United States Government Accountability Office

GAO

Report to Congressional Requesters

June 2009

FOOD AND DRUG ADMINISTRATION

FDA Faces Challenges Meeting Its Growing Medical Product Responsibilities and Should Develop Complete Estimates of Its Resource Needs

GAO-09-581

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Highlights

Highlights of GAO-09-581, a report to congressional requesters

Why GAO Did This Study

Twenty years ago, GAO reported that the Food and Drug Administration (FDA) was concerned that it lacked resources to fulfill its mission, which includes oversight of the safety and effectiveness of medical products—human drugs, biologics, and medical devices—marketed for sale in the United States. Since then, FDA, GAO, and others have raised concerns regarding FDA's ability to meet its oversight responsibilities.

GAO was asked to review the resources supporting FDA's medical product oversight responsibilities. GAO examined trends in (1) FDA's funding and staffing resources for its medical product oversight responsibilities from fiscal years 1999 through 2008, and (2) FDA's medical product oversight responsibilities during this same period. GAO analyzed FDA data on the agency's resources and workload, reviewed relevant federal laws, and interviewed FDA officials. GAO also examined more-detailed data on FDA's fiscal year 2004 through 2008 resources and workload in four key areas, representing a range of FDA's oversight responsibilities, both before and after a medical product is marketed in the United States.

What GAO Recommends

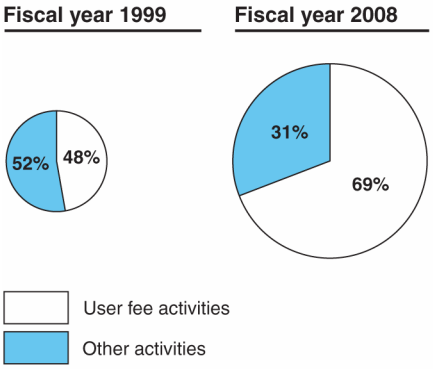
GAO recommends that the Commissioner of FDA take steps to establish a comprehensive and reliable basis for substantiating the agency's resource needs. FDA agreed with our recommendations.

View GAO-09-581 or key components.
For more information, contact Marcia Crosse at (202) 512-7114 or crossem@gao.gov.

What GAO Found

Funding and staffing resources for FDA's medical product programs increased between fiscal years 1999 and 2008, primarily as a result of increased user fees paid by industry, which are made available through appropriations acts to support the agency's processes for reviewing new medical products. Total funding increased from about $562 million in fiscal year 1999 to about $1.2 billion in fiscal year 2008, with user fee funding accounting for more than half of this increase. A large and growing portion of funding supported activities for which user fees are collected, resulting in a declining share of funding available for other activities. FDA officials said that this has seriously limited the agency's ability to fulfill its oversight responsibilities in some areas, particularly those not funded with user fees.

Portion of Total Medical Product Program Funding Allocated to User Fee and Other Activities, Fiscal Years 1999 and 2008



Source: GAO analysis of FDA data.

FDA faced challenges fulfilling and managing its growing medical product oversight responsibilities, which agency officials attributed to resource constraints. FDA's statutory responsibilities grew during this period and a growing number of medical products subject to FDA oversight and establishments manufacturing these products for the U.S. market also added to the agency's workload. However, FDA could not provide data showing its workload and accomplishments in some areas, such as its review of reports identifying potential safety issues with specific medical products. Without such information, FDA cannot develop complete and reliable estimates of its resource needs. While FDA officials said that the funding amounts requested for and provided to FDA during the past 2 years will permit the agency to respond to its most urgent needs and priorities, officials also noted that they did not receive enough resources to meet some statutory requirements, such as biennially inspecting certain manufacturing establishments. Furthermore, officials said that the agency faces significant challenges fulfilling its mission to oversee the safety and effectiveness of medical products.

