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MEDICAL DEVICES

FDA Faces Challenges in Conducting Inspections of Foreign Manufacturing Establishments

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Highlights of [GAO-08-780T](#), a testimony before the Subcommittee on Health, Committee on Energy and Commerce, House of Representatives

Why GAO Did This Study

As part of the Food and Drug Administration's (FDA) oversight of the safety and effectiveness of medical devices marketed in the United States, it inspects certain foreign and domestic establishments where these devices are manufactured. To help FDA address shortcomings in its inspection program, the Medical Device User Fee and Modernization Act of 2002 required FDA to accredit third parties to inspect certain establishments. In response, FDA has implemented two voluntary programs for that purpose.

This statement is based primarily on GAO testimonies from January 2008 ([GAO-08-428T](#)) and April 2008 ([GAO-08-701T](#)). In this statement, GAO assesses (1) FDA's program for inspecting foreign establishments that manufacture medical devices for the U.S. market and (2) FDA's programs for third-party inspections of those establishments. For GAO's January and April 2008 testimonies, GAO interviewed FDA officials, analyzed information from FDA, and updated GAO's previous work on FDA's programs for inspections by accredited third parties. GAO updated selected information for this statement in early May 2008.

To view the full product, including the scope and methodology, click on [GAO-08-780T](#). For more information, contact Marcia Crosse at (202) 512-7114 or crossem@gao.gov.

MEDICAL DEVICES

FDA Faces Challenges in Conducting Inspections of Foreign Manufacturing Establishments

What GAO Found

FDA faces challenges managing its program to inspect foreign establishments that manufacture medical devices. GAO testified in January 2008 that two databases that provide FDA with information about foreign medical device establishments and the products they manufacture for the U.S. market contained inaccurate information about establishments subject to FDA inspection. In addition, comparisons between these databases—which could help produce a more accurate count—had to be done manually. Recent changes FDA made to its registration database could improve the accuracy of the count of establishments, but it is too soon to tell whether these and other changes will improve FDA's management of its foreign inspection program. Another challenge is that FDA conducts relatively few inspections of foreign establishments; officials estimated that the agency inspects foreign manufacturers of high-risk devices (such as pacemakers) every 6 years and foreign manufacturers of medium-risk devices (such as hearing aids) every 27 years. Finally, inspections of foreign manufacturers pose unique challenges to FDA, such as difficulties in recruiting investigators to travel to certain countries and in extending trips if the inspections uncovered problems. FDA is pursuing initiatives that could address some of these unique challenges, but it is unclear whether FDA's proposals will increase the frequency with which the agency inspects foreign establishments.

Few inspections of foreign medical device manufacturing establishments have been conducted through FDA's two accredited third-party inspection programs—the Accredited Persons Inspection Program and the Pilot Multi-purpose Audit Program (PMAP). Under FDA's Accredited Persons Inspection Program, from March 11, 2004—the date when FDA first cleared an accredited organization to conduct independent inspections—through May 7, 2008, four inspections of foreign establishments had been conducted by accredited organizations. An incentive to participation in the program is the opportunity to reduce the number of inspections conducted to meet FDA's and other countries' requirements. Disincentives include bearing the cost for the inspection, particularly when the consequences of an inspection that otherwise might not occur in the near future could involve regulatory action. The Food and Drug Administration Amendments Act of 2007 made several changes to program eligibility requirements that could result in increased participation by manufacturers. PMAP was established on September 7, 2006, as a partnership between FDA and Canada's medical device regulatory agency and allows accredited organizations to conduct a single inspection to meet the regulatory requirements of both countries. As of May 7, 2008, two inspections of foreign establishments had been conducted by accredited organizations through this program. The small number of inspections completed to date by accredited third-party organizations raises questions about the practicality and effectiveness of these programs to quickly help FDA increase the number of foreign establishments inspected.

Mr. Chairman and Members of the Subcommittee:

I am pleased to be here today as you examine the Food and Drug Administration's (FDA) program for inspecting foreign manufacturers of medical devices for the U.S. market. FDA is responsible for the regulation of medical devices¹ marketed in the United States, including those manufactured in foreign establishments.² FDA classifies medical devices into one of three classes based on degree of potential risk and level of control needed to reasonably ensure safety and effectiveness.³ According to FDA data, a wide variety of class II (medium risk) and III (high risk) medical devices may be manufactured for the U.S. market by foreign establishments. Such devices include defibrillators, contact lenses, pacemakers, hip prostheses, and coronary stents.⁴ FDA is responsible for inspecting certain foreign and domestic establishments to ensure they meet required manufacturing standards; such inspections are FDA's primary means of assuring that the safety and effectiveness of medical devices are not jeopardized by poor manufacturing practices.

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA) addressed concerns about FDA's ability to meet its responsibilities for inspecting medical device manufacturing establishments.⁵ MDUFMA included provisions designed to (1) increase the number of inspected medical device manufacturing establishments and (2) help medical device manufacturers meet the inspection requirements of both the United States

¹Medical devices include instruments, apparatuses, machines, and implants that are intended for use to diagnose, cure, treat, or prevent disease, or to affect the structure or any function of the body. 21 U.S.C. § 321(h).

²FDA regulations define an establishment as a place of business under one management at one general physical location at which a device is manufactured, assembled, or otherwise processed. 21 C.F.R. § 807.3(c) (2007). Medical device manufacturers may have more than one establishment. We use the term "manufacture" to refer to activities including manufacturing, preparing, and processing devices.

³21 U.S.C. § 360c. Medical devices are classified into one of three classes. Class I includes "low risk" devices, such as tongue depressors, elastic bandages, and bedpans. Class II includes "medium risk" devices, such as syringes, hearing aids, and electrocardiograph machines. Class III includes "high risk" devices, such as heart valves, pacemakers, and defibrillators.

