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DRUG SAFETY

FDA's Future Inspection Plans Need to Address Issues Presented by COVID-19 Backlog

Statement of Mary Denigan-Macauley, Director,
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GAO Highlights

Highlights of [GAO-21-409T](#), a testimony before the Subcommittee on Agriculture, Rural Development, Food and Drug Administration, and Related Agencies, Committee on Appropriations, House of Representatives

Why GAO Did This Study

The outbreak of COVID-19 has called greater attention to the United States' reliance on foreign drug manufacturers. FDA reports that 74 percent of establishments manufacturing active ingredients and 54 percent of establishments manufacturing finished drugs for the U.S. market were located overseas, as of May 2020. FDA is responsible for overseeing the safety and effectiveness of all drugs marketed in the United States, regardless of where they are produced, and it conducts inspections of both foreign and domestic manufacturing establishments.

GAO has had long-standing concerns about FDA's ability to oversee the increasingly global pharmaceutical supply chain, an issue highlighted in GAO's High Risk Series since 2009.

This statement is largely based on GAO's Drug Manufacturing Inspections enclosure in its January 2021 CARES Act report, as well as GAO's December 2019 and June 2020 testimonies. Specifically, it discusses (1) the number of FDA's foreign inspections, (2) FDA's response to the COVID-19 pandemic pause in inspections, and (3) persistent foreign inspection challenges. For that work, GAO examined FDA data from fiscal years 2012 through 2020, interviewed FDA investigators, and reviewed documents related to drug oversight during the COVID-19 pandemic, among other things.

View [GAO-21-409T](#). For more information, contact Mary Denigan-Macauley at (202) 512-7114 or deniganmacauleym@gao.gov.

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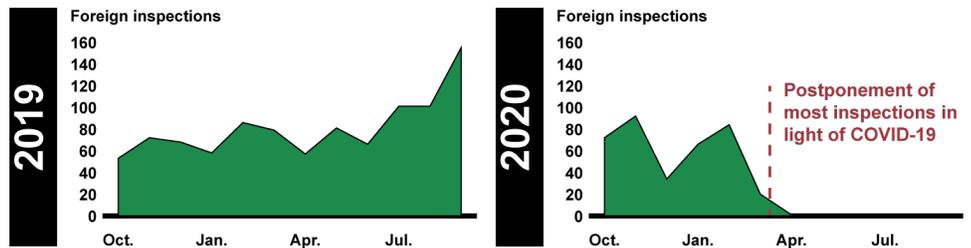
DRUG SAFETY

FDA's Future Inspection Plans Need to Address Issues Presented by COVID-19 Backlog

What GAO Found

Fiscal year 2015 was the first time that the Food and Drug Administration (FDA) conducted more inspections of foreign drug manufacturers than domestic manufacturers, with the majority conducted in China and India. However, in June 2020, GAO reported that from fiscal year 2016 through fiscal year 2018, both foreign and domestic inspections decreased, in part due to staffing vacancies. While foreign inspections increased in 2019, since March 2020, FDA has largely paused foreign and domestic inspections due to the Coronavirus Disease 2019 (COVID-19) pandemic, conducting only those deemed mission critical. In January 2021, GAO reported that FDA conducted three foreign inspections in fiscal year 2020 following the pause—significantly less than in recent years.

Number of FDA-Conducted Foreign Drug Manufacturing Establishment Inspections, Fiscal Years 2019–2020, by Month



Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-21-409T

Data table for Number of FDA-Conducted Foreign Drug Manufacturing Establishment Inspections, Fiscal Years 2019–2020, by Month

	FY 2019	FY2020
Oct.	53	72
Nov.	72	92
Dec.	68	34
Jan.	58	66
Feb.	86	84
March	79	20 /a/
Apr.	57	1
May	81	0
June	66	0
July	101	1
Aug.	101	0
Sept.	155	0

Note /a/: Early March 2020: Postponement of most inspections in light of COVID19

FDA has used alternative inspection tools to maintain some oversight of drug manufacturing quality while inspections are paused. These tools include relying on inspections conducted by foreign regulators, requesting and reviewing records and other information, and sampling and testing drugs. FDA has determined that inspections conducted by certain European regulators are equivalent to and can be substituted for an FDA inspection. Other tools provide useful information but

are not equivalent. In addition, FDA was unable to complete more than 1,000 of its planned fiscal year 2020 inspections and will likely face a backlog of inspections in future years. In January 2021, GAO recommended that FDA ensure that inspection plans for future fiscal years respond to the issues presented by the backlog and that FDA fully assess the agency's alternative inspection tools. FDA concurred with both recommendations.

Even before the COVID-19 pandemic, FDA faced persistent challenges conducting foreign inspections. GAO found in December 2019 that there continued to be vacancies among the investigators who conduct foreign inspections. GAO further found that FDA's practice of preannouncing foreign inspections up to 12 weeks in advance could give manufacturers the opportunity to fix problems ahead of the inspection and raised questions about their equivalence to domestic inspections. In light of COVID-19, FDA is now preannouncing both foreign and domestic inspections for the safety of its staff and manufacturers. GAO also found that language barriers can create challenges during foreign inspections as FDA generally relies on the establishment for translation services.

Chairman Bishop, Ranking Member Fortenberry, 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 The outbreak of Coronavirus Disease 2019 (COVID-19) has called greater attention to the United States' reliance on foreign drug manufacturers and highlighted once again the importance of ensuring a secure pharmaceutical supply chain. Like the majority of other drugs manufactured for the U.S. market, much of the manufacturing of drugs for treating COVID-19 occurs overseas.

