



## Testimony

Before the Subcommittee on Oversight  
and Investigations, Committee on  
Energy and Commerce, House of  
Representatives

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# DRUG SAFETY

## Preliminary Findings Indicate Persistent Challenges with FDA Foreign Inspections

### Accessible Version

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# GAO Highlights

Highlights of [GAO-20-262T](#), a testimony before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives

## Why GAO Did This Study

More than 60 percent of establishments manufacturing drugs for the U.S. market were located overseas in fiscal year 2018. FDA has estimated that about 40 percent of finished drugs and 80 percent of active drug ingredients are manufactured overseas. FDA is responsible for overseeing the safety and effectiveness of all drugs marketed in the United States, regardless of where they are produced and conducts inspections of both foreign and domestic drug manufacturing establishments. GAO has had long-standing concerns about FDA's ability to oversee the increasingly global supply chain, an issue highlighted in GAO's High Risk Series for the last 10 years. GAO recommended in 2008 (GAO-08-970) that FDA increase the number of inspections of foreign drug establishments. GAO found in 2010 (GAO-10-961) and 2016 (GAO-17-143) that FDA was conducting more of these foreign drug inspections, but GAO also reported that FDA may have never inspected many establishments manufacturing drugs for the U.S. market.

This statement is based on ongoing work and provides preliminary GAO observations on 1) the number of foreign inspections FDA has conducted, 2) inspection staffing levels, and 3) challenges unique to foreign inspections. For this work, GAO examined FDA data, visited FDA foreign offices in China and India, and interviewed drug investigators based in these offices and in the United States.

## What GAO Recommends

GAO will continue to assess these issues as part of ongoing work, and make recommendations as appropriate.

View [GAO-20-262T](#). For more information, contact Mary Denigan-Macauley at (202) 512-7114 or [deniganmacauleym@gao.gov](mailto:deniganmacauleym@gao.gov).

December 10, 2019

## DRUG SAFETY

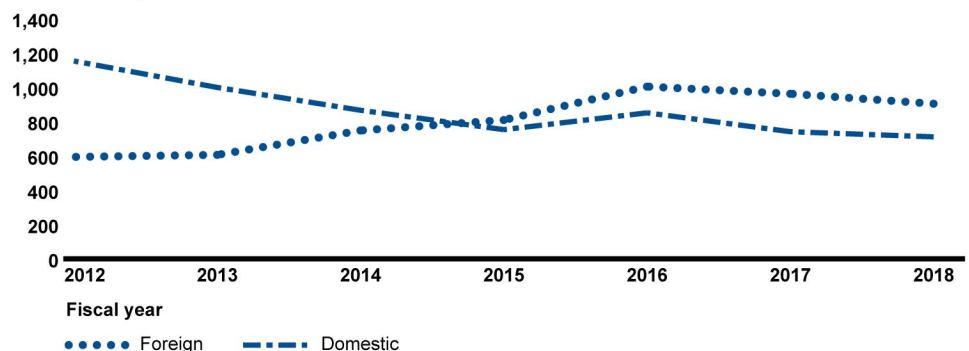
### Preliminary Findings Indicate Persistent Challenges with FDA Foreign Inspections

## What GAO Found

GAO's preliminary analysis of Food and Drug Administration (FDA) data shows that from fiscal year 2012 through 2016, the number of foreign drug manufacturing establishment inspections increased. From fiscal year 2016 through 2018, both foreign and domestic inspections decreased—by about 10 percent and 13 percent, respectively. However, the total number of foreign inspections surpassed the number of domestic inspections in 2015, and a growing percentage of FDA's foreign inspections (43 percent in 2018) were conducted in China and India, where most establishments that ship drugs to the United States were located. FDA officials attributed the decline, in part, to vacancies among investigators available to conduct inspections. GAO previously noted the vital role that inspections play in FDA's oversight of foreign establishments.

#### FDA Inspections of Foreign and Domestic Drug Establishments, Fiscal Year 2012 through 2018

Number of inspections



Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-20-262T

#### Accessible Data for FDA Inspections of Foreign and Domestic Drug Establishments, Fiscal Year 2012 through 2018

| Fiscal year | Number of inspections : (Foreign) | Number of inspections: (Domestic) |
|-------------|-----------------------------------|-----------------------------------|
| 2012        | 625                               | 1184                              |
| 2013        | 637                               | 1030                              |
| 2014        | 779                               | 897                               |
| 2015        | 840                               | 784                               |
| 2016        | 1035                              | 882                               |
| 2017        | 993                               | 772                               |
| 2018        | 935                               | 742                               |

FDA has vacancies among each of the groups of investigators who conduct foreign inspections. FDA had 190 investigators in the United States who conduct

the majority of foreign inspections, but an additional 58 positions were vacant. FDA was in the process of filling 26 of these vacancies, with 32 remaining. However, according to FDA officials, it could be 2 to 3 years before new staff are experienced enough to conduct foreign inspections. FDA also faces persistent vacancies among investigators in its foreign offices.

FDA investigators identified persistent challenges conducting foreign inspections, raising questions about the equivalence of foreign to domestic inspections. For example, while domestic inspections are almost always unannounced, FDA's practice of preannouncing foreign inspections up to 12 weeks in advance may give manufacturers the opportunity to fix problems. Investigators from FDA's China and India offices do conduct some unannounced inspections, but they are involved in a small percentage of inspections in these countries (27 percent and 10 percent, respectively). Further, FDA continues to rely on translators provided by the foreign establishments being inspected, which investigators said can raise questions about the accuracy of information FDA investigators collect.

Chair DeGette, Ranking Member Guthrie, and Members of the Subcommittee:

I am pleased to be here today to discuss our ongoing work on the Food and Drug Administration's (FDA) oversight of drugs manufactured overseas.<sup>1</sup> More than 60 percent of establishments manufacturing drugs—including brand-name, generic, and over-the-counter finished drugs and their active ingredients—for the U.S. market were located overseas in fiscal year 2018.<sup>2</sup> FDA is responsible for overseeing the safety and effectiveness of all drugs marketed in the United States, regardless of where they are manufactured. FDA conducts several types of inspections of foreign manufacturing establishments, as testing a drug

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<sup>1</sup>Drugs 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.” Our ongoing work focuses on human drugs and not on most biologics, veterinary medicines, or other items or products for which FDA conducts inspections. (Biologics are materials, such as viruses, therapeutic sera, toxins, antitoxins, vaccines or analogous products, to prevent, treat, or cure human diseases or injuries, and are derived from natural sources, such as humans, animals, and microorganisms. See 42 U.S.C. § 262(i); 21 C.F.R. § 600.3(h) (2019).)

<sup>2</sup>U.S. Food and Drug Administration, Center for Drug Evaluation and Research, Office of Pharmaceutical Quality, *Report on the State of Pharmaceutical Quality: Assuring quality medicines are available for the American public*, (Silver Spring, Md.: May 2019), 3. We previously reported that nearly 40 percent of finished drugs and approximately 80 percent of active ingredients are manufactured overseas, according to FDA. See GAO, *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).