⁴A coronary stent is a small tube that is placed within a coronary artery to keep the vessel open.

⁵See Pub. L. No. 107-250, § 201, 116 Stat. 1588, 1602-09 (2002) (codified as amended at 21 U.S.C. § 374(g)).

and foreign countries in a single inspection. Specifically, MDUFMA required FDA to accredit third-party organizations to conduct inspections of certain foreign and domestic establishments.⁶ In response, FDA implemented its Accredited Persons Inspection Program, which permits certain establishments to voluntarily request inspections from third-party organizations to meet inspectional requirements. In January 2007, we reported on the status of this program citing, among other things, concerns regarding its implementation and potential incentives and disincentives that may influence manufacturers' participation.⁷ Additionally, in partnership with Health Canada,⁸ FDA established in September 2006 another program for inspection by accredited third parties—the Pilot Multi-purpose Audit Program (PMAP)—that allows accredited organizations to conduct a single inspection to meet the regulatory requirements of both countries.

My remarks today are based primarily on our January 2008 statement, which updated our January 2007 report, on FDA's management of its medical device inspection program and our April 2008 statement on a number of new FDA initiatives related to foreign inspections of FDA regulated products, including medical devices.⁹ My remarks will focus on our assessment of (1) FDA's program for inspecting foreign establishments that manufacture medical devices for the U.S. market and (2) FDA's programs for third-party inspections of foreign medical device manufacturing establishments.

⁶In this report, unless otherwise noted, when we discuss inspections, we are referring to those conducted by FDA investigators.

⁷GAO, *Medical Devices: Status of FDA's Program for Inspections by Accredited Organizations*, [GAO-07-157](#) (Washington, D.C.: Jan. 5, 2007).

⁸Health Canada is the governmental entity that regulates medical devices marketed in Canada.

⁹GAO, *Medical Devices: Challenges for FDA in Conducting Manufacturer Inspections*, [GAO-08-428T](#) (Washington, D.C.: Jan. 29, 2008) and GAO, *Drug Safety: Preliminary Findings Suggest Recent FDA Initiatives Have Potential, but Do Not Fully Address Weaknesses in Its Foreign Drug Inspection Program*, [GAO-08-701T](#) (Washington, D.C.: Apr. 22, 2008).

To address these objectives, we used work completed for our January 2008 statement on FDA's medical device inspection program, for which we interviewed officials from FDA's Center for Devices and Radiological Health (CDRH) and Office of Regulatory Affairs (ORA), which have responsibilities for managing the medical device inspection program.¹⁰ To assess FDA's program for inspecting foreign establishments that manufacture medical devices, we obtained information from FDA's Device Registration and Listing System (DRLS), as of September 19, 2007; Field Accomplishments and Compliance Tracking System (FACTS) for fiscal year 2002 through fiscal year 2007; and Operational and Administrative System for Import Support (OASIS) for fiscal year 2007. We assessed the reliability of these data by (1) reviewing existing information about the data and the databases that produced them, (2) interviewing agency officials knowledgeable about the data, and (3) performing electronic testing of data elements from DRLS and FACTS. We found the data in the FACTS database sufficiently reliable for our purposes. We also found that DRLS was sufficiently reliable, to the extent that it accurately reflects information provided by foreign establishments that register to market medical devices in the United States. However, we determined that these data do not necessarily reflect the number of establishments that manufacture medical devices for the U.S. market. In addition, we found that OASIS is likely to overestimate the number of foreign establishments whose medical devices have been imported into the United States because of uncorrected errors in the data. Therefore, we present information from both DRLS and OASIS to illustrate the variability in information that FDA's databases provide on this topic. These data represent the best information available and are what FDA relies on to manage its foreign medical device inspection activities. In addition, in preparation for our April 2008 statement, we obtained information from FDA officials to learn about recent initiatives to improve the agency's program for inspecting establishments manufacturing FDA-regulated products, including medical devices. For today's statement, we obtained additional data from FDA to update selected information from our January 2008 statement.

To examine FDA's programs for third-party inspections of foreign medical device manufacturing establishments, we updated work completed for our

¹⁰Within FDA, the Center for Biologics Evaluation and Research regulates medical devices involved in human immunodeficiency virus (HIV) testing and the collection, processing, testing, manufacture, and administration of licensed blood, blood components, and cellular products. We did not include medical devices regulated by this center in the scope of our work.

January 2008 statement. We obtained FDA data on the number of inspections conducted by accredited third parties from March 11, 2004—the date when FDA first cleared an accredited organization to conduct inspections—through May 7, 2008. For our January 2008 statement, we also obtained information from FDA about other critical aspects of its programs for inspections by accredited third parties. To gain perspective on recent changes to FDA’s programs for inspections by accredited third parties, we contacted representatives of the same 13 affected entities we interviewed for our January 2007 report on this topic.¹¹ We received responses from 2 of 4 accredited organizations, 1 of 6 medical device manufacturers, and 2 of 3 organizations that represent medical device manufacturers. We shared the facts contained in our current statement with FDA officials. FDA provided technical comments, which are appropriately addressed in the testimony. We conducted audit work for the January 2008 statement from December 2007 to January 2008; for our April 2008 statement, from March 2008 through April 2008; and updated our work on medical devices in early May 2008 for this statement. We conducted this work 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.