We have had long-standing concerns about FDA's ability to oversee the increasingly global pharmaceutical supply chain, 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. The COVID-19 pandemic has further complicated FDA's foreign inspection activities. Citing concern for the safety of its employees, FDA announced in March 2020 that it was postponing most inspections of foreign manufacturing establishments. Only inspections deemed mission critical would still be considered on a case-by-case basis. In its announcement, FDA stated that it had other tools to ensure

¹Drugs are defined to include, among other things, 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, among other things, 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 (2019). In this testimony, we refer both to drug products—drugs in their finished dosage forms—and to active pharmaceutical ingredients as “drugs.”

²See GAO, *High-Risk Series: Substantial Efforts Needed to Achieve Greater Progress on High-Risk Areas*, [GAO-19-157SP](#) (Washington, D.C.: Mar. 6, 2019). See also 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: Better Data Management and More Inspections Are Needed to Strengthen FDA's Foreign Drug Inspection Program*, [GAO-08-970](#) (Washington, D.C.: Sept. 22, 2008).

the safety of the U.S. drug supply and that it was evaluating additional ways to conduct its inspections.

My remarks today primarily discuss findings on FDA's foreign drug inspection program that we previously reported in December 2019 and June 2020 testimonies, and in our Drug Manufacturing Inspections enclosure in the January 2021 CARES Act report.³ Specifically, this statement provides observations on

- (1) the number of FDA's foreign inspections,
- (2) FDA's response to the COVID-19 pandemic pause in inspections, and
- (3) persistent foreign inspection challenges.

For our prior work, we analyzed FDA data from fiscal year 2012 through fiscal year 2020 on inspections of foreign drug manufacturing establishments and interviewed FDA drug investigators. Further, we reviewed agency documents, and interviewed FDA officials related to the agency's drug oversight activities during the COVID-19 pandemic. More detailed information on our objectives, scope, and methodology for that work can be found in the two testimonies and January 2021 report.⁴ We also obtained updates from FDA on the status of inspections, as of February 2021, for this testimony statement. The work on which this statement is based was conducted 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.

³See GAO, *Drug Safety: Preliminary Findings Indicate Persistent Challenges with FDA Foreign Inspections*, [GAO-20-262T](#) (Washington, D.C.: Dec. 10, 2019); *Drug Safety: COVID-19 Complicates Already Challenged FDA Foreign Inspection Program*, [GAO-20-626T](#) (Washington, D.C.: June 2, 2020); and *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).

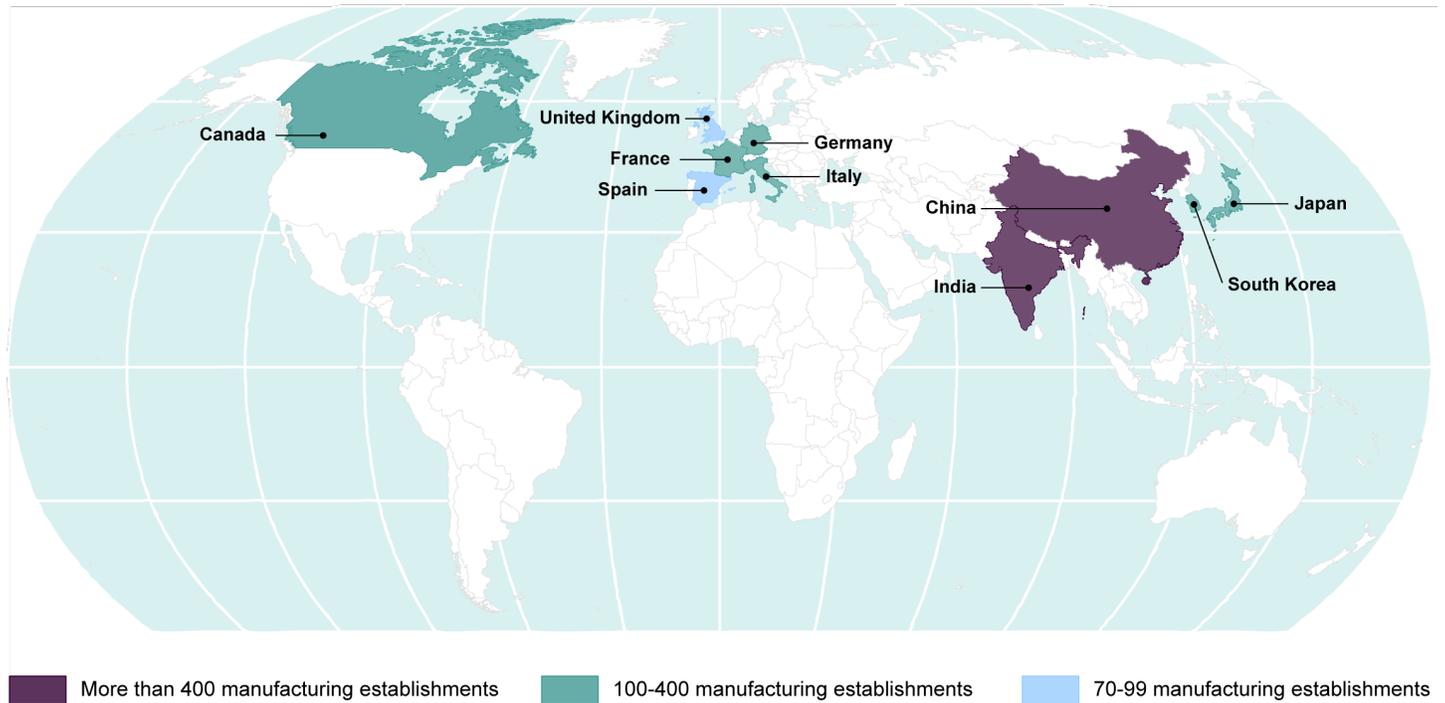
⁴[GAO-20-262T](#), [GAO-20-626T](#), and [GAO-21-265](#).