FDA defines manufacturing to include the manufacture, preparation, propagation, compounding, or processing of a drug. 21 C.F.R. § 207.1 (2019). FDA defines an establishment as a place of business under one management at one general physical location. 21 C.F.R. § 207.1 (2019).

at the U.S. border cannot reliably determine whether the drug was manufactured in compliance with FDA regulations.<sup>3</sup>

We have had long-standing concerns about FDA's ability to oversee the increasingly global supply chain, an issue highlighted in our High Risk Series.<sup>4</sup> In 1998, and again in 2008, we found that FDA inspected relatively few foreign drug manufacturing establishments—an estimated 8 percent of those subject to inspection for our 2008 report—and that challenges unique to foreign inspections influenced the manner in which FDA conducted such inspections.<sup>5</sup> In our 2008 report we recommended that FDA increase the number of foreign inspections it conducts, and FDA agreed with our recommendation.<sup>6</sup> We found in 2010, and again in 2016, that FDA was conducting more inspections of foreign establishments (inspecting about 11 percent and 21 percent of those subject to inspection for our 2010 and 2016 reports, respectively). However, we also reported that many establishments manufacturing drugs for the U.S. market may never have been inspected by FDA.<sup>7</sup> In addition, in the summer of 2018, FDA began announcing recalls of blood pressure medications manufactured overseas and tainted with a potential

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<sup>3</sup>Establishments in foreign countries engaged in the manufacture, preparation, propagation, compounding or processing of drugs for importation into the United States are required to register annually with FDA. 21 U.S.C. § 360(i)(1). This registration information, along with registration information from domestic establishments, is maintained in FDA's drug registration database.

<sup>4</sup>See GAO, *High-Risk Series: Substantial Efforts Needed to Achieve Greater Progress on High-Risk Areas*, [GAO-19-157SP](#) (Washington, D.C.: Mar. 6, 2019).

<sup>5</sup>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: 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).

<sup>6</sup>See [GAO-08-970](#), 43. Following our recommendation, FDA started conducting more foreign inspections and changed how it selects establishments for inspection to ensure that foreign establishments be inspected at a frequency comparable to domestic establishments with similar characteristics.

<sup>7</sup>See 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 [GAO-17-143](#).

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carcinogen, raising further questions about FDA's oversight of foreign-manufactured drugs.<sup>8</sup>

My testimony today is based on our ongoing examination of FDA's foreign drug inspection program and provides preliminary observations on

1. the number of FDA's foreign inspections,
2. inspection staffing levels, and
3. any challenges unique to foreign inspections.

To develop our preliminary observations, we analyzed data from FDA's Field Accomplishments and Compliance Tracking System, which contains information on inspections of drug manufacturing establishments. Specifically, we examined FDA data from fiscal year 2012 through fiscal year 2018 to determine: (1) the number of foreign and domestic inspections conducted by FDA, (2) the type of inspections, (3) the country in which the inspections took place, and (4) inspection results.<sup>9</sup> This date range was selected to allow for an analysis of trends over time through 2018, the last full fiscal year of data available when we began our analysis. To assess the reliability of these data, we reviewed related documentation, interviewed knowledgeable agency officials, conducted electronic data testing for missing data and outliers, and compared the data to published information from the same database. On the basis of these steps, we found these data sufficiently reliable for the purposes of our reporting objectives. We also visited FDA's foreign offices in China and in India, the countries where FDA performs the largest number of foreign drug inspections and which are FDA's offices that have drug investigators who conduct inspections—a unique aspect of these offices. At these two offices we interviewed a nongeneralizable selection of the

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<sup>8</sup>Food and Drug Administration, *FDA Updates and Press Announcements on Angiotensin II Receptor Blocker (ARB) Recalls (Valsartan, Losartan, and Irbesartan)*, accessed December 1, 2019, <https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-angiotensin-ii-receptor-blocker-arb-recalls-valsartan-losartan>

<sup>9</sup>Our analysis focused on inspections related to the drug approval process or inspections conducted to determine an establishment's ongoing compliance with laws and regulations in the manufacture of human drugs already marketed in the United States. FDA conducts additional drug inspections that are beyond the scope of our review, such as to determine whether drug manufacturers are submitting to FDA, as required, complete and accurate data on adverse drug experiences associated with marketed drugs, inspections conducted for the President's Emergency Plan for AIDS Relief, and inspections of clinical trial sites, compounding pharmacies, and medical gas manufacturers.

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six FDA drug investigators available in the offices at the time of our visits about their inspection efforts. (We plan to interview the remaining drug investigators deployed to these offices as part of our ongoing work.) While in those countries, we also accompanied investigators to two drug manufacturing establishments to observe inspection procedures. We also interviewed all 12 members of FDA's calendar year 2019 cadre of investigators who are based in the United States but exclusively conduct foreign drug inspections. Finally, we reviewed information from FDA on their inspection staffing levels since our last report in 2016.

The ongoing work on which this statement is based is being 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.

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## Background

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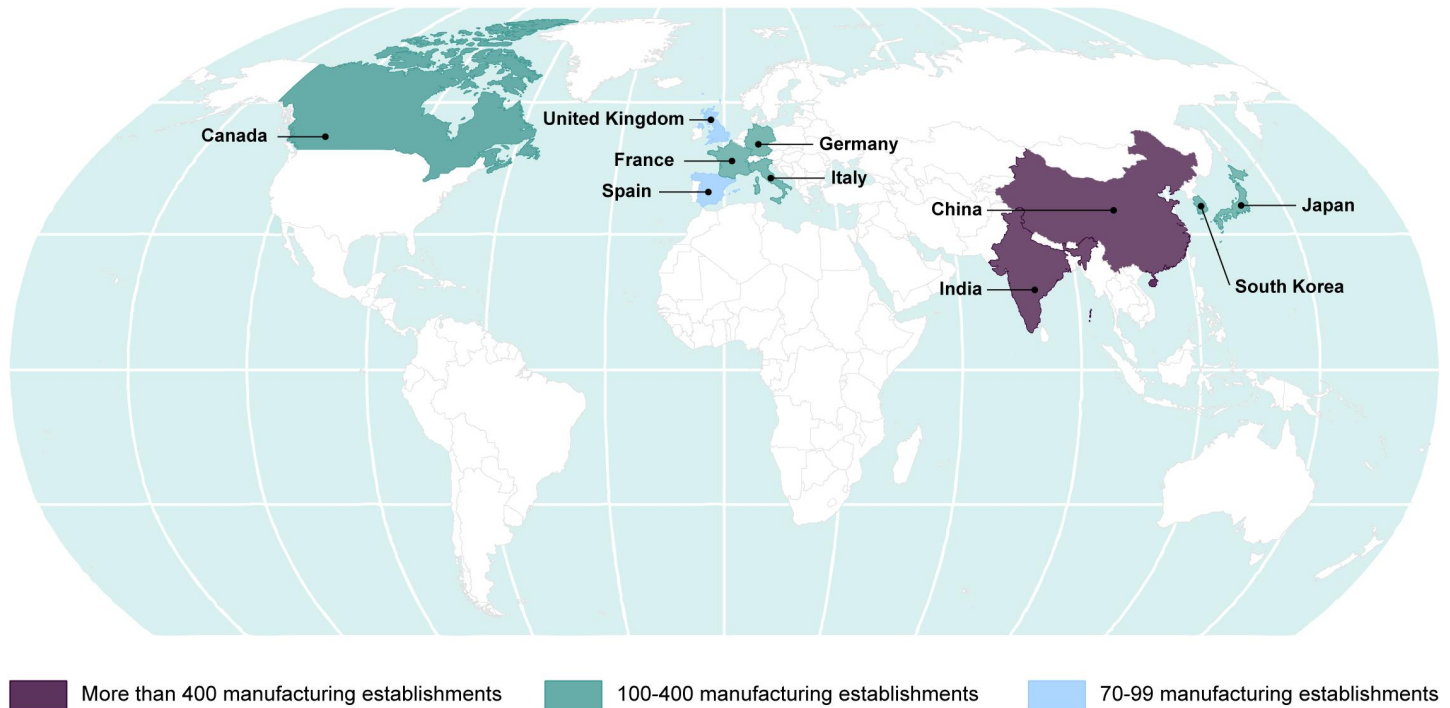
### Globalization of Drug Manufacturing

Drugs sold in the United States—including active pharmaceutical ingredients and finished dosage forms—are manufactured throughout the world. According to a May 2019 FDA report, in fiscal year 2018 about 40 percent of establishments manufacturing drugs for the U.S. market were located domestically and more than 60 percent of establishments manufacturing for the U.S. market were located overseas.<sup>10</sup> As of March 2019, FDA data show 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.)