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Abbreviations

ANDA	abbreviated new drug application
BLA	biologics license application
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CRS	Congressional Research Service
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FTE	full-time equivalent
GDP	gross domestic product
HHS	Department of Health and Human Services
IND	investigational new drug
MDUFMA	Medical Device User Fee and Modernization Act of 2002
NDA	new drug application
OMB	Office of Management and Budget
ORA	Office of Regulatory Affairs
PDUFA	Prescription Drug User Fee Act of 1992
PREA	Pediatric Research Equity Act of 2003

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United States Government Accountability Office
Washington, DC 20548

June 19, 2009

Congressional Requesters

Twenty years ago, we reported that the Food and Drug Administration (FDA), an agency of the Department of Health and Human Services (HHS), was concerned that it lacked sufficient funding and staffing resources.[1] FDA reported that its lack of resources prevented it from adequately fulfilling its mission, which includes overseeing the safety and effectiveness of medical products—human drugs, biologics,[2] and medical devices[3]—marketed for sale in the United States.[4] We concluded that, while the agency was experiencing significant resource challenges, it lacked a comprehensive and reliable basis to substantiate its estimates of resource requirements. On several occasions since then, senior FDA officials have testified before Congress and the agency issued a report noting that the agency's funding and staffing resources do not enable it to meet its growing oversight responsibilities.[5]

Lingering questions regarding the agency's resources have added to concerns about FDA's ability to protect Americans from unsafe and ineffective medical products. FDA's Science Board reported in November 2007 that the agency could not fulfill its growing responsibilities because it

[1]GAO, *FDA Resources: Comprehensive Assessment of Staffing, Facilities, and Equipment Needed*, GAO/HRD-89-142 (Washington, D.C.: Sept. 15, 1989).

[2]Biologics are derived from living sources (such as humans, animals, and microorganisms), unlike drugs, which are chemically synthesized. Biologics include blood, vaccines, allergenic products, certain tissues, and cellular and gene therapies. 42 U.S.C. § 262(i).

[3]Medical 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).

[4]FDA considers oversight of animal drugs and feeds, and research conducted by FDA's National Center for Toxicological Research, among its medical product responsibilities. We have excluded these efforts from the definition of medical product oversight used in this report.

[5]For example, see Statement of Michael A. Friedman, FDA Deputy Commissioner for Operations, before the Committee on Labor and Human Resources, United States Senate (Washington, D.C.: Mar. 19, 1997); Statement of Jane E. Henney, FDA Commissioner, before the Subcommittee on Oversight and Investigations, Committee on Commerce, House of Representatives (Washington, D.C.: Oct. 3, 2000); and FDA, *FDA's Growing Responsibilities for the Year 2001 and Beyond* (Rockville, Md.: June 13, 2001).

did not have sufficient resources.[6] In fiscal years 2007 and 2008, the HHS Office of Inspector General listed FDA's oversight of drug and device safety as one of the department's top management and performance challenges in HHS' annual financial reports.[7] And in January 2009, we added FDA's oversight of medical products to our High-Risk Series, which is intended to raise the priority and visibility of government programs that are in need of broad-based transformation to address major economy, efficiency, or effectiveness challenges.[8]

To enhance its ability to meet its mission, particularly to address challenges related to the globalization of medical product development and manufacturing, FDA requested an additional appropriation from Congress in May 2008. This request was designed to supplement resources for, among other things, FDA's three medical product programs—the drugs, biologics, and devices programs. In June 2008, the administration officially amended its fiscal year 2009 budget request for FDA to include an additional $100 million for these programs.

Questions have been raised regarding the sufficiency of the resources available to FDA to fulfill its medical product oversight responsibilities, including recurring responsibilities required by statute, such as inspecting certain manufacturing establishments at prescribed intervals. This report examines (1) trends in FDA's funding and staffing resources for its medical product programs from fiscal year 1999 through fiscal year 2008, and (2) trends in FDA's medical product oversight responsibilities from fiscal year 1999 through fiscal year 2008.