Background

Drugs sold in the United States—including active pharmaceutical ingredients and finished dosage forms—are manufactured throughout the world. According to FDA, as of May 2020, 74 percent of establishments manufacturing active pharmaceutical ingredients and 54 percent of establishments manufacturing finished drugs for the U.S. market were located overseas.⁵ As of March 2019, FDA data showed that India and China had the most manufacturing establishments shipping drugs to the United States, with about 40 percent of all foreign establishments in these two countries. (See fig. 1.)

⁵Judith A. McMeekin, Pharm.D., Associate Commissioner for Regulatory Affairs, Office of Regulatory Affairs, Mark Abdoo, Associate Commissioner for Global Policy and Strategy, and Douglas Throckmorton, M.D., Deputy Director for Regulatory Programs, Center for Drug Evaluation and Research, Food and Drug Administration, *COVID-19 and Beyond: Oversight of the FDA's Foreign Drug Manufacturing Inspection Process*, testimony before the Senate Committee on Finance, 116th Cong., 2nd sess., June 2, 2020. According to FDA, although the agency has information on the location of drug manufacturing establishments, it does not have information on the volume of drug ingredients these establishments manufacture for the U.S. market.

Figure 1: The 10 Countries with the Most Foreign Drug Establishments Shipping to the United States as of March 2019



Source: GAO analysis of Food and Drug Administration data (data); National Atlas (base map). | GAO-21-409T

Text of Figure 1: The 10 Countries with the Most Foreign Drug Establishments Shipping to the United States as of March 2019

	Countries
More than 400 manufacturing establishments	China, India
100-400 manufacturing establishments	Canada, Germany, France, Italy, Japan, South Korea
70-99 manufacturing establishments	Spain, United Kingdom

Source: GAO analysis of Food and Drug Administration data | GAO21-409T

Note: This figure includes the 10 countries with the most foreign drug establishments shipping to the United States and does not include those countries with fewer than 70 establishments. The count of foreign establishments represents the number of establishments that were known to ship or were likely to ship a drug to the United States as of March 2019. This count excludes about 380 establishments that participate in some aspect of the manufacturing process, such as sterilizers and analytical labs, but do not ship products to the United States directly. Such establishments are also subject to inspection.

FDA is responsible for overseeing the safety and effectiveness of all drugs marketed in the United States, regardless of where they are manufactured. Drugs manufactured overseas to be offered for import and sale in the United States must meet the same statutory and regulatory standards as those manufactured in this country. FDA's Center for Drug Evaluation and Research establishes standards for the safety, quality, and effectiveness of, and manufacturing processes for, over-the-counter and prescription drugs. FDA's Office of Regulatory Affairs inspects both domestic and foreign establishments to ensure that drugs are produced in conformance with applicable laws of the United States, including current good manufacturing practice (CGMP) regulations.⁶

FDA typically conducts 1) preapproval inspections before approving a new brand name or generic drug; 2) surveillance inspections periodically based on a risk analysis after a drug is marketed to ensure continued compliance with applicable laws and regulations; and 3) for-cause inspections to investigate specific issues or follow-up on previous FDA regulatory action. To prioritize establishments for surveillance inspections, FDA applies a risk-based site selection model to its catalog of establishments to identify those establishments (both domestic and foreign) that, based on the characteristics of the drugs being manufactured, pose the greatest potential public health risk should they experience a manufacturing defect. Through this process, FDA develops a ranked list of establishments for inspection.

In 1998, and again in 2008, we found that FDA inspected relatively few foreign drug manufacturing establishments and that challenges unique to foreign inspections influenced the manner in which FDA conducted such inspections.⁷ In our 2008 report we recommended that FDA increase the number of foreign inspections it conducts, and FDA agreed with our recommendation. We found in 2010, and again in 2016, that FDA was conducting more inspections of foreign establishments.⁸ In our 2008

⁶CGMPs provide for systems that assure proper design, monitoring, and control of manufacturing processes and facilities. See 21 C.F.R. pts. 210, 211, 212 (2019). FDA considers nearly all drug establishment inspections to include an assessment of CGMPs.

⁷[GAO/HEHS-98-21](#) and [GAO-08-970](#).

⁸See GAO, *Drug Safety: FDA Has Conducted More Foreign Inspections and Begun to Improve Its Information on Foreign Establishments, but More Progress Is Needed*, [GAO-10-961](#) (Washington, D.C.: Sept. 30, 2010) 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).

report we also found that, because of inaccurate information in FDA's databases, the agency did not know how many foreign drug establishments were subject to inspection.⁹ We recommended that FDA take steps to improve the accuracy of this registration information. In our 2010 and 2016 reports we found that FDA had taken steps to improve the accuracy and completeness of information in its catalog of drug establishments subject to inspection, such as using contractors to conduct site visits to verify the existence of registered foreign establishments and confirm that they manufacture the products that are recorded in U.S. import records.

FDA's Foreign Inspections Declined in Recent Years After Several Years of Increases, and Then Mostly Stopped Due to the COVID-19 Pandemic

Prior to the COVID-19 Pandemic, FDA Foreign Drug Inspections Had Increased for Several Years, but Started Trending Downward in Fiscal Year 2017

As we reported in our June 2020 testimony, the number of FDA foreign drug manufacturing establishment inspections increased from fiscal year 2012 through fiscal year 2016, surpassing the number of domestic inspections for the first time.¹⁰ However, we found that from fiscal year 2016 through 2018, both foreign and domestic inspections decreased—by about 10 percent and 13 percent, respectively. FDA officials attributed the decrease to vacancies in the number of investigators available to conduct inspections (which we discuss later in this testimony statement) and to inaccurate data used to select establishments for inspection in

⁹[GAO-08-970](#).