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<sup>10</sup>U.S. Food and Drug Administration, *Report on the State of Pharmaceutical Quality*, 3.

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



Source: GAO analysis of Food and Drug Administration data (data); National Atlas (base map). | GAO-20-262T

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 likely would 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 would not ship products to the United States directly. Such establishments are also subject to inspection.

## Types of Inspections

Drugs manufactured overseas must meet the same statutory and regulatory requirements as those manufactured in the United States. FDA's Center for Drug Evaluation and Research (CDER) establishes standards for the safety, quality, and effectiveness of, and manufacturing processes for, over-the-counter and prescription drugs. CDER requests that FDA's Office of Regulatory Affairs (ORA) inspect 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.<sup>11</sup>

FDA investigators generally conduct three main types of drug manufacturing establishment inspections: preapproval inspections, surveillance inspections, and for-cause inspections, as described in table 1. At times, FDA may conduct an inspection that combines both preapproval and surveillance inspection components in a single visit to an establishment.<sup>12</sup>

**Table 1: Types of Drug Manufacturing Establishment Inspections Conducted by the Food and Drug Administration (FDA)**

| Type of inspection       | Purpose of inspection   |
|--------------------------|---|
| Preapproval inspections  | FDA conducts preapproval inspections before approving a new brand name or generic drug to be marketed in the United States. These inspections are designed to verify the accuracy and authenticity of drug application data (such as manufacturing records) and assess whether the establishment can manufacture the product in the application in conformance with applicable regulations to assure a drug’s identity, strength, quality, and purity. <sup>a</sup>   |
| Surveillance inspections | Surveillance inspections are conducted at establishments when drugs are already marketed in the United States—either after FDA approval or after marketing for drugs that do not require FDA preapproval—and focus on compliance with system-wide controls for ensuring that the manufacturing processes produce high-quality drugs. <sup>b</sup> Systems examined during these inspections include those related to materials, quality control, production, facilities and equipment, packaging and labeling, and laboratory controls. These systems may be involved in the manufacture of multiple drugs. |
| For-cause inspections    | For-cause inspections are conducted to investigate specific issues, such as those raised in consumer complaints, indications of potential manufacturing problems submitted by the manufacturers themselves, or to follow-up on previous FDA regulatory action, among other reasons.   |

Source: GAO analysis of FDA information. | GAO-20-262T

<sup>a</sup>When FDA receives an application for drug approval (or a supplement to that application related to a manufacturing change), officials review the inspection history of each establishment listed on the application, among other things. According to FDA officials, if an establishment listed on the application has received a satisfactory good manufacturing practices inspection in the previous 2 years for a similar or more complex product, and the agency has no new concerns, FDA may consider this inspection sufficient and not perform a preapproval inspection of this establishment.

<sup>b</sup>Certain drugs, such as some over-the-counter drugs, may not require FDA approval before marketing in the United States.

**FDA uses multiple databases to select foreign and domestic establishments for surveillance inspections, including its registration**

<sup>11</sup>CGMPs 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.

<sup>12</sup>Most combined inspections occur when FDA conducts a surveillance inspection at an establishment where a preapproval inspection was also being conducted.

database and inspection database. Because the establishments are continuously changing as they begin, stop, or resume marketing products in the United States, CDER creates an establishment catalog monthly. The catalog is prioritized for inspection twice each year.

In our 2008 report we found that, because of inaccurate information in FDA's databases, the agency did not know how many foreign drug establishments were subject to inspection.<sup>13</sup> For example, some establishments included in FDA's registration database may have gone out of business and did not inform FDA that they had done so or did not actually manufacture drugs for the U.S. market. In our report, we noted that some foreign establishments may register because, in foreign markets, registration may erroneously convey an "approval" or endorsement by FDA, when in fact the establishment may never have been inspected by FDA. 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.<sup>14</sup>

To prioritize establishments for surveillance inspections, CDER 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. This model analyzes several factors, including inherent product risk, establishment type, inspection history, and time since last inspection, to develop a list of establishments that FDA considers to be a priority for inspection.<sup>15</sup> Through this process, CDER develops a ranked list of foreign and domestic establishments selected for inspection that is submitted to ORA. To be efficient with its resources, according to FDA officials, ORA staff may shift the order of establishments to be inspected on CDER's prioritized list based on geographic proximity to other planned inspection trips.

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<sup>13</sup>[GAO-08-970](#).

<sup>14</sup>See [GAO-10-961](#) and [GAO-17-143](#).

<sup>15</sup>Establishments may also be selected for surveillance inspections for other reasons, such as FDA's focus on a particular product.

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## FDA Inspection Workforce

Investigators from ORA and, as needed, ORA laboratory analysts with certain expertise are responsible for inspecting drug manufacturing establishments.<sup>16</sup> FDA primarily relies on three groups of investigators to conduct foreign inspections:

- ORA investigators based in the United States, who primarily conduct domestic drug establishment inspections but may sometimes conduct foreign inspections.
- Members of ORA's dedicated foreign drug cadre, a group of domestically based investigators, who exclusively conduct foreign inspections.
- Investigators assigned to and living in the countries where FDA has foreign offices, including staff based in the foreign offices full time and those on temporary duty assignment to the foreign offices. FDA began opening offices around the world in 2008 to obtain better information on the increasing number of products coming into the United States from overseas, to build relationships with foreign stakeholders, and to perform inspections.<sup>17</sup> FDA full-time foreign office staff are posted overseas for 2-year assignments. FDA staff can also be assigned to the foreign offices on temporary duty assignments for up to 120 days. In fiscal year 2019, there were full-time and temporary duty drug investigators assigned to FDA foreign offices in China and India.

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## Post-Inspection Activities

FDA's process for determining whether a foreign establishment complies with CGMPs involves both CDER and ORA. During an inspection, ORA investigators are responsible for identifying any significant objectionable conditions and practices and reporting these to the establishment's management. Investigators suggest that the establishment respond to FDA in writing concerning all actions taken to address the issues identified during the inspection.

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<sup>16</sup>ORA investigators lead inspections and are responsible for performing or overseeing all aspects of an inspection. ORA laboratory analysts are chemists or microbiologists and have expertise in laboratory testing. In some instances, staff from CDER, such as subject matter experts or drug application reviewers, may participate in inspections.

<sup>17</sup>Currently, FDA has foreign offices in China, Europe, India, and Latin America, but does not have drug investigators in the Europe or Latin America offices.

Once ORA investigators complete an inspection, they are responsible for preparing an establishment inspection report to document their inspection findings. Inspection reports describe the manufacturing operations observed during the inspection and any conditions that may violate U.S. statutes and regulations. Based on their inspection findings, ORA investigators make an initial recommendation regarding whether regulatory actions are needed to address identified deficiencies using one of three classifications: no action indicated (NAI); voluntary action indicated (VAI); or official action indicated (OAI).<sup>18</sup> Inspection reports and initial classification recommendations for regulatory action are to be reviewed within ORA. For inspections classified as OAI—where ORA identified serious deficiencies—such inspection reports and classification recommendations are to be reviewed within CDER. CDER is to review the ORA recommendations and determine whether regulatory action is necessary. CDER also is to review inspection reports and initial classification recommendations for all for-cause inspections, regardless of whether regulatory action is recommended by ORA.

According to FDA policy, inspections classified as OAI may result in regulatory action, such as the issuance of a warning letter. FDA issues warning letters to those establishments manufacturing drugs for the U.S. market that are in violation of applicable U.S. laws and regulations and may be subject to enforcement action if the violations are not promptly and adequately corrected. In addition, warning letters may notify foreign establishments that FDA may refuse entry of their drugs at the border or recommend disapproval of any new drug applications listing the establishment until sufficient corrections are made.<sup>19</sup> FDA may take other regulatory actions if it identifies serious deficiencies during the inspection of a foreign establishment. For example, FDA may issue an import alert, which instructs FDA staff that they may detain drugs manufactured by the violative establishment that have been offered for entry into the United

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<sup>18</sup>FDA officials told us that investigators are responsible for checking on previously identified deficiencies in any subsequent inspections of the same establishment. Officials told us that repeated identification of the same deficiency could result in regulatory action.

