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DRUG SAFETY

FDA Has Faced Persistent Challenges Overseeing Foreign Drug Manufacturing

Accessible Version

Statement of Mary Denigan-Macauley, Director, Health Care

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Chair Griffith, Ranking Member Castor, and Members of the Subcommittee:

I am pleased to be here today to discuss our work on the Food and Drug Administration's (FDA) oversight of drugs manufactured overseas.[1] FDA is responsible for ensuring the safety and effectiveness of all drugs marketed in the U.S., regardless of where they are produced. An increasingly global supply chain and disruptions caused by the COVID-19 pandemic have complicated FDA's oversight of the more than 4,800 establishments manufacturing drugs for the U.S. market. FDA reported that 58 percent of establishments manufacturing drugs for the U.S. market were located overseas as of October 2022. We have identified long-standing weaknesses in FDA's ability to oversee this manufacturing, an issue highlighted in our High-Risk Series since 2009.[2]

A critical element in FDA's oversight of overseas manufacturing is its inspection of foreign manufacturing establishments. My remarks today discuss our findings related to FDA's foreign drug inspection program, which we have reported on over two decades, including findings that we reported in January 2022 and in our April 2023 High-Risk Series.[3] Specifically, this statement provides observations on FDA's inspections of foreign drug manufacturers, challenges unique to conducting foreign inspections, and FDA's foreign inspection workforce.

For our prior work, we analyzed FDA inspection and workforce data, interviewed FDA staff—including drug investigators who conduct foreign inspections—and reviewed agency documents. More detailed information on our objectives, scope, and methodology for that work can be found in our January 2022 report. This statement also includes updates on the status of agency efforts to implement recommendations that we have

[1]Drugs are defined to include articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, and include components of those articles. See 21 U.S.C. §§ 321(g)(1)(B), (D). An active pharmaceutical ingredient includes any component that is intended to provide pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease. See 21 C.F.R. § 207.1 (2023). In this testimony, we refer both to drug products—drugs in their finished dosage forms—and to active pharmaceutical ingredients as "drugs." This testimony focuses on human drugs and not on most biologics, veterinary medicines, or other items or products for which FDA conducts inspections.

[2]See GAO, *High-Risk Series: Efforts Made to Achieve Progress Need to Be Maintained and Expanded to Fully Address All Areas*, GAO-23-106203 (Washington, D.C.: Apr. 20, 2023).

[3]GAO, *Drug Safety: FDA Should Take Additional Steps to Improve Its Foreign Inspection Program*, GAO-22-103611 (Washington, D.C.: Jan. 7, 2022) and GAO-23-106203.

made in our prior work. FDA has partially addressed or otherwise taken steps to respond to each of our recommendations.

We conducted the work on which this statement is based in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

FDA Inspections of Foreign Manufacturers

Over the years, we have reported on efforts by FDA to increase the number of foreign drug manufacturing establishments it inspects. FDA inspected a relatively small number of foreign establishments in fiscal year 1997 but made significant increases over the next two decades, with a peak in fiscal year 2016.[4] Most recently, after decreases from fiscal years 2016 through 2018, FDA began to increase the number of inspections of foreign establishments in fiscal year 2019, as we reported in January 2022.[5] In that same report, we found that, in fiscal year 2019, FDA conducted the largest number of foreign inspections in India and China, where more than one-third of foreign establishments supplying the U.S. market were located. However, beginning in March 2020, FDA postponed most inspections because of the COVID-19 pandemic.

In January 2022, we also reported that FDA used alternative inspection tools to maintain oversight of drug manufacturing quality while inspections were paused.[6] These tools included relying on inspections conducted by foreign regulators, requesting and reviewing records and other information, and using teleconferences, livestream video, and screen sharing of data and documents as part of a remote interactive evaluation. In a January 2021 report, we recommended that FDA fully assess these

[4]See GAO, *Food and Drug Administration: Improvements Needed in the Foreign Drug Inspection Program*, GAO/HEHS-98-21 (Washington, D.C.: Mar. 17, 1998) and *Drug Safety: FDA Has Improved Its Foreign Drug Inspection Program, but Needs to Assess the Effectiveness and Staffing of Its Foreign Offices*, GAO-17-143 (Washington, D.C., Dec. 16, 2016).

[5]GAO-22-103611.

[6]GAO-22-103611.

alternatives and others and consider their applicability for future use.[7] FDA concurred with this recommendation. See our website for more information about this recommendation and its status.[8] We will continue to monitor FDA's progress towards implementing it.