To examine trends in FDA's funding and staffing resources, we reviewed funding and staffing data as reported in FDA's congressional budget justifications for the agency's medical product programs from fiscal years 1999 through 2008. We compared changes in funding for FDA's medical product programs to the 10-year inflation rate as measured by the gross

[6]FDA's Science Board, an advisory board to the FDA commissioner, provides advice on, among other things, specific complex and technical issues as well as emerging issues within the scientific community, in industry, and in academia. See FDA Science Board, Subcommittee on Science and Technology, *FDA Science and Mission at Risk* (Rockville, Md.: November 2007).

[7]U.S. Department of Health and Human Services, *Agency Financial Report: Fiscal Year 2007* (Washington, D.C.: Nov. 15, 2007), and U.S. Department of Health and Human Services, *Agency Financial Report: Fiscal Year 2008* (Washington, D.C.: Nov. 17, 2008).

[8]GAO, *High-Risk Series: An Update*, GAO-09-271 (Washington, D.C.: January 2009).

domestic product (GDP) price index for nondefense goods and services.[9] We reviewed Office of Management and Budget (OMB) data on HHS and federal government funding for fiscal years 1999 through 2008 and compared trends in HHS and federal government funding to trends in FDA funding over this period. We reported staffing resources by the number of full-time equivalent (FTE) staff; one FTE represents 40 hours of work per week conducted by a federal government employee over the course of 1 year. FTEs do not include contractors and therefore provide a partial measure of staffing resources. We reviewed HHS' online employee directory as of March 2009 to obtain an estimate of the number of contractors working with FDA's medical product programs. We also interviewed FDA officials regarding trends in hiring, retention, and retirement, and the effect of funding and staffing resource trends on the agency's ability to meet its medical product oversight responsibilities. To supplement our analysis of trends in FDA's resources from fiscal years 1999 through 2008, we obtained and reviewed more-detailed data on how the agency used its funding and staffing resources for specific activities within the three medical product programs during a shorter time period, fiscal years 2004 through 2008. For these areas, we compared changes in funding levels to the 5-year inflation rate as measured by the GDP price index.

To examine trends in FDA's medical product oversight responsibilities from fiscal year 1999 through fiscal year 2008, we reviewed changes in the volume of work that FDA was responsible for conducting related to its oversight of medical products. To determine if FDA's responsibilities changed during this time period, we reviewed FDA documents and Congressional Research Service (CRS) reports identifying laws that affected FDA's medical product responsibilities and we also examined those federal laws. We did not conduct a comprehensive search of all federal laws. To review trends in the volume of FDA's work related to its oversight responsibilities, we analyzed FDA data on the number of medical product applications and other materials submitted to the agency for review between fiscal years 1999 and 2008. We also reviewed FDA data on the cumulative number of medical products approved or cleared for marketing in the United States and the number of establishments registered with the agency to produce marketed medical products—a proxy for the number of establishments subject to FDA oversight and

[9]The GDP price index for nondefense goods and services measures the change in the value of nondefense related goods and services produced by the U.S. economy in a given period.

inspection—in fiscal years 1999 and 2008.[10] We interviewed FDA officials to obtain detailed information on how changes in the agency's medical product oversight responsibilities affected the amount of work it conducted over this 10-year period.

To supplement our examination of trends in FDA's medical product oversight resources and responsibilities, we reviewed FDA's oversight of four key areas within its three medical product programs for a shorter time period—fiscal years 2004 through 2008. We selected these four areas to represent a broad range of the agency's medical product oversight responsibilities, including FDA's oversight responsibilities both before and after a product is marketed in the United States, and areas funded with and without user fees. The four key areas we examined were FDA's (1) review of generic drug, new drug, and new biologic applications, (2) inspections of medical product research activities and manufacturing establishments, (3) review of adverse event[11] reports, and (4) examination of advertising and promotional materials. For each key area, we interviewed FDA officials and analyzed FDA data on the resources it used to conduct its work during this period.