In summary, we found that FDA faces challenges in its program to inspect foreign establishments manufacturing medical devices. In January 2008, we testified that two databases that provide FDA with information about foreign medical device establishments and the products they manufacture for the U.S. market contained inaccurate information about establishments subject to FDA inspection and could not exchange information. Since then, FDA has made changes to its registration process that could improve its database and provide the agency with a more accurate count of foreign establishments that manufacture medical devices. While the agency has initiated other steps to improve its databases, it is too soon to know if these changes will improve FDA’s management of its foreign inspection program. Another challenge is that FDA conducts relatively few inspections of foreign establishments that manufacture medical devices. Officials estimated the agency had inspected foreign class II

¹¹These affected entities included accredited organizations, organizations that represent medical device manufacturers, and medical device manufacturers.

manufacturers every 27 years and foreign class III manufacturers every 6 years. Finally, inspections of foreign medical device manufacturing establishments pose unique challenges to FDA, such as difficulties in recruiting investigators to voluntarily travel to certain countries and in extending trips if problems are identified during inspections. FDA is pursuing initiatives that could address some of these challenges, but it is unclear whether the agency's proposals will increase the frequency with which FDA inspects foreign establishments.

Few inspections of foreign medical device manufacturing establishments have been conducted through FDA's two programs for inspections by accredited third parties—the Accredited Persons Inspection Program and PMAP. Under FDA's Accredited Persons Inspection Program, from March 11, 2004—the date when FDA first cleared an accredited organization to conduct inspections—through May 7, 2008, four inspections of foreign establishments had been conducted by accredited organizations. To participate in this program, manufacturers must decide to request an inspection by an accredited organization, and this decision might be influenced by both potential incentives and disincentives. An incentive to participation in the program is the opportunity to reduce the number of inspections conducted to meet FDA and other countries' requirements. Disincentives include bearing the cost for the inspection, particularly when the consequences of an inspection that otherwise may not occur in the near future could involve regulatory action. The Food and Drug Administration Amendments Act of 2007 (FDAAA) changed the requirements for inspections by accredited third parties in several ways, which could result in increased participation by manufacturers, although it is too soon to tell. For example, a requirement that foreign establishments be periodically inspected by FDA before being eligible for third-party inspections was eliminated. Device manufacturers may also request an inspection by an accredited third party through PMAP, which was established on September 7, 2006, and is limited to a partnership with Canada. As of May 7, 2008, two inspections of foreign establishments had been conducted by an accredited organization through PMAP. The small number of inspections completed by accredited third-party organizations raises questions about the practicality and effectiveness of these programs to help FDA conduct additional foreign inspections.

Background

FDA is responsible for overseeing the safety and effectiveness of medical devices that are marketed in the United States, whether manufactured in domestic or foreign establishments. All establishments that manufacture medical devices for marketing in the United States are required to register annually with FDA.¹² As part of its efforts to ensure the safety, effectiveness, and quality of medical devices, FDA is responsible for inspecting certain foreign and domestic establishments to ensure that, among other things, they meet manufacturing standards established in FDA's quality system regulation.¹³ Within FDA, CDRH is responsible for assuring the safety and effectiveness of medical devices. Among other things, CDRH works with ORA, which conducts inspections of foreign establishments. FDA may conduct inspections before and after medical devices are approved or otherwise cleared to be marketed in the United States.

- Premarket inspections are conducted before FDA approves U.S. marketing of a new medical device that is not substantially equivalent to one that is already on the market.¹⁴ Premarket inspections primarily assess manufacturing facilities, methods, and controls and may verify pertinent records.
- Postmarket inspections are conducted after a medical device has been approved or otherwise cleared to be marketed in the United States and include several types of inspections: (1) Quality system inspections are conducted to assess compliance with applicable FDA regulations, including the quality system regulation to ensure good manufacturing practices and the regulation requiring reporting of adverse events.¹⁵ These inspections may be comprehensive or abbreviated, which differ in the scope of inspectional activity. Comprehensive postmarket inspections

¹²21 U.S.C. § 360(b), (i).

¹³21 C.F.R. pt. 820 (2007). The quality system regulation requires, among other things, that domestic or foreign manufacturers have a quality system in place to implement current good manufacturing practices in the design, manufacture, packaging, labeling, storage, installation, and servicing of finished medical devices intended for human use in the United States. A quality system includes the organizational structure, responsibilities, procedures, processes, and resources for implementing quality management.

¹⁴Currently, most medical devices are cleared for marketing in the United States because they are determined to be "substantially equivalent" to a marketed device. FDA generally does not conduct premarket inspections of establishments manufacturing these types of medical devices.

¹⁵21 C.F.R. pt. 803 (2007).

assess multiple aspects of the manufacturer's quality system, including management controls, design controls, corrective and preventative actions, and production and process controls. Abbreviated postmarket inspections assess only some of these aspects, but always assess corrective and preventative actions. (2) For-cause and compliance follow-up inspections are initiated in response to specific information that raises questions or problems associated with a particular establishment. (3) Postmarket audit inspections are conducted within 8 to 12 months of a premarket application's approval to examine any changes in the design, manufacturing process, or quality assurance systems.

Requirements governing foreign and domestic inspections differ. Specifically, FDA is required to inspect domestic establishments that manufacture class II or III medical devices every 2 years.¹⁶ There is no comparable requirement to inspect foreign establishments. FDA does not have authority to require foreign establishments to allow the agency to inspect their facilities. However, if an FDA request to inspect is denied, FDA may prevent the importation of medical devices from that foreign establishment into the United States. In addition, FDA has the authority to conduct physical examinations of products offered for import and, if there is sufficient evidence of a violation, prevent their entry at the border.¹⁷ Unlike food, for which FDA primarily relies on inspections at the border, physical inspection of manufacturing establishments is a critical mechanism in FDA's process to ensure that medical devices are safe and effective and that manufacturers adhere to good manufacturing practices.