¹⁰[GAO-20-626T](#).

fiscal years 2017 and 2018.¹¹ FDA conducted more foreign inspections in fiscal year 2019 than in fiscal year 2018, but the total number of inspections continued to decline from the fiscal year 2016 peak.

In addition, we found that FDA continued to conduct the largest number of foreign inspections in India and China, with almost half of fiscal year 2019 foreign inspections conducted in these two countries. (See table 1.) In addition to India and China, the rest of the countries in which FDA most frequently conducted inspections has generally been the same since our 2008 report.¹²

Table 1: Total Number of FDA Foreign Drug Inspections, by Country, Fiscal Years 2012 through 2019

Country	2012	2013	2014	2015	2016	2017	2018	2019
India	140	110	114	204	207	219	252	305
China	59	74	113	127	173	165	153	167
Canada	49	51	39	52	56	72	48	70
Germany	59	60	72	68	72	69	68	69
Japan	49	28	47	31	65	46	43	51
All other countries	269	314	394	358	462	422	371	315
Total foreign	625	637	779	840	1,035	993	935	977
Total domestic	1,184	1,030	897	784	882	772	742	694
Total inspections	1,809	1,667	1,676	1,624	1,917	1,765	1,677	1,671

Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-21-409T

Note: The total number of inspections includes those conducted for preapproval, surveillance, and for-cause purposes.

FDA Postponed Most Foreign Inspections since March 2020 Due to the COVID-19 Pandemic

In our January 2021 report, we found that the total number of FDA inspections of foreign establishments was about 60 percent lower in fiscal

¹¹We reported in December 2019 that an FDA effort to inspect approximately 1,000 foreign establishments that lacked an inspection history contributed to the decline in the number of foreign inspections because a sizeable percentage of these establishments were not actually subject to inspection. Therefore, these establishments were removed from the inspection list. FDA officials told us that domestic establishments replaced these removed establishments as they were the next highest priority establishments identified through the model.

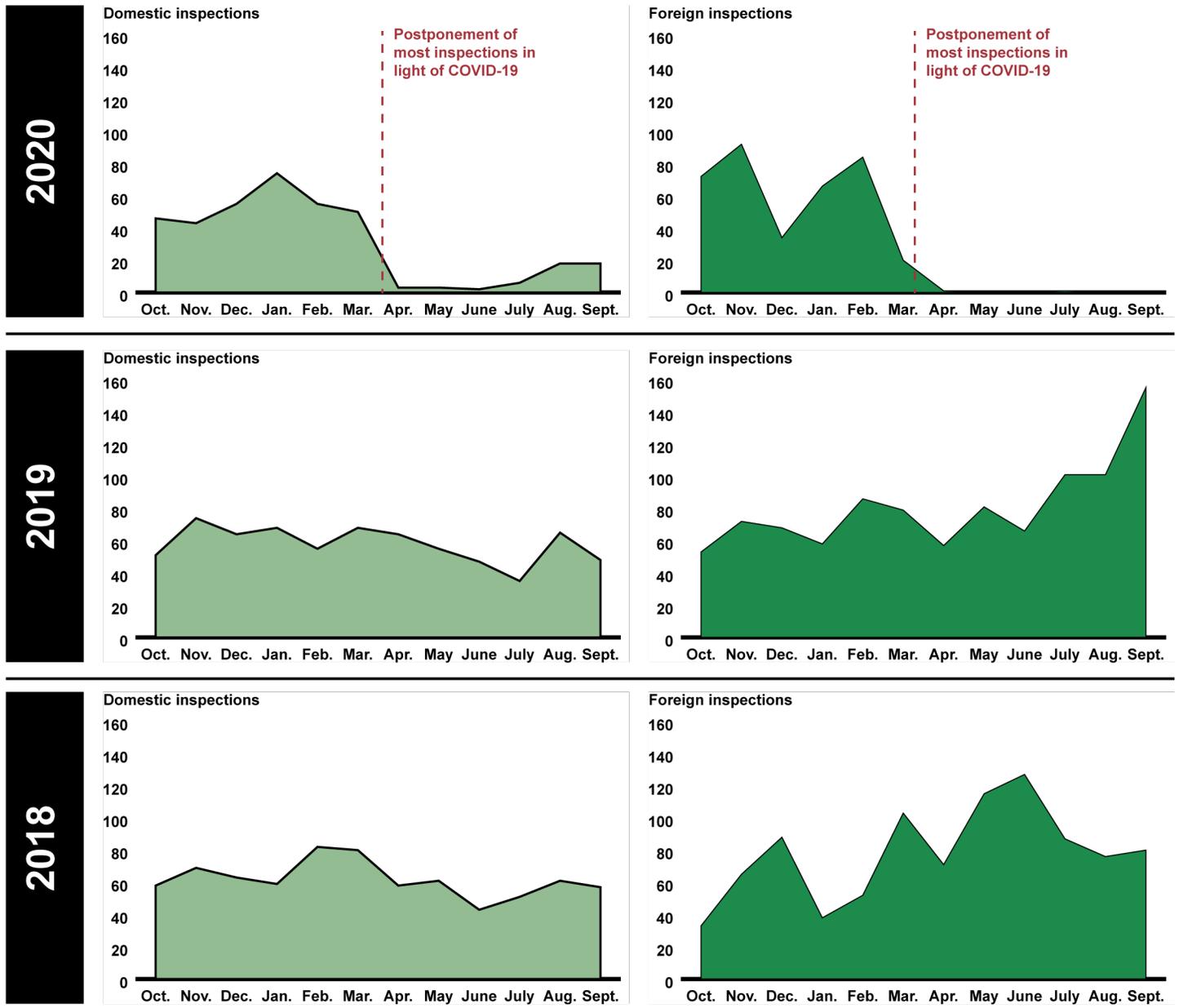
¹²[GAO-08-970](#).

year 2020 than during each of the previous 2 fiscal years.¹³ From March 2020 (when FDA announced it would temporarily not conduct any foreign or domestic inspections other than those deemed mission critical) through the end of the fiscal year, FDA conducted three foreign mission critical inspections—one each in Canada, Germany, and India. In contrast, during the same time frame in each of the prior 2 years, FDA conducted more than 600 foreign inspections. FDA’s domestic inspection activities also decreased significantly in 2020, though FDA conducted more domestic inspections than foreign inspections during the pandemic—52 from March through October 1, 2020.¹⁴ (See fig. 2.)