Inspection classifications are publicly available for some inspections on FDA's website: <https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/inspection-classification-database/>

<sup>19</sup>Warning letters are publicly available on FDA's website: <https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters>.

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States.<sup>20</sup> In addition, FDA may conduct regulatory meetings with the violative establishment. Regulatory meetings may be held in a variety of situations, such as a follow-up to the issuance of a warning letter to emphasize the significance of the deficiencies or to communicate documented deficiencies that do not warrant the issuance of a warning letter.

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## The Number Of Foreign Inspections Declined In Recent Years, And The Majority Of Such Inspections Identified Deficiencies

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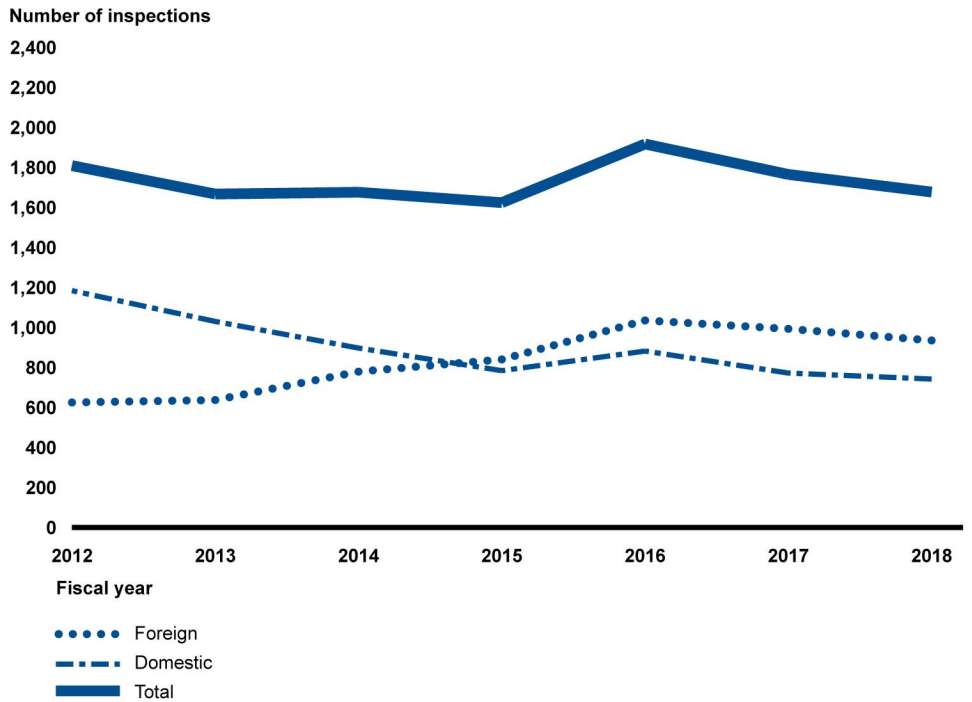
### Total Number of FDA Foreign Drug Inspections Has Decreased Since Fiscal Year 2016 after Several Years of Increases

Our preliminary analysis of FDA data shows that from fiscal year 2012 through fiscal year 2016, the number of FDA foreign drug manufacturing establishment inspections increased but then began to decline after fiscal year 2016 (see fig. 2). In fiscal year 2015, the total number of foreign inspections surpassed the number of domestic inspections. From fiscal year 2016 to 2018, both foreign and domestic inspections decreased—by about 10 percent and 13 percent, respectively.

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<sup>20</sup>An import alert can apply to specific drugs or all drugs manufactured by an establishment. Import alerts are publicly available on FDA's website: <https://www.fda.gov/industry/actions-enforcement/import-alerts>.

**Figure 2: Total Number of FDA Inspections of Foreign and Domestic Drug Establishments, Fiscal Year 2012 through 2018**



Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-20-262T

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

**Accessible Data for Figure 2: Total Number of FDA Inspections of Foreign and Domestic Drug Establishments, Fiscal Year 2012 through 2018**

| Fiscal year | Number of inspections: (Foreign) | Number of inspections: (Domestic) | Number of inspections: (Total) |
|-------------|----------------------------------|-----------------------------------|--------------------------------|
| 2012        | 625                              | 1184                              | 1809                           |
| 2013        | 637                              | 1030                              | 1667                           |
| 2014        | 779                              | 897                               | 1676                           |
| 2015        | 840                              | 784                               | 1624                           |
| 2016        | 1035                             | 882                               | 1917                           |
| 2017        | 993                              | 772                               | 1765                           |
| 2018        | 935                              | 742                               | 1677                           |

FDA officials attributed this 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 fiscal years 2017 and 2018. Despite steps taken to improve the accuracy and completeness of FDA data on foreign establishments, data challenges we identified in our 2008 report continue to make it difficult for FDA to accurately identify establishments subject to inspection. Specifically, since 2017, FDA has pursued an initiative to inspect approximately 1,000 foreign establishments that lacked an inspection history and, as of November 2019, officials said all of these establishments had either been inspected or were determined to not be subject to inspection.<sup>21</sup> However, officials told us that this effort contributed to the decline in the number of foreign inspections conducted because of how data inaccuracies affected the process for selecting establishments for inspection. Specifically, after selecting uninspected foreign establishments for inspection, FDA determined that a sizeable percentage of these establishments were not actually subject to inspection (e.g., about 40 percent of those assigned to the China Office in fiscal years 2017 and 2018).<sup>22</sup> These foreign establishments were thus removed from the list for inspection for the given year. FDA officials told us that the next highest priority establishments identified through the risk-based model to replace those establishments were domestic. As a result, the number of foreign establishments actually inspected decreased. As part of our ongoing work, we plan to examine the accuracy and completeness of information FDA maintains about foreign establishments and the application of its risk-based site selection process.

FDA continues to conduct the largest number of foreign inspections in India and China, with inspections in these two countries representing about 40 percent of all foreign drug inspections from fiscal year 2016 (when we last reported on this issue) through 2018. (See table 2.) 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.

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<sup>21</sup>We previously reported that as of 2016, FDA lacked the inspection history of 33 percent of the foreign establishments in its catalog of establishments subject to inspection.

<sup>22</sup>FDA officials said that some of these establishments were registered with FDA but did not actually manufacture drugs for the U.S. market, and others were drug manufacturers but had not shipped drugs to the United States in the previous 3 years. FDA officials told us that, once identified, they removed such establishments from the catalog of establishments subject to surveillance inspection to which the agency applies its risk-based model each year, but they retained information on these establishments in the larger inventory of establishments should these establishments begin shipping drugs to the United States in the future.





