



MEMORANDUM

December 6, 2019

To: Subcommittee on Oversight and Investigations Members and Staff

Fr: Committee on Energy and Commerce Staff

Re: Hearing on “Securing the U.S. Drug Supply Chain: Oversight of FDA’s Foreign Inspection Program”

On **Tuesday, December 10, at 10 a.m. in the John D. Dingell Room, 2123 Rayburn House Office Building**, the Subcommittee on Oversight and Investigations will hold a hearing entitled, “Securing the U.S. Drug Supply Chain: Oversight of FDA’s Foreign Inspection Program.” The hearing will examine the Food and Drug Administration’s (FDA) ability to effectively oversee the quality of drug products manufactured in foreign countries.

I. BACKGROUND

To receive approval to market a drug product in the United States, pharmaceutical manufacturers must comply with FDA’s Current Good Manufacturing Practice (CGMP) regulations. The CGMP regulations lay out “minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packing of a drug product. The regulations make sure that a product is safe for use, and that it has the ingredients and strength it claims to have.”¹ While FDA requires that manufacturers implement CGMPs to ensure the safety and efficacy of the drugs they produce, FDA is ultimately the entity charged with ensuring the integrity of the drug supply of the United States.² FDA is tasked with inspecting foreign and domestic firms, both of which are held to the same manufacturing standards.³

One of the primary mechanisms for overseeing the United States’ drug supply is through FDA inspections. FDA conducts three types of inspections of drug manufacturing firms: (1)

¹ Food and Drug Administration, *Current Good Manufacturing Practice (CGMP) Regulations* (Mar. 2018) (www.fda.gov/drugs/pharmaceutical-quality-resources/current-good-manufacturing-practice-cgmp-regulations).

² Food and Drug Administration, *Facts About the Current Good Manufacturing Practices (CGMP)* (Jun. 2018) (www.fda.gov/drugs/pharmaceutical-quality-resources/facts-about-current-good-manufacturing-practices-cgmps).

³ Government Accountability Office, *Drug Safety: FDA Has Improved Its Foreign Drug Inspection Program, but Needs to Assess the Effectiveness and Staffing of Its Foreign Offices* (Dec. 2016) (GAO-17-143).

preapproval inspections; (2) surveillance inspections; and (3) for-cause inspections. FDA conducts a preapproval inspection of firms' manufacturing facilities prior to allowing their product on the market in the United States, inspecting the firm to ensure that it can manufacture the drug in compliance with CGMPs. Once a drug is marketed in the United States, the firm is then subject to periodic surveillance inspections by FDA to ensure the firm has adequate controls to produce high-quality drugs. Finally, FDA may conduct for-cause inspections for reasons such as manufacturing problems, adverse health events associated with a product, or complaints from consumers or health care providers.⁴

A large portion of the drug supply in the United States originates abroad. FDA has estimated that nearly 40 percent of finished drug products⁵ and 72 percent of active pharmaceutical ingredients (API)⁶ are manufactured outside the United States. Specifically, FDA reported that as of August 2019, 18 percent of API manufacturing facilities were located in India and 13 percent were located in China, after the number in China more than doubled since 2010.⁷

Brand and generic drug firms are held to the same quality standards. Brand and generic versions of a drug must contain the same API, and generic drugs are the same as a brand-name product in dosage, safety, effectiveness, strength, stability, and quality, as well as in the way the product is taken and should be used.⁸ Because a large portion of the United States' supply of API is manufactured overseas, both the brand and generic versions of many drugs may use API sourced from the same foreign API manufacturer.

II. FDA FOREIGN INSPECTIONS: A LONG HISTORY OF OVERSIGHT

As far back as 1998, the Government Accountability Office (GAO) and the Committee have repeatedly raised concerns with FDA's foreign drug inspection program. For example, in 1998, GAO noted concerns about FDA's infrequent inspections of foreign firms, a finding reiterated in later GAO reports.⁹

⁴ *Id.*

⁵ *Id.*

⁶ House Committee on Energy and Commerce, Statement of Dr. Janet Woodcock, Director, Center for Drug Evaluation and Research, Food and Drug Administration, *Safeguarding Pharmaceutical Supply Chains in a Global Economy*, 116th Cong. (2019).

⁷ *Id.*

⁸ Food and Drug Administration, *Generic Drug Facts* (June 2018) (www.fda.gov/drugs/generic-drugs/generic-drug-facts); *see* note 3.