¹³[GAO-21-265](#).

¹⁴In July 2020, FDA announced that it planned to resume domestic inspections, contingent on a rating system that incorporates information on COVID-19 infection trends in a geographic area. Depending on an area’s rating, FDA’s inspection activities were to range from mission critical inspections only to the resumption of all inspections. According to FDA’s area rating data, as of December 3, 2020, conditions were appropriate for conducting routine surveillance inspections in 49 U.S. counties, with regulatory activity limited to mission critical inspections only in the more than 3,000 remaining counties.

Figure 2: Domestic and Foreign Drug Manufacturing Establishment Inspections Conducted by FDA, Fiscal Years 2018-2020, by Month



Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-21-409T

Chairman Bishop, Ranking Member Fortenberry, and Members of the Subcommittee:

Data table for Figure 2: Domestic and Foreign Drug Manufacturing Establishment Inspections Conducted by FDA, Fiscal Years 2018-2020, by Month

	2020		2019		2018	
	Domestic	Foreign	Domestic	Foreign	Domestic	Foreign
Oct.	46	72	51	53	58	33
Nov.	43	92	74	72	69	65
Dec.	55	34	64	68	63	88
Jan.	74	66	68	58	59	38
Feb.	55	84	55	86	82	52
Mar. /a/, /b/	50	20	68	79	80	103
Apr.	3	1	64	57	58	71
May	3	0	55	81	61	115
Jun.	2	0	47	66	43	127
Jul.	6	1	35	101	51	87
Aug.	18	0	65	101	61	76
Sept.	18	0	48	155	57	80

Note /a/: Mid March 2020: Postponement of most inspections in light of COVID19

Note /b/: Early March 2020: Postponement of most inspections in light of COVID19

As of February 2021, FDA had begun conducting some foreign inspections, but had not set a date for resuming routine foreign surveillance inspections in all countries. FDA said it continues to monitor the global situation and remains in contact with foreign regulators in individual countries to inform FDA’s assessment of the feasibility of resuming foreign surveillance inspections as conditions improve. FDA reported that, in October 2020, staff in the agency’s China office had begun conducting inspections in China. According to FDA, between October 26, 2020, and January 14, 2021, these staff had conducted nine preapproval inspections, but no surveillance inspections. FDA officials told us that staff in the agency’s India office began conducting inspections in India in January 2021 and had conducted two inspections as of February 25, 2021.

COVID-19 Pandemic Has Forced FDA to Rely on Alternatives to Inspections and the Agency

Will Likely Face an Inspection Backlog in the Future

FDA Has Relied on Alternative Tools in Lieu of Inspections During the Pandemic, but They Are Not a Comprehensive or Long-Term Substitute

In January 2021, we reported that FDA used alternative tools to oversee drug manufacturing quality while inspections have been paused, including the use of inspections conducted by foreign regulators, requesting and reviewing records and other information, and sampling and testing drugs.¹⁵ These tools provide useful information, but are not all considered equivalent to an inspection conducted by FDA.

Inspections conducted by some foreign regulators, when available, can substitute for FDA inspections. In light of the COVID-19 pause in inspections, FDA expanded the use of the mutual recognition agreement it has with the European Union to include inspections conducted outside of Europe by European regulators as a full substitute for FDA inspections.¹⁶ However, this only applies to certain European regulators whose inspections FDA has found to be equivalent to its own.¹⁷ Inspections from other select countries (such as Australia and Japan) can be used for oversight purposes, but are not considered by FDA as substitutes for an FDA inspection.

FDA can request and review records and other information to substitute for FDA preapproval inspections in certain circumstances. During the COVID-19 pandemic, FDA substantially increased use of its authority to request that establishments provide records in advance of or in lieu of an inspection, requesting records from

¹⁵[GAO-21-265](#).

¹⁶For the purposes of this report, when we refer to European regulators, we are referring to the 27 European regulators that are part of the mutual recognition agreement with FDA, plus the United Kingdom, which has a separate mutual recognition agreement.

¹⁷Inspections conducted outside of Europe by 19 of these 28 regulators can be substituted for an FDA inspection as of January 2021.

establishments in China, India, and the United States, among others.¹⁸ In certain cases, FDA can substitute the review of records and other information for conducting a preapproval inspection, but such information alone cannot be used as a substitute for an FDA surveillance inspection.

Sampling and testing are not a substitute for an inspection. In response to the COVID-19 pandemic, FDA has adjusted the tool it uses to automatically screen drug imports to help FDA determine where to focus its sampling at the U.S. border, according to FDA officials. However, sampling and testing alone do not specifically confirm adherence to quality standards and thus cannot fully replace an FDA inspection.

