generic medicines and mitigate drug shortages. We also support continued inclusion of resources and performance goals for FDA foreign inspections in GDUFA II – these are important drivers of essential oversight activities that protect patients.

References:

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[3] IBID

[4] IBID

[5] Warning Letter WL 320-08-01, April 21, 2008. To: Dr. Yan Wang, Ph.D., General Manager, Changzhou SPL Company, Ltd (a/k/a "Kaipu"). From: Food and Drug Administration, Division of Manufacturing and Product Quality Office of Compliance Center for Drug Evaluation and Research.

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[7] Department of Health and Human Services Fiscal Year 2016 Food and Drug Administration Justification of Estimates for Appropriations Committees.
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