**Table 2: Total Number of FDA Foreign Drug Inspections, by Country, Fiscal Years 2012 through 2018**

| Country               | 2012         | 2013         | 2014       | 2015       | 2016         | 2017       | 2018       |
|-----------------------|--------------|--------------|------------|------------|--------------|------------|------------|
| India                 | 140          | 110          | 114        | 204        | 207          | 219        | 252        |
| China                 | 59           | 74           | 113        | 127        | 173          | 165        | 153        |
| Germany               | 59           | 60           | 72         | 68         | 72           | 69         | 68         |
| Canada                | 49           | 51           | 39         | 52         | 56           | 72         | 48         |
| Italy                 | 38           | 45           | 50         | 41         | 69           | 46         | 45         |
| Japan                 | 49           | 28           | 47         | 31         | 65           | 46         | 43         |
| South Korea           | 4            | 7            | 8          | 5          | 13           | 56         | 40         |
| France                | 25           | 37           | 44         | 45         | 55           | 42         | 36         |
| Switzerland           | 23           | 23           | 37         | 31         | 37           | 25         | 32         |
| United Kingdom        | 29           | 27           | 33         | 43         | 41           | 40         | 12         |
| All other countries   | 150          | 175          | 222        | 193        | 247          | 213        | 206        |
| <b>Total foreign</b>  | <b>625</b>   | <b>637</b>   | <b>779</b> | <b>840</b> | <b>1,035</b> | <b>993</b> | <b>935</b> |
| <b>Total domestic</b> | <b>1,184</b> | <b>1,030</b> | <b>897</b> | <b>784</b> | <b>882</b>   | <b>772</b> | <b>742</b> |

Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-20-262T

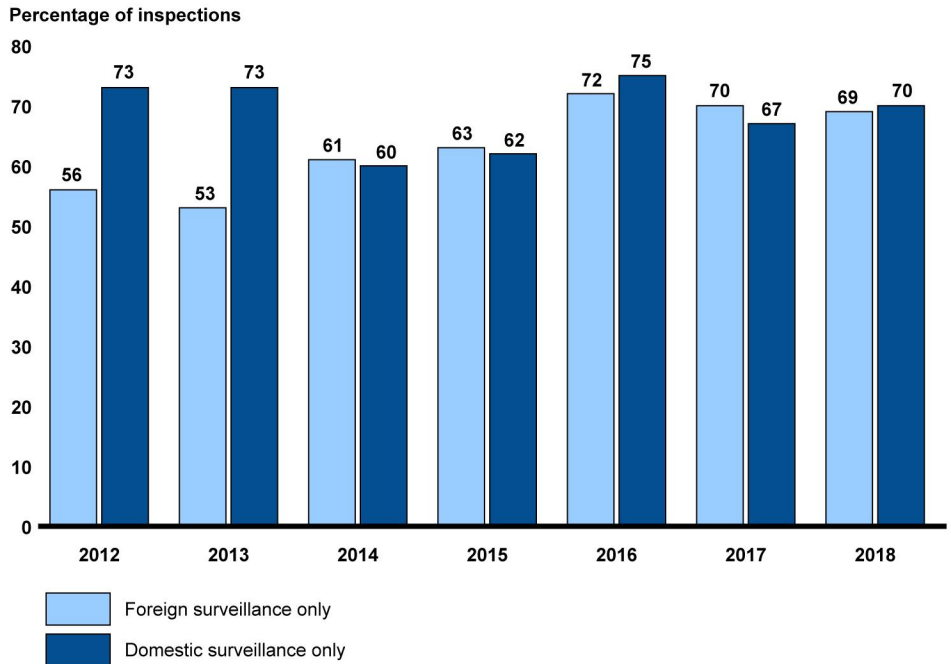
Note: The total number of inspections includes those conducted for preapproval, surveillance, and for-cause purposes.

## Most Foreign Inspections Are Surveillance Inspections

Our preliminary analysis of FDA data shows that each year from fiscal year 2012 through 2018, at least 50 percent of FDA’s foreign inspections were surveillance inspections. In contrast to preapproval inspections, surveillance inspections are used to ensure drugs already on the market are manufactured in compliance with FDA regulations. In recent years, the proportion of foreign surveillance inspections has increased. As figure 3 shows, in fiscal year 2012, 56 percent of foreign inspections were surveillance-only inspections; in contrast, from fiscal year 2016 through 2018, about 70 percent of foreign inspections were surveillance-only, which was comparable to the percentage for domestic inspections during that period. This is a significant increase from the 13 percent of foreign inspections that were surveillance-only when we made our 2008 recommendation that FDA inspect foreign establishments at a

comparable frequency to their domestic counterparts (85 percent of which were surveillance-only at that time).<sup>23</sup>

**Figure 3: Percentage of FDA Foreign and Domestic Drug Inspections Conducted for Surveillance Purposes, Fiscal Years 2012 through 2018**



Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-20-262T

Note: FDA conducts surveillance inspections to monitor the ongoing compliance of establishments manufacturing drugs that are already on the market. This figure depicts surveillance -only inspections. FDA conducted additional inspections that had a surveillance component combined with another type of inspection.

**Accessible Data for Figure 3: Percentage of FDA Foreign and Domestic Drug Inspections Conducted for Surveillance Purposes, Fiscal Years 2012 through 2018**

| Fiscal year | Foreign surveillance (percentage of inspections) | Domestic surveillance (percentage of inspections) |
|-------------|--|---|
| 2012        | 56   | 73  |
| 2013        | 53   | 73  |
| 2014        | 61   | 60  |
| 2015        | 63   | 62  |
| 2016        | 72   | 75  |

<sup>23</sup>See [GAO-08-970](#), 27.

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| Fiscal year | Foreign surveillance<br>(percentage of inspections) | Domestic surveillance<br>(percentage of inspections) |
|-------------|---|--|
| 2017        | 70  | 67   |
| 2018        | 69  | 70   |

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FDA has implemented changes to its foreign drug inspection program since our 2008 report that may have contributed to the increase in surveillance inspections. Prior to 2012, FDA was required to inspect domestic establishments that manufacture drugs marketed in the United States every 2 years, but there was no similar requirement for foreign establishments. As a result, and as we reported in 2008, foreign inspections were often preapproval inspections driven by pending applications for new drugs. FDA thus conducted relatively few surveillance-only inspections to monitor the ongoing compliance of establishments manufacturing drugs that were already on the market, with just 13 percent of foreign inspections conducted for surveillance purposes at the time of our 2008 report. However, in 2012, the Food and Drug Administration Safety and Innovation Act eliminated the 2-year requirement for domestic inspections, directing FDA to inspect both domestic and foreign establishments on a risk-based schedule determined by an establishment's known safety risks, which was consistent with our 2008 recommendation.<sup>24</sup>

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### FDA Identified Deficiencies during the Majority of Foreign Inspections

Our preliminary analysis of FDA data shows that from fiscal year 2012 through 2018, FDA identified deficiencies in approximately 64 percent of foreign drug manufacturing establishment inspections (3,742 of 5,844 inspections). This includes deficiencies necessitating a classification of VAI or the more serious OAI, as described in the text box.

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<sup>24</sup>Pub. L. No. 112-144, § 705, 126 Stat. 993, 1066 (2012) (codified at 21 U.S.C. 360(h)). This established a comparable inspection frequency for foreign and domestic establishments with similar characteristics, consistent with our 2008 recommendation.

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**Inspection Classifications**

Based on their inspection findings, FDA investigators make an initial recommendation regarding the classification of each inspection:

- **No action indicated (NAI)** means that insignificant or no deficiencies were identified during the inspection.
- **Voluntary action indicated (VAI)** means that deficiencies were identified during the inspection, but the agency is not prepared to take regulatory action, so any corrective actions are left to the establishment to take voluntarily.
- **Official action indicated (OAI)** means that serious deficiencies were found that warrant regulatory action.