FDA determines which establishments to inspect using a risk-based strategy. High priority inspections include premarket approval inspections for class III devices, for-cause inspections, inspections of establishments that have had a high frequency of device recalls, and other devices and manufacturers FDA considers high risk. The establishment's inspection history may also be considered. A provision in FDAAA may assist FDA in making decisions about which establishments to inspect because this law authorizes the agency to accept voluntary submissions of audit reports

¹⁶21 U.S.C. § 360(h). There is no statutory requirement for inspection of class I medical device manufacturing establishments, and FDA does not routinely inspect them. However, FDA periodically inspects establishments manufacturing surgeon's gloves and patient examination gloves, which are both class I medical devices, due to ongoing problems with leakage. FDA also periodically inspects manufacturers of randomly selected class I devices.

¹⁷21 U.S.C. § 381(a); 21 C.F.R. § 820.1(d) (2007).

addressing manufacturers' conformance with internationally established standards for the purpose of setting risk-based inspectional priorities.¹⁸

FDA's programs for foreign and domestic inspections by accredited third parties provide an alternative to the traditional FDA-conducted comprehensive postmarket quality system inspection for eligible manufacturers of class II and III medical devices. MDUFMA required FDA to accredit third persons—which are organizations—to conduct inspections of certain establishments. In describing this requirement, the House of Representatives Committee on Energy and Commerce noted that some manufacturers have faced an increase in the number of inspections required by foreign countries and that the number of inspections could be reduced if the manufacturers could contract with a third-party organization to conduct a single inspection that would satisfy the requirements of both FDA and foreign countries.¹⁹ Manufacturers that meet eligibility requirements may request a postmarket inspection by an FDA-accredited organization.²⁰ The eligibility criteria for requesting an inspection of an establishment by an accredited organization include that the manufacturer markets a medical device in the United States and markets (or intends to market) a medical device in at least one other country and that the establishment to be inspected must not have received warnings for significant deviations from compliance requirements on its last inspection.²¹

¹⁸Pub. L. No. 110-85, § 228, 121 Stat. 823, 858 (2007).

¹⁹H.R. Rep. No. 107-728, pt. 1, at 32-36 (2002). Some foreign countries have accredited, certified, or otherwise recognized organizations to conduct inspections. We use the term “single inspection” to mean a complete inspection that covers all requirements of two or more countries, without repeating those activities covered under more than one set of requirements. A complete inspection can be conducted during a single block of time or in multiple phases. Two or more separate inspection reports could be generated on the basis of that single inspection.

²⁰Accredited organizations may conduct comprehensive postmarket quality system inspections, but not other types of inspections of establishments that FDA has the authority to conduct, such as premarket or for-cause inspections. FDA may conduct its own inspections of establishments even after inspection by an accredited organization.

²¹See 21 U.S.C. § 374(g)(6). FDAAA eliminated certain previously established eligibility requirements. For example, it eliminated a limitation on the number of consecutive inspections allowed by an accredited organization and a limitation that foreign establishments must be inspected periodically by FDA.

MDUFMA also established minimum requirements for organizations to be accredited to conduct third-party inspections, including protections against financial conflicts of interest and assurances of the competence of the organization to conduct inspections. FDA developed a training program for inspectors from accredited organizations that involves both formal classroom training and completion of three joint training inspections with FDA. Each individual inspector from an accredited organization must complete all training requirements successfully before being cleared to conduct independent inspections. FDA relies on manufacturers to volunteer to host these joint inspections, which count as FDA postmarket quality system inspections.

A manufacturer that is cleared to have an inspection by an accredited third party enters an agreement with the approved accredited organization and schedules an inspection. Once the accredited organization completes its inspection, it prepares a report and submits it to FDA, which makes the final assessment of compliance with applicable requirements. FDAAA added a requirement that accredited organizations notify FDA of any withdrawal, suspension, restriction, or expiration of certificate of conformance with quality systems standards (such as those established by the International Organization for Standardization) for establishments they inspected for FDA.²²

In addition to the Accredited Persons Inspection Program, FDA has a second program for accredited third-party inspections of medical device establishments. On September 7, 2006, FDA and Health Canada announced the establishment of PMAP. This pilot program was designed to allow qualified third-party organizations to perform a single inspection that would meet the regulatory requirements of both the United States and Canada. The third-party organizations eligible to conduct inspections through PMAP are those that FDA accredited for its Accredited Persons Inspection Program (and that completed all required training for that program) and that are also authorized to conduct inspections of medical device establishments for Health Canada. To be eligible to have a third-party inspection through PMAP, manufacturers must meet all criteria established for the Accredited Persons Inspection Program. As with the Accredited Persons Inspection Program, manufacturers must apply to participate and be willing to pay an accredited organization to conduct the inspection.

²²21 U.S.C. § 374(g)(3)(F).

FDA relies on multiple databases to manage its program for inspecting medical device manufacturing establishments.

- FDA's medical device registration and listing database contains information on domestic and foreign medical device establishments that have registered with FDA. Establishments that are involved in the manufacture of medical devices intended for commercial distribution in the United States are required to register annually with FDA. These establishments provide information to FDA, such as an establishment's name and its address and the medical devices it manufactures. Prior to October 1, 2007, this information was maintained in DRLS. As of October 1, 2007, establishments are required to register electronically through FDA's Unified Registration and Listing System and certain medical device establishments pay an annual establishment registration fee, which in fiscal year 2008 is \$1,706.²³
- OASIS contains information on medical devices and other FDA-regulated products imported into the United States, including information on the establishment that manufactured the medical device. The information in OASIS is automatically generated from data managed by Customs and Border Protection (CBP). These data are originally entered by customs brokers based on the information available from the importer.²⁴ CBP specifies an algorithm by which customs brokers generate a manufacturer identification number from information about an establishment's name, address, and location.
- FACTS contains information on FDA's inspections, including those of domestic and foreign medical device establishments. FDA investigators enter information into FACTS following completion of an inspection.