To further examine trends in FDA's responsibilities, we examined the extent to which the agency met selected statutory requirements and performance goals that set expectations for FDA between fiscal years 2004 and 2008 in two of the four key areas we reviewed—FDA's review of generic drug, new drug, and new biologic applications, and inspections of medical product research activities and manufacturing establishments.[12] Specifically, we reviewed FDA data on the timeliness of the agency's

[10]In prior reports we found that FDA's establishment registration databases contain inaccurate information on the number of establishments manufacturing drugs and devices. However, these data represent the best information available and are what FDA relies on to manage its inspection activities. For more information about these databases, see GAO, *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); and *Medical Devices: FDA Faces Challenges in Conducting Inspections of Foreign Manufacturing Establishments*, GAO-08-780T (Washington, D.C.: May 14, 2008).

[11]Adverse event is the term used by FDA to refer to any untoward medical event associated with the human use of a medical product.

[12]FDA did not have statutory requirements or performance goals related to its work in the other two key areas we reviewed—review of adverse event reports and examination of advertising and promotional materials—for all medical products during the entire period, fiscal years 2004 through 2008. For these two areas, we limited our examination to reviewing trends in the amount of work FDA conducted.

review of generic drug applications compared with a statutory requirement that the agency review these applications within a certain time frame. We reviewed published FDA reports and FDA data on the timeliness of the agency's review of new drug and new biologic applications compared with certain performance goals. We also examined FDA's estimated inspection frequency for six types of establishments—domestic drug manufacturing, foreign drug manufacturing, domestic blood banks, domestic human tissue banks, domestic device manufacturing, and foreign device manufacturing. We selected these six types of establishments because they included inspections for drugs, biologics, and devices, and because they also include establishment types with and without statutory requirements regarding the frequency of inspections. We provide FDA's estimated inspection frequency because, as we have noted in prior reports, FDA does not know how many establishments are subject to inspection, and therefore the percentage of those that have been inspected cannot always be calculated with certainty.[13] The results of our review of these four key areas were used to provide detailed illustrations that are neither representative of all agency activities nor generalizable to the agency as a whole.

To assess the reliability of FDA data on funding, staffing, and workload, we discussed the data with the responsible agency officials, reviewed related documentation, and examined the data for consistency. We determined that FDA data were sufficiently reliable for their use in this report.

We conducted this performance audit from April 2008 to June 2009 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.

Background

FDA receives annual appropriations to conduct its medical product responsibilities; these appropriations include amounts derived from user fees paid by industry in connection with FDA activities. FDA's medical product responsibilities include oversight of the safety and effectiveness

[13]See, for example, GAO-08-970.

of medical products marketed for sale in the United States, regardless of whether they are manufactured domestically or overseas. The agency's role is far-reaching and its responsibilities include oversight of medical products both before and after they are marketed in the United States.

FDA Funding and Organization

Each year, the request for FDA's resources is submitted to Congress as part of the President's Budget request. FDA develops and submits supporting information for the request in the budget justification that is submitted to the subcommittees with jurisdiction over FDA funding as part of the annual appropriations process. This information reflects how FDA proposes to meet its mission, goals, and objectives and assists Congress in understanding whether FDA will require significant changes in levels of appropriations. Guidance issued by OMB, which assists the President in overseeing the preparation of the federal budget, directs agencies to incorporate the cost of fulfilling all statutory requirements and responsibilities in their submissions to OMB for consideration in developing the President's Budget request. We have also issued guidance on the development of comprehensive and reliable resource estimates, which includes recognition of the basic elements of such estimates. For example, these elements include complete and reliable data, such as data on the agency's current resources, workload and performance; provisions for program uncertainties; adjustment for inflation; recognition of any exclusions; and an independent review of the estimates.[14]

In fiscal year 2008, FDA's funding totaled $2.2 billion. Of this amount, about $500 million was derived from user fees collected from industry and made available until expended.[15] The remaining amounts, about $1.7 billion, were derived from the General Fund of the Treasury and available during fiscal year 2008.[16] Both user fee funding and fiscal year appropriations are made available through the annual appropriations

[14]For additional information on the elements of reliable cost estimates, see GAO, *GAO Cost Estimating and Assessment Guide: Best Practices for Developing and Managing Capital Program Costs*, GAO-09-3SP (Washington, D.C.: March 2009).