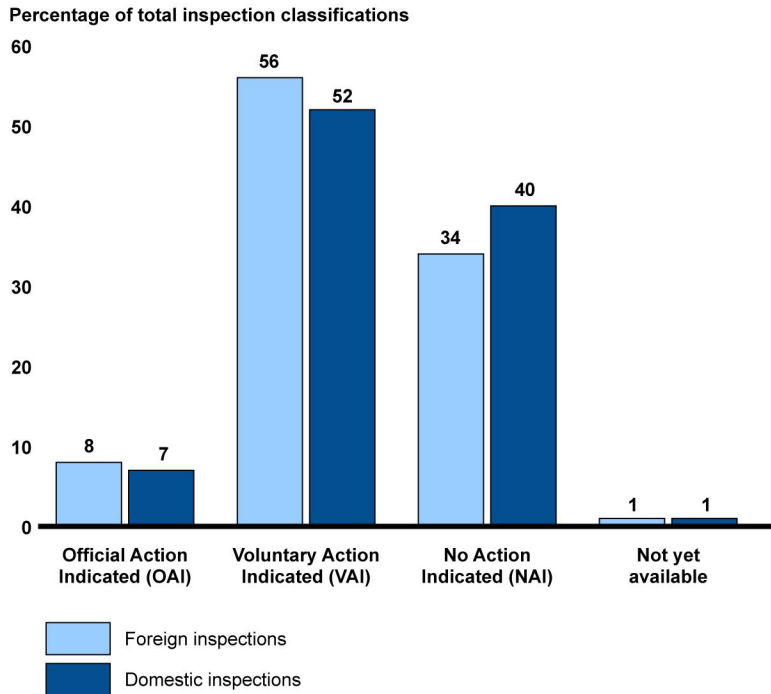
Source: GAO. | GAO-20-262T

About 59 percent of domestic inspections (3,702 out of 6,291) identified deficiencies during this time period. (See fig. 4.) This proportion is similar to what we found when we last looked at this issue in 2008, when FDA identified deficiencies in about 62 percent of foreign inspections and 51 percent of domestic inspections from fiscal years 2002 through 2006.<sup>25</sup>

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<sup>25</sup>In our 2008 report we found that FDA's data did not provide reliable information about the number of foreign inspections with serious deficiencies classified specifically as OAI. Therefore, we reported data on the percentage of inspections classified as either VAI or OAI together. See [GAO-08-970](#), 29. We recommended that FDA correct this issue and they did so beginning in October 2011, but for comparison purposes, we continue to report combined VAI and OAI inspection data here.

**Figure 4: FDA Inspection Classifications for Foreign and Domestic Drug Establishments by Type of Classification, Fiscal Year 2012 through 2018**



Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-20-262T

Notes: Based on their inspection findings, FDA investigators make an initial recommendation regarding the classification of each inspection: NAI means that insignificant or no deficiencies were identified during the inspection; VAI means that deficiencies were identified during the inspection, but the agency is not prepared to take regulatory action, so any corrective actions are left to the establishment to take voluntarily; and OAI means that serious deficiencies were found that warrant regulatory action, such as issuing a warning letter or import alert.

The analysis presented in this figure is based on 5,844 foreign inspections and 6,291 domestic inspections conducted from fiscal year 2012 through 2018. Totals do not sum to 100 due to rounding. Some classifications were not yet available at the time of our analysis (1 percent of both foreign and domestic inspections). Finally, less than 1 percent of both foreign and domestic inspections received another interim classification, which is not reflected in this figure.

**Accessible Data for Figure 4: FDA Inspection Classifications for Foreign and Domestic Drug Establishments by Type of Classification, Fiscal Year 2012 through 2018**

| Category                         | Foreign inspections (percentage of total inspection classifications) | Domestic inspections (percentage of total inspection classifications) |
|----------------------------------|--|---|
| Official Action Indicated (OAI)  | 8  | 7   |
| Voluntary Action Indicated (VAI) | 56   | 52  |

| Category                  | Foreign inspections<br>(percentage of total<br>inspection<br>classifications) | Domestic inspections<br>(percentage of total<br>inspection classifications) |
|---------------------------|---|---|
| No Action Indicated (NAI) | 34  | 40  |
| Not yet available         | 1   | 1   |

Our preliminary analysis showed that serious deficiencies identified during foreign drug inspections classified as OAI—which represented 8 percent of inspections from fiscal year 2012 through 2018—include CGMP violations such as those related to production and process controls, equipment, records and reports, and buildings and facilities. For example:

- **Failure to maintain the sanitation of the buildings used in the manufacturing processing, packing, or holding of a drug product (21 C.F.R. § 211.56(a) (2019)).** At an establishment in India producing finished drug products, the investigator reported observing a live moth floating in raw material used in the drug production, and that the facility staff continued to manufacture the drug products using the raw material contaminated by the moth, despite the investigator pointing out its presence.
- **Failure to perform operations relating to the manufacture, processing, and packing of penicillin in facilities separate from those used for other drug products (21 C.F.R. § 211.42 (d) (2019)).** At an establishment in Turkey that manufactured penicillin and other drugs, the investigator reported that the manufacturer had detected penicillin outside the penicillin manufacturing area of the establishment multiple times. According to FDA, penicillin contamination of other drugs presents great risk to patient safety, including potential anaphylaxis (even at extremely low levels of exposure) and death.

The identification of serious deficiencies is not unique to foreign inspections. For example, at a domestic establishment producing finished drug products, the investigator observed brown stains, white residues, and brown stagnant water in manufacturing equipment.

Some investigators who conduct foreign inspections expressed concern with instances in which ORA or CDER reviewers reclassify the investigator’s initial inspection classification recommendations of OAI to

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the less serious classification of VAI. We plan to examine this issue as part of our ongoing work.

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## FDA Continues To Face Challenges Filling Vacancies Among Staff Conducting Foreign Inspections

Our ongoing work showed FDA's foreign inspection workforce has staff vacancies, which FDA officials said contributed to the recent decline in inspections. As previously mentioned, FDA uses multiple types of staff resources to conduct foreign drug inspections—including ORA investigators based in the United States, members of ORA's dedicated foreign drug cadre based in the United States, and investigators assigned to FDA's foreign offices.<sup>26</sup> However, each of these groups has current vacancies. According to FDA officials, the agency is trying to fill vacancies in each of these groups, but the lower staff numbers may limit FDA's ability to conduct more foreign inspections.

**ORA investigators based in the United States.** This group of investigators conducts the majority of foreign inspections; about 76 percent of foreign inspections in fiscal year 2018 involved an ORA investigator based in the United States who conducts both foreign and domestic inspections.<sup>27</sup> FDA officials said that the more experienced investigators from this group are expected to conduct three to six foreign inspections per year, and investigators hired using generic drug user fees are expected to inspect nine to 12 foreign establishments per year.<sup>28</sup> As of June 2019, there were 190 investigators eligible to conduct foreign drug inspections, but officials said that as of November 2019, the agency had an additional 58 vacancies in this group. Officials said that the agency was in the process of hiring 26 ORA investigators based in the

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<sup>26</sup>In addition to these categories, there are a variety of other FDA staff who, on occasion, may participate in an inspection if certain subject matter expertise is needed.

<sup>27</sup>Inspections can be conducted by one investigator or multiple investigators. Therefore, investigators from more than one group could be involved with a single inspection.

<sup>28</sup>Beginning in 2014, FDA began to use the user fees collected from manufacturers of generic drugs to hire additional investigators focused on inspecting generic drug manufacturers. According to FDA officials, these investigators have primarily been assigned to conduct foreign inspections.

United States to fill these vacancies, with 32 vacancies remaining.<sup>29</sup> FDA officials attributed the vacancies to multiple factors: investigator retirements, investigator movement to other parts of FDA, and the need to hire to additional investigator positions using generic drug user fees. Officials also said that a reorganization within ORA led to a reduced number of investigators who conduct drug manufacturing establishment inspections. While FDA recently filled several of the vacancies, officials told us that new investigators are not typically used for foreign inspections until they have been with the agency for 2 to 3 years.

**ORA dedicated foreign drug cadre.** About 15 percent of foreign inspections in fiscal year 2018 involved an investigator from ORA's dedicated foreign drug cadre—a group of ORA investigators based in the United States who exclusively conduct foreign inspections. FDA officials said that members of the cadre are expected to conduct 16 to 18 foreign inspections each year. According to FDA, the cadre had 20 investigators in 2012 and 15 investigators in 2016. However, the cadre had only 12 investigators as of November 2019, out of 20 available slots. According to FDA officials, the agency is attempting to fill these positions from the current ORA investigator pool, but officials are not confident that all 20 slots will be filled.