²³21 U.S.C. §§ 360(i)(1), (p), 379i(13), 379j(a)(3), (b), (h). The registration user fee will increase by 8.5 percent per year, to \$2,364 in fiscal year 2012. Fees are available for obligation only to the extent and in the amount provided in advance in annual appropriations acts. FDA's authority to assess registration fees terminates on October 1, 2012. Pub. L. No. 110-85, § 217; 121 Stat. 823, 852 (2007).

²⁴Customs brokers are private individuals, partnerships, associations, or corporations licensed, regulated, and empowered by CBP to assist in meeting federal requirements governing imports and exports.

According to FDA data, there are more registered establishments in China and Germany reporting that they manufacture class II or III medical devices than in any other foreign countries.²⁵ Canada and the United Kingdom also have a large number of registered establishments.

FDA Faces Challenges Conducting Inspections of Foreign Establishments That Manufacture Medical Devices

FDA faces challenges in its program to inspect foreign establishments manufacturing medical devices. The databases that provide FDA with data about the number of foreign establishments manufacturing medical devices for the U.S. market have not provided it with an accurate count of foreign establishments for inspection. In addition, FDA conducted relatively few inspections of foreign establishments. Moreover, inspections of foreign medical device manufacturing establishments pose unique challenges to FDA—both in human resources and logistics.

FDA Lacks Accurate Data on the Number of Foreign Establishments Subject to Inspection, but Has Made Recent Attempts to Improve Its Data

FDA's databases on registration and imported medical devices have not provided an accurate count of establishments subject to inspection, although recent improvements to FDA's medical device registration database may address some weaknesses. In January 2008, we testified that DRLS provided FDA with information about foreign medical device establishments and the products they manufacture for the U.S. market. According to DRLS, as of September 2007, 4,983 foreign establishments that reported manufacturing a class II or III medical device for the U.S. market had registered with FDA.²⁶ However, these data contained inaccuracies because establishments may register with FDA but not actually manufacture a medical device or may manufacture a medical device that is not marketed in the United States. In addition, FDA did not routinely verify the data within this database.

Recent changes to FDA's medical device establishment registration process could improve the accuracy of its database. In fiscal year 2008, FDA implemented, in addition to its annual user fee, electronic

²⁵Counts of registered establishments in China do not include establishments registered in Hong Kong or Taiwan as these establishments are tracked separately.

²⁶DRLS contained one additional registered establishment for which location information was not available.

registration and an active re-registration process for medical device establishments.²⁷ According to FDA, about half of previously registered establishments had reregistered using the new system as of April 11, 2008.²⁸ While FDA officials expect that additional establishments will reregister, they expect that the final result will be the elimination of establishments that do not manufacture medical devices for the U.S. market and thus a smaller, more accurate database of medical device establishments. FDA officials indicated that implementation of electronic registration and the annual user fee seemed to have improved the data so FDA can more accurately identify the type of establishment registered, the devices manufactured at an establishment, and whether or not an establishment should be registered. According to FDA officials, the revenue from device registration user fees is applied to the process for the review of device applications, including premarket inspections.²⁹

FDA has also proposed, but not yet implemented, the Foreign Vendor Registration Verification Program, which could also help improve the accuracy of information FDA maintains on registered foreign establishments. Through this program, FDA plans to contract with an external organization to conduct on-site verification of the registration data and product listing information of foreign establishments shipping medical devices and other FDA-regulated products to the United States. FDA has solicited proposals for this contract, but it is still developing the specifics of the program. For example, as of April 2008, the agency had not yet established the criteria it would use to determine which establishments would be visited for verification purposes or determined how many establishments it would verify annually. FDA plans to award this contract in June 2008. Given the early stages of this process, it is too soon to

²⁷FDA indicated that it will deactivate the registrations of those establishments that fail to complete the annual registration. Officials noted that many establishments that had previously registered had not updated those registrations in several years.

²⁸According to FDA, the agency sent letters on April 11, 2008 and April 14, 2008 to establishments that had registered in the past but had not completed their registration for fiscal year 2008 advising them that they must register using the new system and must pay the registration fee, if applicable, to be considered registered. Establishments that do not reregister within a month of those letters would be considered inactive. As of May 6, 2008, prior to the mid-May deadline, FDA reported that 4,284 registered foreign establishments reported that they manufacture class II or class III medical devices. This total also includes some establishments that may not reregister.

²⁹See 21 U.S.C. §§ 379i(8), 379j(h)(1), (2).

determine whether this program will improve the accuracy of the data FDA maintains on foreign medical device establishments.

FDA also obtains information on foreign establishments from OASIS, which tracks the importation of medical devices and other FDA-regulated products. While not intended to provide a count of establishments, OASIS does contain information about the medical devices actually being imported into the United States and the establishments manufacturing them. However, inaccuracies in OASIS prevent FDA from using it to develop a list of establishments subject to inspection. OASIS contains an inaccurate count of foreign establishments manufacturing medical devices imported into the United States as a result of unreliable identification numbers generated by customs brokers when the product is offered for entry.³⁰ FDA officials told us that these errors result in the creation of multiple records for a single establishment, which results in inflated counts of establishments offering medical devices for entry into the U.S. market. According to OASIS, in fiscal year 2007, there were as many as 22,008 foreign establishments that manufactured class II medical devices for the U.S. market and 3,575 foreign establishments that manufactured class III medical devices for the U.S. market.³¹

FDA has supported a proposal with the potential to address weaknesses in OASIS, but FDA does not control the implementation of this proposed change. FDA is pursuing the creation of a governmentwide unique establishment identifier, as part of the Shared Establishment Data Service (SEDS), to address these inaccuracies.³² Rather than relying on the creation and entry of an identifier at the time of import, SEDS would provide a unique establishment identifier and a centralized service to provide commercially verified information about establishments.³³ The

³⁰The algorithm currently used by customs brokers to assign the manufacturer identification number does not provide for a number that is reliably reproduced or inherently unique.