Alternative tools allowed FDA to take some regulatory action against foreign drug manufacturing establishments with manufacturing deficiencies during the inspection pause. From March 1, 2020, to December 1, 2020, FDA placed 64 foreign establishments on import alert for the following reasons:

- one based on issues identified in a foreign regulator inspection report;
- nine for refusing FDA records requests or for deficiencies identified during the agency's review of records provided in response to an FDA records request; and
- 54 based on issues identified from sampling. In addition, in January, 2021, FDA placed all alcohol-based hand sanitizers from Mexico on import alert because it identified a high proportion of methanol contamination in these drug products.¹⁹

¹⁸See 21 U.S.C. § 374(a)(4). Prior to the COVID-19 pandemic, FDA used this authority in a more limited capacity to oversee 10 establishments that the agency would not routinely inspect because of travel warnings. In fiscal year 2019, for example, this included establishments in Colombia, Egypt, Israel, Mexico, Pakistan, and Saudi Arabia, among others.

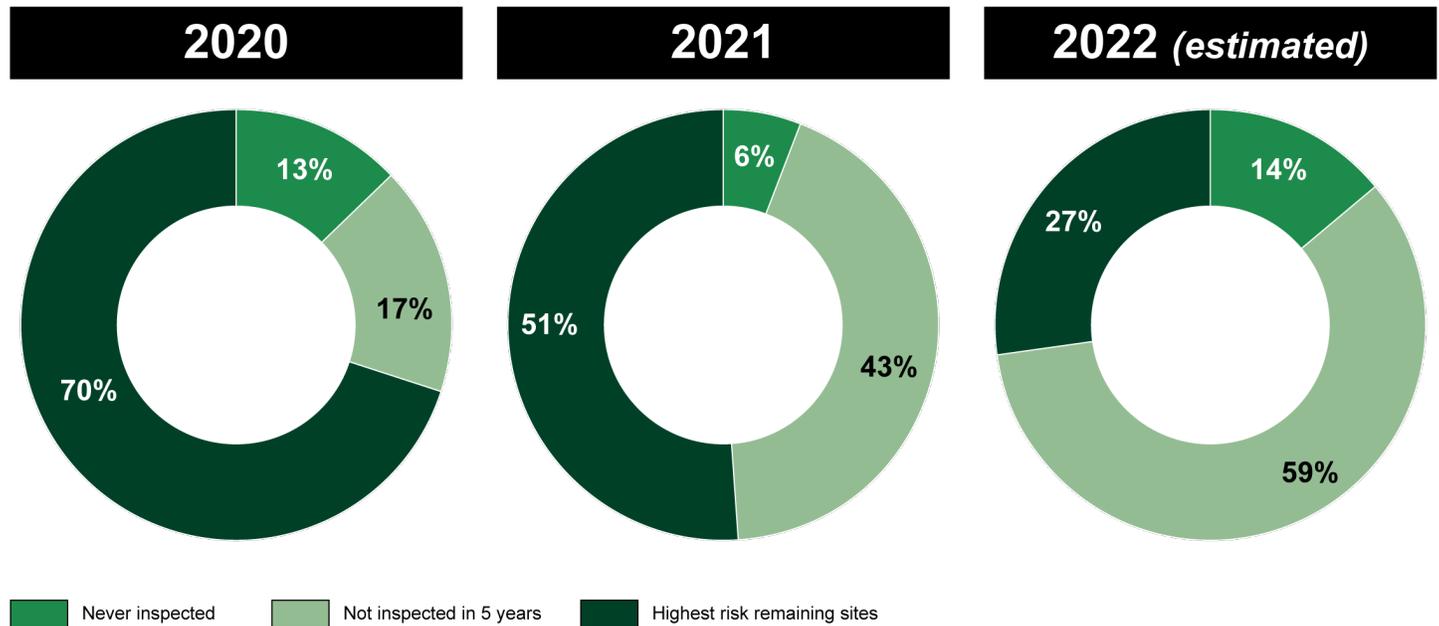
¹⁹Food and Drug Administration, *FDA Takes Action to Place All Alcohol-Based Hand Sanitizers from Mexico on Import Alert to Help Prevent Entry of Violative and Potentially Dangerous Products into U.S., Protect U.S. Consumers*, accessed February 22, 2021, <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-takes-action-place-all-alcohol-based-hand-sanitizers-mexico-import>.

FDA May Face an Inspection Backlog and Drug Approval Challenges as a Result of the Pause in Inspections

As a result of the pause in inspections during the COVID-19 pandemic, FDA was unable to complete more than 1,000 of its planned fiscal year 2020 surveillance inspections. In selecting establishments for surveillance inspection each year, FDA prioritizes, as mandatory, those establishments never inspected or not inspected within 5 years. According to FDA officials, such establishments represent significant risks to drug quality, but the extent of these risks is uncertain.

In order to achieve the agency's strategic goal of risk-driven surveillance inspections, with any resources remaining after mandatory inspections, FDA seeks to maximize the number of inspections of establishments prioritized by its risk-based site selection model each year. However, due to the ongoing COVID-19 pandemic, domestic inspections continue to be limited and the vast majority of foreign inspections continue to be postponed, as of February 2021. If inspections continue to be postponed, the backlog of mandatory inspections this will create could both extend the maximum interval between inspections beyond FDA's 5-year policy and reduce the resources available in fiscal year 2022 for inspecting the other highest priority establishments identified by its model (see fig. 3).