**Investigators assigned to FDA's foreign offices.** Approximately 7 percent of foreign inspections in fiscal year 2018 involved investigators from FDA's foreign offices. The investigators conducting these inspections are those based in the China and India foreign offices—the countries where most drug inspections occur—and also include those on temporary duty assignment to these offices.<sup>30</sup> According to FDA officials, these investigators are expected to conduct 15 foreign inspections each year. We have noted high vacancy rates for these foreign offices in past reports.<sup>31</sup> While these vacancy rates have decreased over time, vacancies persist. As of November 2019, FDA's China office had three of

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<sup>29</sup>FDA officials indicated that filling these vacancies was a priority for the agency and noted that their recent implementation of direct-hire authority has helped them fill these positions.

<sup>30</sup>The percentage of inspections involving these groups of investigators do not equal 100 percent because some inspections may involve only non-investigator staff, such as CDER drug application reviewers.

<sup>31</sup>See GAO, *Food and Drug Administration: Overseas Offices Have Taken Steps to Help Ensure Import Safety, but More Long-Term Planning Is Needed*, [GAO-10-960](#) (Washington, D.C.: Sep. 30, 2010), and [GAO-17-143](#).



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10 drug investigator positions vacant (a 30 percent vacancy rate), while FDA's India office had two of six drug investigator positions vacant (a 33 percent vacancy rate).

FDA has taken steps to address vacancies in the foreign offices, but continues to face challenges. In our 2010 report, we recommended that FDA develop a strategic workforce plan to help recruit and retain foreign office staff.<sup>32</sup> FDA released such a plan in March 2016, but the long-standing vacancies in the foreign offices raise questions about its implementation. FDA officials told us that one challenge in recruiting investigators for the foreign offices is that well-qualified investigators for those positions need foreign inspection experience. For example, an official in FDA's India office told us that foreign inspections can be challenging and the India office does not have the resources to develop or train new investigators. Therefore, it is important to recruit investigators who have experience conducting foreign inspections, and such investigators are recruited from ORA. Thus, vacancies in the other two groups of investigators can influence the number of staff available to apply for positions in the foreign offices. Further, according to FDA officials, after employees have accepted an in-country position, the agency can experience significant delays before they are staffed in the office due to delays in processing assignments. For example, an official in FDA's India office said that investigators need to complete a week-long security training program and must obtain the security clearance needed to work at the U.S. Embassy, which is where FDA's foreign office is located. However, the official told us that there are limited availabilities for that training and background checks for security clearances can take time.<sup>33</sup> According to this official, FDA investigators do not usually receive first priority for the training. FDA estimates that it can take as little as 1 year to over 2 years to clear background and medical checks and arrive at a foreign office. For example, an investigator in FDA's China office told us that as a result of these requirements and other issues, it took nearly 2 years for the investigator to arrive at the office after FDA had accepted the investigator's application. According to FDA's own strategic workforce plan for the foreign offices, these types of delays have resulted in staff changing their decision after accepting a position in the foreign offices.

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<sup>32</sup>[GAO-10-960](#).

<sup>33</sup>We have highlighted timeliness concerns with the government-wide personnel security clearance process in our High Risk series. See [GAO-19-157SP](#).

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## Persistent Challenges Unique To Foreign Inspections Raise Questions About Their Equivalence To Domestic Inspections

Our preliminary analysis indicates that FDA continues to face unique challenges when inspecting foreign drug establishments—as compared to domestic establishments—that raise questions about the equivalence of these inspections. Specifically, based on our interviews with drug investigators in the dedicated foreign drug cadre and FDA’s foreign offices in China and India, we identified four challenge areas related to conducting foreign inspections, which are described below. Of the four challenge areas identified, three areas—preannouncing inspections, language barriers, and lack of flexibility—were also raised in our 2008 report.<sup>34</sup>

**Preannouncing Inspections.** As we reported in 2008, the amount of notice FDA generally gives to foreign drug establishments in advance of an inspection is different than for domestic establishments.<sup>35</sup> Domestic drug establishment inspections are almost always unannounced, whereas foreign establishments generally receive advance notice of an FDA inspection. According to FDA officials, FDA is not required to preannounce foreign inspections. However, they said the agency generally does so to avoid wasting agency resources, obtain the establishment’s assistance to make travel arrangements, and ensure the safety of investigators when traveling in country.

FDA does conduct some unannounced foreign inspections, particularly if the investigators conducting the inspection are based in FDA’s foreign offices. However, FDA officials told us that FDA 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.<sup>36</sup> However, the officials estimated that the agency generally

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<sup>34</sup>[GAO-08-970](#).

<sup>35</sup>[GAO-08-970](#).

<sup>36</sup>According to FDA officials, FDA plans to add a new variable to its data to identify preannounced and unannounced inspections.

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 3).

**Table 3: 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 <sup>a</sup>  |
|--|---|--|
| China office investigator                                      | Announcement: 0-5 days<br>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, 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 preannounced to the drug establishments in advance. | Involved in 27 percent of total number of inspections in China   |
| India office investigator                                      | Announcement: 0-5 days<br>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   |
| Domestic investigator (Including dedicated foreign drug cadre) | Announcement: generally 12 weeks<br>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"> <li>• 75 percent of total number of inspections in China</li> <li>• 90 percent of total number of inspections in India</li> <li>• 100 percent of total number of inspections in other foreign countries</li> </ul> |

Source: Interviews with Food and Drug Administration (FDA) officials and GAO analysis of FDA data. | GAO-20-262T

<sup>a</sup>These percentages add up to over 100 percent as some inspections may involve more than one type of investigator.

Our preliminary work indicates that preannouncing foreign inspections can create challenges and raises questions about the equivalence to domestic inspections. Of the 18 investigators we interviewed, 14 said that there are downsides to preannouncing foreign inspections, particularly that providing advance notice gives foreign establishments the opportunity to fix problems before the investigator arrives. For example, when an inspection is preannounced, it gives establishments time to clean up their facility and update or generate new operating procedures. However, establishments are expected to be in a constant state of

compliance and always ready for an FDA inspection, and several investigators told us seeing the true day-to-day operating environment for an establishment is more likely during an unannounced inspection.

Of the 18 investigators we interviewed, 12 said that unannounced inspections are generally preferable to preannounced inspections. One investigator told us that, although they believe the best way to ensure industry compliance to CGMPs is for establishments to not know when FDA is coming for an inspection, there is no data that would allow the agency to evaluate whether unannounced inspections are better than preannounced inspections. In addition, some investigators told us that it is still possible to identify serious deficiencies during preannounced inspections. For example, investigators can still identify issues by looking at the firm's electronic records, including time-stamped data relating to the creation, modification, or deletion of a record. Three investigators also told us that in some cases there can be benefits to announcing inspections in advance. For example, for preapproval inspections, announcing the inspection in advance gives the establishment time to organize the documentation and staff needed to conduct the inspection.

**Language Barriers.** Our preliminary work indicates that language barriers—which we first reported as a challenge to conducting foreign inspections in our 2008 report—can add time to inspections and raise questions about the accuracy of information FDA investigators collect and thus about the equivalence to domestic inspections.<sup>37</sup> FDA generally does not send translators on inspections in foreign countries. Rather, investigators rely on the drug establishment to provide translation services, which can be an English-speaking employee of the establishment being inspected, an external translator hired by the establishment, or an English-speaking consultant hired by the establishment.

Of the 18 investigators that we interviewed, 14 said that language barriers can be a challenge to conducting foreign inspections and were especially challenging in parts of Asia, including China and Japan. Seven investigators told us this is less of a challenge for inspections conducted in other foreign countries, including India and countries in Europe, because workers at establishments in these countries are more likely to speak English, and documentation is also more likely to be in English.

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<sup>37</sup> [GAO-08-970](#).