³¹According to FDA officials, a single establishment could be manufacturing more than one class of device.

³²The SEDS concept was developed by a working group with representatives from FDA, the Environmental Protection Agency, and the departments of Agriculture, Commerce, Defense, and Homeland Security.

³³If an establishment did not already have an identification number, it would request an identification number through SEDS, which would verify the data about the establishment through a commercial service. This commercial service would provide researched and validated records on domestic and foreign establishments.

standard identifier would be submitted as part of import entry data when required by FDA or other government agencies. SEDS could thus eliminate the problems that have resulted in multiple identifiers associated with an individual establishment. The implementation of SEDS is dependent on action from multiple federal agencies, including the integration of the concept into a CBP import and export system under development and scheduled for implementation in 2010. In addition, once implemented by CBP, participating federal agencies would be responsible for bearing the cost of integrating SEDS with their own operations and systems. FDA officials are not aware of a specific time line for the implementation of SEDS. Developing an implementation plan for SEDS was recommended by the Interagency Working Group on Import Safety.³⁴

Although comparing information from its registration and import databases could help FDA determine the number of foreign establishments marketing medical devices in the United States, the databases do not exchange information to be compared electronically and any comparisons are done manually. FDA is in the process of implementing additional initiatives to improve the integration of its databases, and these changes could make it easier for the agency to establish an accurate count of foreign manufacturing establishments subject to inspection. The agency's Mission Accomplishments and Regulatory Compliance Services (MARCS) is intended to help FDA electronically integrate data from multiple systems. It is specifically designed to give individual users more complete information about establishments. FDA officials estimated that MARCS, which is being implemented in stages, could be fully implemented by 2011 or 2012. However, FDA officials told us that implementation has been slow because the agency has been forced to shift resources away from MARCS and toward the maintenance of current systems that are still heavily used, such as FACTS and OASIS. Taken together, changes to FDA's databases could provide the agency with more accurate information on the number of establishments subject to inspection. However, it is too early to tell whether this will improve FDA's management of its inspection program.

³⁴Interagency Working Group on Import Safety, *Action Plan for Import Safety: A Roadmap for Continual Improvement* (Nov. 2007) (www.importsafety.gov/report/actionplan.pdf, accessed May 6, 2008).

FDA Inspects Relatively Few Foreign Medical Device Establishments

From fiscal year 2002 through fiscal year 2007, FDA inspected relatively few foreign medical device establishments and primarily inspected establishments located in the United States. During this period, FDA conducted an average of 247 foreign establishment inspections each year, compared to 1,494 inspections of domestic establishments.³⁵ This average number of foreign inspections suggests that each year FDA inspects about 6 percent of registered foreign establishments that reported manufacturing class II or class III medical devices.³⁶ FDA officials estimated the agency had inspected foreign class II manufacturers every 27 years and foreign class III manufacturers every 6 years. The inspected foreign establishments were in 44 foreign countries and more than two-thirds were in 10 countries. Most of the countries with the highest number of inspections were also among those with the largest number of registered establishments that reported manufacturing class II or III medical devices. The lowest rate of inspections in these 10 countries was in China, where 64 inspections were conducted in this 6-year period and 568 establishments were registered as of May 6, 2008. (See table 1.)

³⁵We were unable to differentiate inspections according to medical device classification. FDA's inspection database contains the most recent information available to FDA about the class of device manufactured at the establishment and consequently does not contain readily available information about the class of devices manufactured at the time of a specific inspection. As a result, the data we present include all inspections, regardless of the classification of the manufactured device or devices. According to FDA officials, FDA primarily conducts inspections of establishments manufacturing class II or III medical devices.

³⁶This calculation is based on the 4,284 registered establishments that reported that they manufacture class II or III medical devices, as of May 6, 2008.

Table 1: Number of FDA Inspections of Foreign Medical Device Establishments, Fiscal Year 2002 through Fiscal Year 2007

Country	Number of inspections ^a							Total	Number of registered class II or III manufacturing establishments ^b
	FY 2002	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007			
Germany	39	30	34	51	25	52	231	460	
United Kingdom	25	31	28	14	25	43	166	277	
Canada	17	17	24	11	13	26	108	282	
Japan	7	8	20	21	16	25	97	210	
Ireland	15	22	13	13	16	11	90	62	
France	16	14	17	14	12	10	83	154	
Switzerland	6	12	19	9	7	18	71	108	
China ^c	0	0	21	19	11	13	64	568 ^d	
Mexico	10	7	12	8	12	11	60	122	
Italy	8	7	10	6	13	11	55	170	
All other countries	66	83	102	67	69	69	456	1,871	
Total	209	231	300	233	219	289	1,481	4,284	

Source: GAO analysis of FDA data.

^aWe were unable to differentiate inspections according to medical device classification. FDA's inspection database contains the most recent information available to FDA about the class of device manufactured at the establishment and consequently does not contain readily available information about the class of devices manufactured at the time of a specific inspection. As a result, the data we present include all inspections, regardless of the classification of the manufactured device or devices. According to FDA officials, FDA primarily conducts inspections of establishments manufacturing class II or III medical devices.

^bThese counts represent the number of registered establishments as of May 6, 2008.

^cThe inspection counts for China do not include inspections conducted in Hong Kong or Taiwan because these inspections are tracked separately in FACTS.

^dCounts of registered establishments in China do not include establishments registered in Hong Kong or Taiwan because these establishments are tracked separately.