Figure 3: Potential Effect of COVID-19 Backlog on Distribution of FDA’s Risk-Based Surveillance Inspections over Time if Fiscal Year 2021 Inspections Continue to be Postponed



Source: GAO analysis of Food and Drug Administration (FDA) information. | GAO-21-409T

Data table for Figure 3: Potential Effect of COVID-19 Backlog on Distribution of FDA’s Risk-Based Surveillance Inspections over Time if Fiscal Year 2021 Inspections Continue to be Postponed

	2020	2021	2022 (estimated)
Never impacted	13%	6%	14%
Not impacted in 5 years	17%	43%	59%
Highest risk remaining sites	70%	51%	27%

Source: GAO analysis of FDA information | GAO-21-409T

Note: Fiscal year 2020 and fiscal year 2021 percentages are based on the list of establishments prioritized for inspection, which is issued in July of each year for the following fiscal year. Fiscal year 2022 percentages are our estimates based on the following assumptions: (1) that FDA will not conduct any inspections of the establishments it has never inspected or for which the inspection is outdated in fiscal year 2021 and so all of those inspections will roll over to fiscal year 2022; (2) that there will be additional establishments that have never been inspected or for which the FDA inspection is outdated (based on the average number of never and outdated inspections FDA identified as mandatory in the last 2 years); and (3) FDA’s inspection capacity of 1,500 surveillance inspections per year will not change. If FDA is able to resume surveillance inspections in fiscal year 2021 or use alternative tools as substitutes for FDA inspections, then it may be able to complete a larger number of inspections of establishments, including those that have never been inspected, that have not been inspected in 5 years, or those that are the highest risk remaining sites than is reflected in our estimates and this figure.

Therefore, in January 2021, we recommended that FDA, as inspection plans for future fiscal years are developed, ensure that such plans identify, analyze, and respond to the issues presented by the backlog of inspections that could jeopardize the goal of risk-driven inspections.²⁰ FDA concurred with the recommendation and stated that it was actively tracking the list of sites that need to be inspected, and noted that the size of the backlog will depend on the extent to which alternative inspection tools are used.

The need to conduct preapproval inspections represents another challenge for FDA. As of November 2020, FDA officials told us that the agency had not experienced a significant effect on approval decisions due to the COVID-19 inspection pause. FDA notes that it is continuing its work to review and approve drug applications and that, as of October 2020, the agency had approved more than 600 brand name and generic drug applications in 2020. Representatives from three associations representing drug manufacturers stated that, because preapproval inspections may happen months before an application is approved, the postponement of inspections has not had a significant effect on FDA's ability to make drug approval decisions yet. However, two of these associations noted that the longer inspections are postponed, the more likely the inability to conduct a preapproval inspection could create larger challenges for FDA's ability to make approval decisions. FDA officials said that they are expanding the use of alternative tools to mitigate the effect of the pandemic on the agency's ability to make approval decisions when inspections are not possible.

FDA Has Not Fully Assessed How Its Alternative Tools or Others Can Be Used to Support Its Current and Future Drug Oversight Activities

In January 2021 we reported that, with the exception of European regulator inspection reports, FDA has not yet fully assessed how its alternative tools can be used to supplement its regular inspection activities, or help meet its drug oversight objectives when inspections are not possible in the future.²¹ We also noted that there may be additional tools for the agency to utilize when inspections are not possible. According to FDA officials, the agency is in the process of assessing the

²⁰[GAO-21-265](#).

²¹[GAO-21-265](#).

potential use, including its authority to use, other tools to serve as supplements to FDA inspections. These include using remote video and other remote and live interactions with establishment staff and records to evaluate drug manufacturing operations.

We recommended that FDA fully assess its alternative inspection tools and consider whether these tools or others could provide the information needed to supplement regular inspection activities or help meet its drug oversight objectives when inspections are not possible in the future. FDA concurred with the recommendation and stated that it would continue to evaluate these alternative tools and that the resulting information will help it determine how such tools can be used to streamline and supplement regular inspection activities and to prioritize inspections when normal inspection operations are not possible. FDA stated that as it pursues continued process improvements, the agency will incorporate this recommendation in its ongoing assessment of these alternative inspection tools.

FDA Faced Persistent Challenges to Conducting Foreign Inspections Prior to the COVID-19 Pandemic

Prior to COVID-19, FDA faced challenges to conducting its foreign inspections. Many of these challenges—including inspection staff vacancies, preannouncing inspections, and translation barriers—are longstanding issues and have been discussed in detail in our prior reports.

Foreign inspection staff vacancies. In December 2019, we found that FDA faced challenges filling staff vacancies in its foreign inspection workforce, and FDA officials said these vacancies contributed to the decline in inspections.²² At that time, FDA officials told us that the agency was trying to fill its vacancies. However, officials have also told us that new investigators are not typically used for foreign inspections until they have been with the agency for 2 to 3 years. In June 2020, FDA testified that it intended to fill all investigator vacancies in 2020, but as of December 2020, investigator vacancies remained.²³ We plan to review

²²[GAO-20-262T](#).

²³McMeekin, Abdo, and Throckmorton, *COVID-19 and Beyond*.

this issue as part of our ongoing examination of FDA's foreign drug inspection program.

Preannouncing inspections. In December 2019, we found that, prior to COVID-19, there were differences in the amount of notice FDA generally gives to foreign and domestic establishments because of challenges inherent in conducting foreign inspections, and that this raises concerns regarding their equivalence to domestic inspections.²⁴ Prior to COVID-19, almost all domestic inspections were unannounced, whereas foreign inspections were generally preannounced, which may give establishments the opportunity to fix problems before the investigator arrives. FDA testified in June 2020 that the agency usually announces foreign surveillance inspections in advance, partly due to logistics such as planning travel, arranging access to facilities, and securing visas, and partly to avoid problems given the high costs of conducting foreign inspections.²⁵

In our June 2020 testimony, we reported that FDA does conduct some unannounced foreign inspections, particularly if the investigators conducting the inspection are based in FDA's foreign offices.²⁶ FDA officials told us that the agency does not have data on the frequency with which foreign drug inspections are unannounced, nor the extent to which the amount of notice provided to foreign establishments varies. According to FDA officials, this is because FDA does not have a data field in its database to systematically track this information.²⁷ However, the officials estimated that the agency generally gives 12 weeks of notice to establishments that investigators are coming when investigators are traveling from the United States. While investigators in FDA's China and India offices do conduct unannounced or short-notice inspections, these staff do not perform most of the inspections in these countries. (See table 2.)