Investigators told us that compared to domestic inspections, it can be more challenging and take longer to complete typical inspection-related activities, such as reviewing documentation or interviewing employees, if the investigator needs to rely on translation.

Fourteen of the 18 investigators we interviewed said that there can be concerns related to relying on establishment staff and independent translators. Specifically, 11 investigators told us 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. For instance, one investigator said that there is more risk of conflict of interest if the establishment uses its own employees to translate. Another investigator said that they went to a drug establishment in China that told FDA it had English-speaking employees to translate the inspection, but that this was not the case, and the investigator had to use an application on their phone to translate the interviews. In addition, the firm representative providing the translation may be someone that does not have the technical language needed, which can make it harder to communicate with firm staff and facilitate the inspection. One investigator told us that the independent translators hired by firms are sometimes consultants and, in those instances, it can seem like the consultants are coaching the firm during the inspection.

FDA officials told us that when they conduct unannounced for-cause inspections in China, investigators bring locally employed staff who work in FDA's China office to act as translators. The investigators we interviewed said that in such instances, they valued knowing that the translation they were getting was accurate. However, FDA does not have the resources to provide locally employed staff on every inspection, according to an FDA official. We will continue to examine this issue with FDA as part of our ongoing work.

**Lack of Flexibility.** Our preliminary work indicates that, as we first reported in 2008, the overseas travel schedule can present unique challenges for FDA's domestically based investigators—including both ORA investigators and members of the dedicated foreign drug cadre—who conduct the majority of foreign inspections.<sup>38</sup> Eight of the 12 dedicated foreign drug cadre investigators that we interviewed told us that

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<sup>38</sup>[GAO-08-970](#).

there is little flexibility to extend foreign inspections conducted by domestically based investigators because the inspections they conduct on an overseas trip are scheduled back-to-back in 3-week trips that may involve three different countries.<sup>39</sup> This raises questions about their equivalence to domestic inspections. For instance, extending one inspection would limit the amount of time the investigator has to complete their other scheduled inspections, some investigators told us. In addition, eight investigators told us that domestically based staff are generally unable to extend the total amount of time spent on an overseas trip—one investigator told us that an investigator would have to find something really bad to justify an extension. In contrast, FDA officials told us that inspections conducted by in-country investigators in China or India, and domestic inspections in the United States, are generally scheduled one at a time and can thus more easily be extended if the investigator needs additional time to pursue potential deficiencies. However, in-country investigators are not involved in the majority of inspections conducted in China or India.

Three investigators from the dedicated foreign drug cadre told us that when they travel overseas, they adjust their inspection approach to help ensure they finish foreign inspections on time. For example, one investigator told us an investigator may start the inspection in an area of the establishment that was noted as having issues during the last inspection. However, one investigator said that sometimes it is not possible to cover everything in depth during a foreign inspection. Another investigator told us that they focus on identifying the most serious issues during a foreign inspection, and that less serious issues can be identified in the establishment inspection report for reference in the next inspection. Five investigators also noted that they work long hours during their inspection to ensure they can complete the needed work.<sup>40</sup> While FDA may assign more than one investigator to an inspection to complete needed work, one investigator said that FDA does not usually assign more than one person to an inspection because investigators are

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<sup>39</sup>According to FDA officials, investigators in the dedicated foreign drug cadre are expected to conduct 16 to 18 foreign inspections per year. To meet this expectation, cadre members travel overseas six times a year, with each trip lasting 3 weeks, and conduct two or three back-to-back inspections per trip.

<sup>40</sup>According to FDA officials, members of the dedicated foreign drug cadre can receive up to 15 hours of overtime per week during an overseas week to complete inspection-related work. For example, investigators may use overtime hours to extend the amount of time on site or to review relevant data and documentation when they return to their hotel at night.

expected to have the experience to conduct inspections by themselves. From fiscal years 2012 to 2018, the majority of both foreign and domestic inspections were conducted by one person—77 percent and 66 percent, respectively.<sup>41</sup>

**Post-Inspection Classification Process.** According to FDA officials, starting in fiscal year 2018, FDA implemented a new post-inspection classification process: when an ORA investigator recommends an OAI classification following an inspection, ORA compliance is required to send that inspection report to CDER for review within 45 calendar days from the inspection closeout. Among other things, the process was intended to help ensure FDA can communicate inspection results to domestic and foreign establishments within 90 days of the inspection closeout, as committed to under the Generic Drug User Fee Amendments of 2017 (GDUFA II).<sup>42</sup> FDA officials told us that the changes also required an additional ORA review for foreign inspection reports to align that process with the process for domestic inspection reports.<sup>43</sup> Although the 45-day reporting time frame for potential OAI classifications is a requirement for both domestic and foreign inspections, adding the additional level of review within ORA effectively shortened the amount of time investigators have to document findings for foreign inspections.

Our preliminary work indicates that the post-inspection reporting time frames can create challenges for domestic investigators that conduct foreign inspections and raise questions about the equivalence to domestic inspections. Eight of the 18 investigators that we interviewed said shortening the time for completing reports and adding a level of review has made it more challenging to meet reporting requirements,

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<sup>41</sup>In addition to the time pressures associated with sending only one investigator on a foreign inspection, two of the investigators we interviewed from the dedicated foreign drug cadre expressed a preference for conducting team inspections as it helps reduce risks to their personal safety.

<sup>42</sup>Pub. L. No. 115-52, §§ 301, 131 Stat. 1005, 1020 (codified in pertinent part at 21 U.S.C. § 379j-41 note). Prior to each user fee program reauthorization, FDA negotiates with representatives of the generic drug industry to identify goals for how FDA should spend those user fees over the next 5-year authorization period.

<sup>43</sup>Prior to this change, officials told us that all foreign inspection reports, regardless of classification type, were sent to CDER for review after being endorsed by ORA supervisors. Under the new process, all foreign inspections are reviewed by ORA compliance after being endorsed by ORA supervisors. Foreign inspection reports now only go to CDER compliance for review in certain circumstances, such as if there is an OAI recommended, which had been the process for domestic inspections.

especially if serious deficiencies are identified during the inspection. Investigators told us that for a potential OAI inspection, they now need to send the inspection report to their supervisor for endorsement within 10 days of the closeout of a foreign inspection, regardless of when the investigator's next inspection is scheduled for, or whether the investigator has to travel from overseas back to the United States after the inspection. For example, if a domestic investigator finds serious deficiencies on the first inspection, thus indicating an initial OAI classification, the investigator needs to write and send the related inspection report to the ORA supervisor for endorsement before returning home from the 3-week overseas trip to meet the required time frame. One investigator told us that, as a result of the time pressures, post-inspection reports may be less thorough, and that some inspection observations could be better supported if investigators had more time to write the reports.

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 first examined this issue, FDA has made significant changes to adapt to the globalization of the drug supply chain and has greatly increased the number of inspections that it conducts of foreign establishments. Notably, it has markedly increased the percentage of foreign inspections conducted to monitor drugs already on the market, which we previously noted were vital to FDA oversight of foreign establishments. However, the agency continues to be faced with many of the same challenges in the oversight of foreign establishments that we identified in our 2008 report. Our preliminary work has identified inspection decreases, related in part to FDA challenges filling investigator vacancies. We have also identified a variety of unique challenges that investigators face in foreign inspections. As we continue to conduct our work, we will further examine the cumulative effect of these challenges that raise questions about FDA's ability to conduct equivalent inspections in foreign establishments. We will examine the extent to which FDA has assessed its oversight of drugs manufactured overseas and the steps it is taking to mitigate any risks, and make recommendations as appropriate.

Chair DeGette, Ranking Member Guthrie, 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.



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## 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](mailto: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); John Lalomio (Analyst-in-Charge); Katherine L. Amoroso; George Bogart; Zhi Boon; Derry Henrick; Laurie Pachter; and Vikki Porter.

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