FDA's inspections of foreign medical device establishments were primarily postmarket inspections. While premarket inspections were generally FDA's highest priority, relatively few have had to be performed in any given year.³⁷ Therefore, FDA focused its resources on postmarket

³⁷Currently, most medical devices are cleared for marketing in the United States because they are determined to be "substantially equivalent" to a marketed device. FDA generally does not conduct premarket inspections of establishments manufacturing these types of medical devices.

inspections. From fiscal year 2002 through fiscal year 2007, 89 percent of the 1,481 foreign establishment inspections were for postmarket purposes.

FDA Faces Unique Challenges in Conducting Foreign Inspections

Inspections of foreign establishments pose unique challenges to FDA—both in human resources and logistics. FDA does not have a dedicated cadre of investigators that only conduct foreign medical device establishment inspections; those staff who inspect foreign establishments also inspect domestic establishments. Among those qualified to inspect foreign establishments,³⁸ FDA relies on staff to volunteer to conduct inspections. FDA officials told us that it has been difficult to recruit investigators to voluntarily travel to certain countries. However, they added that if the agency could not find an individual to volunteer for a foreign inspection trip, it would mandate the travel. Logistically, foreign medical device establishment inspections are difficult to extend even if problems are identified because the trips are scheduled in advance.³⁹ Foreign medical device establishment inspections are also logistically challenging because investigators do not receive independent translational support from FDA or the State Department and may rely on English-speaking employees of the inspected establishment or the establishment's U.S. agent to translate during an inspection.

FDA recently announced proposals to address some of the challenges unique to conducting foreign inspections, but specific steps toward implementation and associated time frames are unclear. FDA noted in its report on revitalizing ORA that it was exploring the creation of a cadre of investigators who would be dedicated to conducting foreign inspections.⁴⁰ However, the report did not provide any additional details or time frames about this proposal. In addition, FDA announced plans to establish a permanent presence overseas, although little information about these plans is available. FDA intends that its foreign offices will improve cooperation and information exchange with foreign regulatory bodies,

³⁸Staff members must meet certain criteria in terms of their experience and training to conduct inspections of foreign establishments. For example, they are required to take certain training courses and have at least 3 years of experience conducting domestic inspections before they can be considered qualified to conduct a foreign inspection.

³⁹Typically, FDA investigators travel abroad for about 3 weeks at a time, during which they inspect approximately three establishments.

⁴⁰See, for example, Food and Drug Administration, *Revitalizing ORA: Protecting the Public Health Together In a Changing World* (Rockville, Md.: January 2008).

improve procedures for expanded inspections, allow it to inspect facilities quickly in an emergency, and facilitate work with private and government agencies to assure standards for quality. FDA's proposed foreign offices are intended to expand the agency's capacity for overseeing, among other things, medical devices, drugs, and food that may be imported into the United States. The extent to which the activities conducted by foreign offices are relevant to FDA's foreign medical device inspection program is uncertain. Initially, FDA plans to establish a foreign office in China with three locations—Beijing, Shanghai, and Guangzhou—comprised of a total of eight FDA employees and five Chinese nationals. The Beijing office, which the agency expects will be partially staffed by the end of 2008, will be responsible for coordination between FDA and Chinese regulatory agencies. FDA staff located in Shanghai and Guangzhou, who are to be hired in 2009, will be focused on conducting inspections and working with Chinese inspectors to provide training as necessary. FDA noted that the Chinese nationals will primarily provide support to FDA staff, including translation and interpretation. The agency is also considering setting up offices in other locations, such as India, the Middle East, Latin America, and Europe, but no dates have been specified. While the establishment of both a foreign inspection cadre and offices overseas have the potential for improving FDA's oversight of foreign establishments, it is too early to tell whether these steps will be effective or will increase the number of foreign medical device establishment inspections.

Few Inspections of Foreign Establishments Have Been Conducted Through FDA's Third-Party Programs, but Recent Changes Could Eliminate Some Obstacles to Manufacturers' Participation

Few inspections of foreign medical device manufacturing establishments—a total of six—have been conducted through FDA's two accredited third-party inspection programs, the Accredited Persons Inspection Program and PMAP. FDAAA specified several changes to the requirements for inspections by accredited third parties that could result in increased participation by manufacturers.

Few inspections have been conducted through FDA's Accredited Persons Inspection Program since March 11, 2004—the date when FDA first cleared an accredited organization to conduct independent inspections. Through May 7, 2008, four inspections of foreign establishments had been conducted independently by accredited organizations.⁴¹

As of May 7, 2008, 16 third-party organizations were accredited, and individuals from 8 of these organizations had completed FDA's training requirements and been cleared to conduct independent inspections.⁴² FDA and accredited organizations had conducted 44 joint training inspections. As we previously reported, fewer manufacturers volunteered to host training inspections than have been needed for all of the accredited organizations to complete their training,⁴³ and scheduling these joint training inspections has been difficult. FDA officials told us that, when appropriate, staff are instructed to ask manufacturers to host a joint training inspection at the time they notify the manufacturers of a pending inspection. FDA schedules inspections a relatively short time prior to an actual inspection,⁴⁴ and as we previously reported, some accredited

⁴¹Two inspections of domestic establishments were also conducted through FDA's Accredited Persons Inspection Program.

⁴²Specific foreign jurisdictions that have certified, accredited, or otherwise recognized one or more of the FDA-accredited organizations that have been cleared to conduct independent inspections include all member states of the European Community, Australia, Canada, New Zealand, Norway, Taiwan, and the United Kingdom. Of the eight third-party organizations that have been cleared to conduct independent inspections through the Accredited Persons Inspection Program, four may conduct inspections through PMAP.

⁴³As we reported in January 2007, some representatives of affected entities speculated that manufacturers might not have volunteered to host training inspections because they believed that training inspections would require more time and effort for their staff (and would thus be more disruptive) than inspections conducted by fully trained personnel, or that manufacturers might have believed that training inspections would be more rigorous than nontraining inspections if the trainees and FDA personnel were to take particular care to demonstrate their thoroughness to each other.