²⁴[GAO-20-262T](#).

²⁵McMeekin, Abdoo, and Throckmorton, *COVID-19 and Beyond*.

²⁶[GAO-20-626T](#).

²⁷In June 2020, we reported that FDA planned to add a new variable to its data to identify preannounced and unannounced inspections, according to FDA officials.

Chairman Bishop, Ranking Member Fortenberry, and Members of the Subcommittee:

Table 2: FDA Estimates of the Amount of Notice It Provides to Foreign Drug Establishments Prior to Inspection, by Investigator Type, and the Percentage of Inspections in Which These Investigator Types Are Involved, Fiscal Year 2018

Type of investigator	Amount of notice provided	Percentage of inspections involving this investigator type in fiscal year 2018 ^a
China office investigator	Announcement: 0-5 days FDA officials stated that investigators based in FDA’s China office will announce surveillance inspections (those related to drugs already on the U.S. market) to drug establishments 5 business days in advance of an inspection. According to FDA officials, for-cause inspections (those conducted in response to specific issues or concerns) conducted by investigators based in the China office are unannounced, meaning that they are not announced to the drug establishments in advance.	Involved in 27 percent of total number of inspections in China
India office investigator	Announcement: 0-5 days FDA officials stated that investigators based in FDA’s India office will announce inspections to drug establishments 3 to 5 days in advance of an inspection and can conduct short-notice inspections that are announced 30 minutes before the inspection.	Involved in 10 percent of total number of inspections in India
U.S.-based investigator (Including dedicated foreign drug cadre)	Announcement: generally 12 weeks FDA officials said that the agency generally announces foreign inspections conducted by domestically based investigators about 12 weeks in advance.	Involved in: <ul style="list-style-type: none"> 73 percent of total number of inspections in China 90 percent of total number of inspections in India 100 percent of total number of inspections in other foreign countries

Source: Interviews with Food and Drug Administration (FDA) officials and GAO analysis of FDA data. | GAO-21-409T

^aThese percentages add up to over 100 percent as some inspections may involve more than one type of investigator.

In our January 2021 report we noted that of FDA’s fiscal year 2021 appropriation, \$3.5 million is to be used for foreign unannounced drug inspection pilots.²⁸ In February 2021, officials told us that FDA is developing plans to implement a pilot. However, they said that in light of the pandemic, FDA was preannouncing all domestic and foreign

²⁸According to the Joint Explanatory Statement accompanying the Consolidated Appropriations Act, 2021, \$3.5 million of FDA’s fiscal year 2021 appropriation is to be used for foreign unannounced human drug inspection pilots. See Explanatory Statement, 166 Cong. Rec. H7891 (daily ed. Dec. 21, 2020) (statement of Rep. Lowey); Pub. L. No. 16-260, § 4, 134 Stat. 1182, 1185 (2020) (clarifying that the explanatory statement regarding this act shall have the same effect as a joint explanatory statement with respect to the allocation of funds and implementation of certain divisions).

inspections for the foreseeable future to help assure the safety of inspection staff and establishment employees.

Language barriers. In December 2019 we found that language barriers continue to be a challenge to conducting foreign inspections.²⁹ Foreign investigators generally rely on the drug establishment to provide translation services, when needed. These services might be provided by an English-speaking employee of the establishment being inspected, or an external translator hired by the establishment. Investigators said that there can be uncertainties regarding the accuracy of the information being translated, particularly when investigators rely on the translation provided by an employee of the establishment being inspected. It can also take longer to complete typical inspection-related activities if the investigator needs to rely on translation services. In January 2021 we found that FDA also relies on drug establishments to translate the records and other information that FDA has the authority to request in advance of or in lieu of an inspection, an authority FDA has increased its use of during the COVID-19 pandemic.³⁰ According to FDA policy, if translated, the manufacturer should provide verification that the translation of the records is complete and accurate, and copies of the original records should also be included. Nevertheless, language barriers continue to present risks for FDA—an area we plan to review as part of our ongoing examination of FDA’s foreign drug inspection program.

We also reported in our December 2019 testimony that the overseas travel schedule can present challenges for FDA’s domestically based investigators, who conduct the majority of foreign inspections. For example, there is little flexibility for domestically based investigators to extend a foreign inspection because their inspections are scheduled back-to-back in 3-week trips—extending one inspection would limit the time on other scheduled inspections. Domestically based investigators also faced challenges meeting post-inspection reporting requirements, especially if serious deficiencies are identified during the inspection.³¹

In conclusion, foreign manufacturing establishments continue to be a critical source of drugs for millions of Americans, and FDA inspections are a key tool to ensure the quality of these drugs. Over the years since we

²⁹[GAO-20-262T](#). We previously reported language barriers as a challenge to conducting foreign inspections in our 2008 report ([GAO-08-970](#)).

³⁰[GAO-21-265](#).

³¹[GAO-20-262T](#).

first examined this issue, FDA has made significant changes to adapt to the globalization of the pharmaceutical supply chain and has greatly increased the number of inspections it conducts of foreign establishments. However, we found in December 2019 that the agency faced many of the same challenges overseeing foreign establishments that we identified over the last two decades. Subsequently, the outbreak of COVID-19 has added a layer of complexity. Therefore, it will be important for FDA to utilize lessons that it has learned during the COVID-19 pandemic to improve its foreign drug inspection program, including efforts to identify alternative mechanisms to satisfy foreign inspection requirements and plans to address its growing backlog of inspections.

Chairman Bishop, Ranking Member Fortenberry, 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); George Bogart; Zhi Boon; Kaitlin Farquharson; Cathleen Hamann; Derry Henrick; John Lalomio; Laurie Pachter; Vikki Porter; and Dan Ries.

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