⁹ Government Accountability Office, *Food and Drug Administration: Improvements Needed in the Foreign Drug Inspection Program* (Mar. 1998) (GAO/HEHS-98-21); Government Accountability Office, *Drug Safety: Better Data Management and More Inspections Are Needed to Strengthen FDA's Foreign Drug Inspection Program* (Sept. 2008) (GAO-08-970).

In 2007, the Subcommittee on Oversight and Investigations held a hearing entitled, “FDA Foreign Drug Inspection Program: A System at Risk.” At that hearing, the Committee noted the increased respective roles of India and China in the United States’ drug supply, and explored challenges related to the frequency of FDA’s foreign inspections, FDA staff presence abroad, the availability of FDA translators in foreign countries, and the quality of FDA’s data on foreign firms, among other things.¹⁰

In 2008, the Subcommittee held a follow-up hearing to explore the capacity of FDA to inspect foreign drug facilities following multiple deaths linked to contaminated heparin imported from China.¹¹ That same year, GAO identified deficiencies in the databases FDA was using to oversee foreign firms, resulting in FDA not knowing how many foreign firms were subject to inspection.¹² Soon after that 2008 report, GAO added FDA’s oversight of medical products (including drugs) to its High-Risk Series, particularly noting vulnerabilities in FDA’s foreign drug inspection program.¹³

In 2010, GAO found that FDA had increased the number of foreign firms that it had inspected, noting, however, that those numbers were still relatively fewer than domestic inspections, and that FDA may have never inspected most foreign firms in its inventory. According to GAO, FDA also was not focusing its foreign inspections on firms deemed to represent the greatest public health risk.¹⁴ In a separate report that year, GAO also found that FDA experienced challenges recruiting and retaining staff for its foreign offices, which provide dedicated in-country staff to inspect foreign firms. GAO noted that these challenges could limit the foreign offices’ effectiveness.¹⁵

More recently in 2016, GAO found that, while FDA increased its foreign drug inspections, it had still never inspected nearly 1,000 foreign firms and it had not yet assessed the

¹⁰ House Committee on Energy and Commerce, *FDA Foreign Drug Inspection Program: A System at Risk*, 110th Cong. (2007).

¹¹ House Committee on Energy and Commerce, *FDA’s Foreign Drug Inspection Program: Weaknesses Place Americans at Risk*, 110th Cong. (2008).

¹² Government Accountability Office, *Drug Safety: Better Data Management and More Inspections Are Needed to Strengthen FDA’s Foreign Drug Inspection Program* (Sept. 2008) (GAO-08-970).

¹³ Government Accountability Office, *High-Risk Series: An Update* (Jan. 2009) (GAO-09-271).

¹⁴ Government Accountability Office, *Drug Safety: FDA Has Conducted More Foreign Inspections and Begun to Improve Its Information on Foreign Establishments, but More Progress Is Needed* (Sept. 2010) (GAO-10-961).

¹⁵ Government Accountability Office, *Food and Drug Administration: Overseas Offices Have Taken Steps to Help Ensure Import Safety, but More Long-Term Planning Is Needed* (Sept. 2010) (GAO-10-960).

effectiveness of its foreign offices, which still suffered from high vacancy rates.¹⁶ GAO also raised concerns about the number of inspections conducted by staff in these foreign offices, noting that inspectors from FDA’s China foreign office participated in an average of only seven inspections per year between fiscal years 2010 and 2015.¹⁷

III. CONGRESSIONAL ACTION TO STRENGTHEN FOREIGN INSPECTIONS

The Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) gave FDA authorities to address some of these challenges, including establishing a risk-based inspections schedule; prohibiting manufacturers from delaying, denying, limiting, or refusing inspection; providing FDA with the authority to destroy products that have been refused admission; allowing FDA to recognize foreign inspections of drug establishments; and extending FDA’s administrative detention authority.¹⁸

The Drug Quality and Security Act of 2013 (DQSA) provided FDA with “track and trace” authority to improve its detection of potentially dangerous drugs in the supply chain.¹⁹ In 2017, Congress reauthorized the Generic Drug User Fee Amendments (GDUFA II), requiring generic firms to pay user fees that fund, among other things, FDA’s foreign inspection program.²⁰

Following the passage of FDASIA in 2012, FDA increased the number of foreign inspections it conducted,²¹ and implemented a risk-based approach to select sites for inspection based on their “known safety risks,” regardless of whether they are domestic or foreign.²² FDA

¹⁶ See note 3.

¹⁷ See note 3.