⁴⁴FDA generally notifies manufacturers about a week in advance of postmarket quality system inspections of domestic establishments and about 6 to 8 weeks in advance of postmarket quality system inspections of foreign establishments.

organizations have not been able to participate because they had prior commitments.

We previously reported that manufacturers' decisions to request an inspection by an accredited organization might be influenced by both potential incentives and disincentives. According to FDA officials and representatives of affected entities, potential incentives to participation include the opportunity to reduce the number of inspections conducted to meet FDA and other countries' requirements. For example, one inspection conducted by an accredited organization was a single inspection designed to meet the requirements of FDA, the European Union, and Canada. Another potential incentive mentioned by FDA officials and representatives of affected entities is the opportunity to control the scheduling of the inspection by an accredited organization by working with the accredited organization. FDA officials and representatives of affected entities also mentioned potential disincentives to having an inspection by an accredited organization. These potential disincentives include bearing the cost for the inspection,⁴⁵ doubts about whether accredited organizations can cover multiple requirements in a single inspection, and uncertainty about the potential consequences of an inspection that otherwise may not occur in the near future—consequences that could involve regulatory action.

Changes specified by FDAAA have the potential to eliminate certain obstacles to manufacturers' participation in FDA's programs for inspections by accredited third parties that were associated with manufacturers' eligibility. For example, a requirement that foreign establishments be periodically inspected by FDA before being eligible for third-party inspections was eliminated. Representatives of the two organizations that represent medical device manufacturers with whom we spoke about FDAAA told us that the changes in eligibility requirements could eliminate certain obstacles and therefore potentially increase manufacturers' participation. These representatives also noted that key incentives and disincentives to manufacturers' participation remain. FDA

⁴⁵In January 2007, we reported that representatives of accredited organizations indicated that the cost to manufacturers would vary depending on such factors as the size of the manufacturer and how much extra time would be required to assess compliance with FDA requirements. Representatives suggested that covering FDA's requirements could take 2 or more days in addition to the time spent assessing other countries' requirements, plus time for advance preparation and writing the inspection report. They speculated that they would probably charge manufacturers from \$1,700 to \$2,500 per day, plus the cost of travel and living expenses.

officials told us that they were revising their guidance to industry in light of FDAAA and expected to issue the revised guidance during fiscal year 2008.⁴⁶ It is too soon to tell what impact these changes will have on manufacturers' participation.

FDA officials have acknowledged that manufacturers' participation in the Accredited Persons Inspection Program has been limited. In December 2007, FDA established a working group to assess the successes and failures of this program and to identify ways to increase participation. Representatives of two organizations that represent medical device manufacturers told us that they believe manufacturers remain interested in the Accredited Persons Inspection Program. The representative of one large, global manufacturer of medical devices told us that it was in the process of arranging to have 20 of its domestic and foreign device manufacturing establishments inspected by accredited third parties.

As of May 7, 2008, two inspections of foreign establishments had been conducted through PMAP,⁴⁷ FDA's second program for inspections by accredited third parties. Although it is too soon to tell what the benefits of PMAP will be, the program is more limited than the Accredited Persons Inspection Program and may pose additional disincentives to participation by both manufacturers and accredited organizations. Specifically, inspections through PMAP would be designed to meet the requirements of the United States and Canada, whereas inspections conducted through the Accredited Persons Inspection Program could be designed to meet the requirements of other countries. In addition, two of the five representatives of affected entities whom we spoke to for our January 2008 statement noted that in contrast to inspections conducted through the Accredited Persons Inspection Program, inspections conducted through PMAP could undergo additional review by Health Canada. Health Canada will review inspection reports submitted through this pilot program to ensure the inspections meet its standards. This extra review poses a greater risk of unexpected outcomes for the manufacturer and the accredited organization, which could be a disincentive to participation in PMAP that is not present with the Accredited Persons Inspection Program.

⁴⁶As of May 6, 2008, this guidance had not been issued.

⁴⁷Three inspections of domestic establishments were conducted through PMAP.

Concluding Observations

Americans depend on FDA to ensure the safety and effectiveness of medical devices manufactured throughout the world. A variety of medical devices are manufactured in other countries, including high-risk devices designed to be implanted or used in invasive procedures. However, FDA faces challenges in inspecting foreign establishments. Weaknesses in its database prevent it from accurately identifying foreign establishments manufacturing medical devices for the United States and prioritizing those establishments for inspection. In addition, staffing and logistical difficulties associated with foreign inspections complicate FDA's ability to conduct such inspections. The agency has recently taken some positive steps to improve its foreign inspection program, such as initiating changes to improve the accuracy of the data it uses to manage this program and announcing plans to increase its presence overseas. However, it is too early to tell whether these steps will ultimately enhance the agency's ability to select establishments to inspect and increase the number of foreign establishments inspected. To date, FDA's programs for inspections by accredited third parties have not assisted FDA in meeting its regulatory responsibilities nor have these programs provided a rapid or substantial increase in the number of inspections performed by these organizations, as originally intended. Recent statutory changes to the requirements for inspections by accredited third parties may encourage greater participation in these programs. However, the lack of meaningful progress in conducting inspections to this point raises questions about the practicality and effectiveness of these programs to help FDA conduct additional foreign inspections.

Mr. Chairman, this completes my prepared statement. I would be happy to respond to any questions you or the other Members of the subcommittee may have at this time.

Contacts and Acknowledgments

For further information about this statement, please contact Marcia Crosse at (202) 512-7114 or crossem@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may found on the last page of this statement. Geraldine Redican-Bigott, Assistant Director; Kristen Joan Anderson; Katherine Clark; William Hadley; Cathleen Hamann; Julian Klazkin; and Lisa Motley made key contributions to this statement.

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