[15]FDA's funding from user fees represents the maximum amount the agency is authorized to collect from industry, as provided in advance in appropriations acts.

[16]In this report, we will use the terms "user fee funding" to describe amounts derived from user fee collections and "fiscal year appropriations" to describe amounts derived from the General Fund of the Treasury to delineate the source of the appropriated amounts.

process.[17] About $1.2 billion—over half of FDA's total funding—supported its medical product programs, including about $750 million in fiscal year appropriations and about $440 million in user fee funding.[18] Over half of this funding—$681 million—supported the drug program, while $234 million supported the biologics program and $275 million supported the devices program.

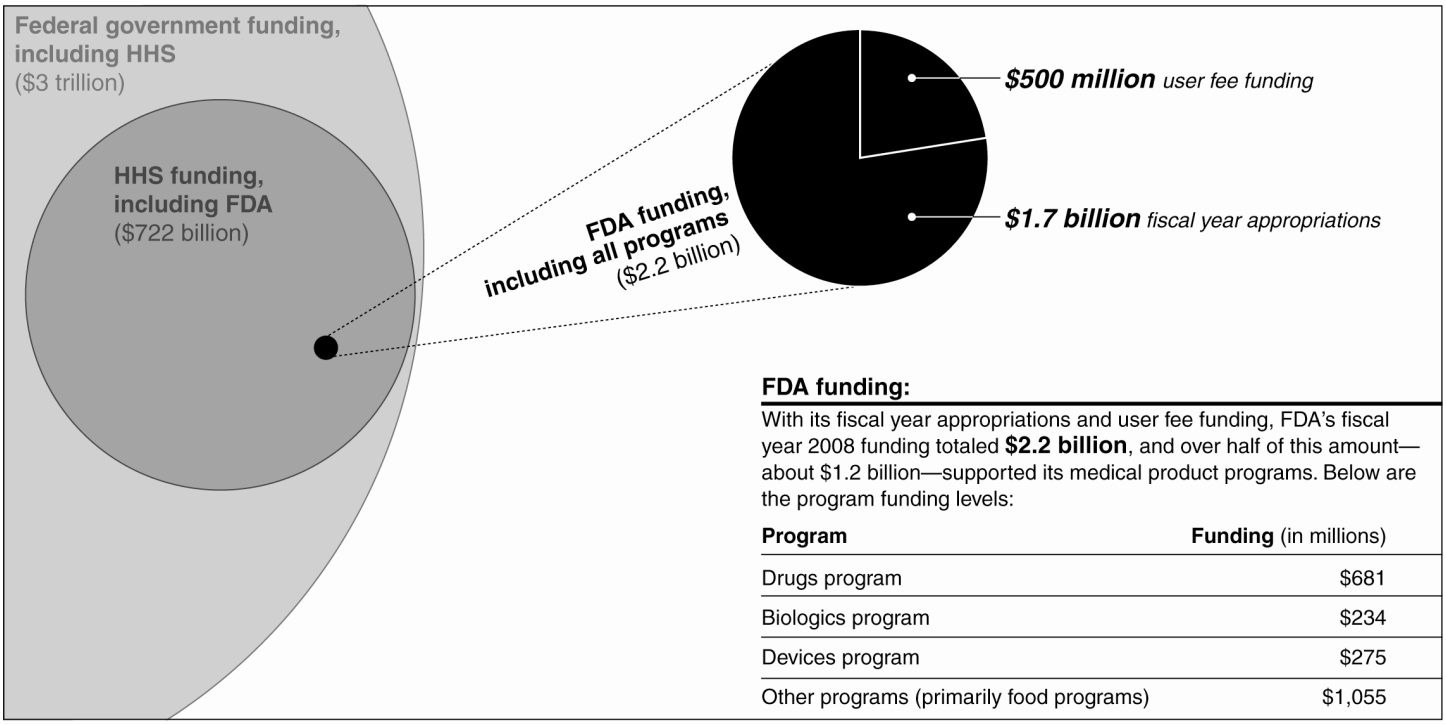
FDA's total funding is a small portion of federal government and HHS funding. In fiscal year 2008, the federal government's funding totaled approximately $3 trillion, of which about $722 billion was made available to fund HHS activities, including those at FDA. These amounts reflect both discretionary spending and mandatory spending.[19] (See fig. 1.) All of FDA's programs involve discretionary spending.