¹⁸ Pub. L. No. 112–144 (July 2012) (www.congress.gov/112/plaws/publ144/PLAW-112publ144.pdf); Food and Drug Administration, *Food and Drug Administration Safety and Innovation Act (FDASIA)* (Mar. 2018) (www.fda.gov/regulatory-information/selected-amendments-fdc-act/food-and-drug-administration-safety-and-innovation-act-fdasia#supplychain).

¹⁹ Pub. L. No. 113–54 (Nov. 2013) (<https://www.congress.gov/113/plaws/publ54/PLAW-113publ54.pdf>); Food and Drug Administration, *Drug Supply Chain Security Act (DSCSA)* (May 2019) (<https://www.fda.gov/drugs/drug-supply-chain-integrity/drug-supply-chain-security-act-dscsa>).

²⁰ Food and Drug Administration, *Generic Drug User Fee Amendments* (Oct. 2019) (www.fda.gov/industry/fda-user-fee-programs/generic-drug-user-fee-amendments).

²¹ See note 3; House Committee on Energy and Commerce, Testimony of Dr. Janet Woodcock, Director, Center for Drug Evaluation and Research, Food and Drug Administration, *Safeguarding Pharmaceutical Supply Chains in a Global Economy*, 116th Cong. (2019).

²² Letter from Traci Vitek, Senior Counselor, U.S. Department of Health and Human Services, to Hon. Frank Pallone, Jr., Chairman, House Committee on Energy and Commerce (Oct. 11, 2019).

also recently reported to the Committee that it had reduced the number of firms that have never been inspected, and conducts surveillance inspections of firms every 2.6 years in China, every 2.5 years in India, and every 2.8 years in the United States (at the median).²³

IV. REMAINING CHALLENGES IN FDA’S FOREIGN DRUG INSPECTION PROGRAM

Despite this progress, FDA’s foreign drug inspection program still faces challenges, partly because FDA has not addressed all of the vulnerabilities previously identified. Over the last two years, the number of FDA inspections has declined for both domestic and foreign firms, attributed at least in part to challenges in hiring FDA inspectors.²⁴ Specifically, FDA still struggles to recruit and retain inspection staff in its foreign offices.²⁵ GAO is also continuing its work at the Committee’s request, and is expected to continue to raise warranted concerns with the declining number of FDA inspections, staffing vacancies, and inspection challenges such as pre-announced inspections and language barriers.²⁶

Earlier this year, the Committee sent two letters to FDA requesting information about its foreign drug inspection program following multiple recalls of blood pressure medication manufactured in China and India that were contaminated with trace amounts of carcinogens.²⁷ A former FDA inspector reportedly raised concerns about “potential systemic problems” at facilities in China and India that produced the API involved in the recalls.²⁸ A number of other press reports have also alleged fraud by foreign firms and called into question FDA’s ability to effectively oversee foreign manufacturing.²⁹

²³ *Id.*

²⁴ House Committee on Energy and Commerce, Testimony of Dr. Janet Woodcock, Director, Center for Drug Evaluation and Research, Food and Drug Administration, *Safeguarding Pharmaceutical Supply Chains in a Global Economy*, 116th Cong. (2019).

²⁵ *Id.*

²⁶ Briefing by Government Accountability Office to House Energy and Commerce Committee Staff (Nov. 19, 2019).

²⁷ Letter from Hon. Frank Pallone, Jr., Chairman, and Hon. Greg Walden, Ranking Member, *et al.*, House Committee on Energy and Commerce, to Dr. Scott Gottlieb, Commissioner, Food and Drug Administration (Feb. 13, 2019); Letter from Hon. Frank Pallone, Jr., Chairman, and Hon. Greg Walden, Ranking Member, *et al.*, House Committee on Energy and Commerce, to Dr. Norman E. Sharpless, Acting Commissioner, Food and Drug Administration (June 28, 2019).

²⁸ *Tainted drugs: Ex-FDA inspector warns of dangers in U.S. meds made in China, India*, NBC News (May 10, 2019).

²⁹ *Allegations of widespread fraud raise questions about the safety of generic drugs made overseas*, CBS News (May 10, 2019); *An Indian drug maker sent records to its scrapyards before*

V. WITNESSES

The following witnesses have been invited to testify:

Mary Denigan-Macauley, Ph.D.

Director, Health Care

Government Accountability Office

Janet Woodcock, M.D.

Director, Center for Drug Evaluation and Research

U.S. Food and Drug Administration

the FDA visited, STAT News (July 17, 2019); *Carcinogens Have Infiltrated the Generic Drug Supply in the U.S.*, Bloomberg (Sept. 12, 2019).