In January 2022, we noted that the postponement of inspections because of the COVID-19 pandemic led to a backlog of establishments never inspected or not inspected within 5 years—categories for which FDA considers inspections mandatory.[9] We reported that this backlog could both extend the interval between inspections and reduce the resources FDA has available for other high-priority inspections. We identified the potential for this backlog in a January 2021 report and recommended that FDA ensure that inspection plans for future fiscal years identify, analyze, and respond to the issues presented by the backlog.[10] FDA concurred with our recommendation. Since then, FDA has issued a plan for addressing this inspection backlog. See our website for more information about this recommendation.[11] We will continue to monitor FDA's progress towards implementing it.

Challenges Unique to Foreign Inspections

Since 2007, we have reported on unique challenges to conducting foreign inspections that can raise questions about their equivalence to domestic inspections.[12] Drugs manufactured overseas for the U.S. market must meet the same requirements as those manufactured in the U.S. However, in January 2022, we reported that, while domestic inspections have almost always been unannounced, FDA's practice of generally preannouncing foreign inspections up to 12 weeks in advance may have given establishments the opportunity to fix problems before the

[7]See GAO, *COVID-19: Critical Vaccine Distribution, Supply Chain, Program Integrity, and Other Challenges Require Focused Federal Attention*, GAO-21-265 (Washington, D.C.: Jan. 28, 2021).

[8]https://www.gao.gov/products/gao-21-265.

[9]GAO-22-103611.

[10]GAO-21-265.

[11]https://www.gao.gov/products/gao-21-265.

[12]GAO, *Drug Safety: Preliminary Findings Suggest Weaknesses in FDA's Program for Inspecting Foreign Drug Manufacturers*, GAO-08-224T (Washington, D.C.: Nov. 1, 2007).

inspection.[13] As a result, investigators may be less likely to see the true day-to-day operating environment of foreign establishments as compared to domestic. We also reported that FDA has relied on translators provided by the foreign establishments being inspected, which investigators told us can raise questions about the accuracy of information FDA investigators collect. We reported that FDA planned on implementing pilot programs focused on evaluating the effect of conducting unannounced inspections and using independent translation services. We recommended that FDA incorporate leading practices into the design of both its unannounced inspection and translation pilot programs. FDA concurred with our recommendations. See our website for more information about these recommendations.[14] We will continue to monitor FDA's progress towards implementing it.

FDA Foreign Inspection Workforce

Vacancies among investigators available to conduct foreign inspections represent another challenge we have identified in multiple reports. In January 2022, we reported that FDA had persistent vacancies among staff who specialize in foreign inspections.[15] This included vacancies among U.S.-based staff who conduct foreign inspections and among staff in FDA's foreign offices located in China and India.[16] We recommended that FDA fully develop tailored strategies to ensure it has a sufficient foreign inspection workforce. FDA concurred with our recommendation. As of March 2023, FDA had made progress implementing strategies in response to this recommendation. See our website for more information about this recommendation.[17] We will continue to monitor FDA's progress towards implementing it.

Following the issuance of our January 2022 report, the Consolidated Appropriations Act, 2023, included a provision for us to conduct additional

[13]GAO-22-103611.

[14]https://www.gao.gov/products/gao-22-103611.

[15]GAO-22-103611.

[16]FDA began opening offices around the world in 2008 to obtain better information on the increasing number of products coming into the U.S. from overseas, to build relationships with foreign stakeholders, and to perform inspections. China and India are the countries where FDA performs the largest number of foreign drug inspections and have foreign office staff that includes investigators to conduct drug inspections.

[17]https://www.gao.gov/products/gao-22-103611.

work on FDA's foreign drug inspection program and its use of alternative inspection tools.[18] We plan to report on all the above issues as part of that ongoing work.

Chair Griffith, Ranking Member Castor, and Members of the Subcommittee, this completes my prepared statement. I would be pleased to respond to any questions that you may have at this time.

GAO Contact and Staff Acknowledgments

If you or your staff have any questions about this testimony, please contact Mary Denigan-Macauley, Director, Health Care at (202) 512-7114 or DeniganMacauleyM@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this statement. GAO staff who made key contributions to this testimony are William Hadley (Assistant Director), Katherine L. Amoroso (Analyst-in-Charge), Sonia Chakrabarty, Taneeka Hansen, Rebecca Hendrickson, Noelle Miesfeld, Laurie Pachter, and Mandy Pusey.

[18]Pub. L. No. 117-328, § 3614, 136 Stat. 4459, 5872 (2022).

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