[17]FDA uses the term "budget authority" to refer to its fiscal year appropriations. Budget authority is, however, the authority provided by federal law to enter into financial obligations that will result in immediate or future outlays involving federal government funds. See GAO, *A Glossary of Terms Used in the Federal Budget Process*, GAO-05-734SP (Washington, D.C.: September 2005). Thus, user fees made available through annual appropriations acts also constitute budget authority.

[18]The remaining portion of FDA's resources—about $1,055 million, which includes about $970 million in fiscal year appropriations and about $80 million in user fee funding—supported the agency's other programs, including FDA's Foods Program, Animal Drugs and Feeds Program, the National Center for Toxicological Research, the Office of the Commissioner, and rent and facilities.

[19]Discretionary spending generally refers to outlays from budget authority that is provided in and controlled by appropriations acts. Mandatory spending refers to budget authority that is provided in and controlled by laws other than appropriations acts.

Figure 1: Federal Government, HHS, and FDA Funding, Fiscal Year 2008



FDA funding:

With its fiscal year appropriations and user fee funding, FDA's fiscal year 2008 funding totaled **$2.2 billion**, and over half of this amount—about $1.2 billion—supported its medical product programs. Below are the program funding levels:

Program	**Funding** (in millions)
Drugs program	$681
Biologics program	$234
Devices program	$275
Other programs (primarily food programs)	$1,055

Source: GAO analysis of FDA and OMB data.

Note: Federal government and HHS funding amounts reflect discretionary and mandatory spending for fiscal year 2008. Specifically, about $1.2 trillion of the federal government's $3 trillion total funding represents discretionary spending, and about $72 billion of HHS' $722 billion total funding represents discretionary spending. All of FDA's fiscal year 2008 funding represents discretionary spending.

User fees are paid in connection with FDA's drugs, biologics, and devices programs' review of applications for new medical products and inspections of mammography facilities.[20] The Prescription Drug User Fee Act of 1992 (PDUFA) was enacted to expedite the review of applications for new drugs and new biologics.[21] PDUFA authorized FDA to collect user

[20]The Mammography Quality Standards Act of 1992 authorized FDA to collect user fees from mammography facilities to fully cover the cost of inspections conducted to determine facilities' compliance with established quality standards for performing mammograms. Pub. L. No. 102-539, 106 Stat. 3547 (codified as amended at 42 U.S.C. § 263b).

[21]Pub. L. No. 102-571, 106 Stat. 4491. PDUFA has been amended and reauthorized several times since enactment, most recently in 2007. References to PDUFA in this report refer to PDUFA as amended, except where otherwise indicated.

fees from drug and biologic sponsors, typically manufacturers, to support the process of reviewing new drug applications (NDA) and biologics license applications (BLA). Likewise, the Medical Device User Fee and Modernization Act of 2002 (MDUFMA) authorized FDA to collect user fees from device sponsors to support the process of reviewing applications for certain new devices.[22] In both cases, FDA's authority to collect fees and use the amounts collected must be provided in appropriations acts. Both PDUFA and MDUFMA require FDA to apply all user fee funding to support the agency's process for reviewing applications for certain new medical products, and preclude the agency from using this funding for other agency activities. In fiscal year 2008, agency activities not funded with user fees included, for example, the agency's oversight of the safety of human tissues, review of applications for generic drugs, inspections unrelated to the agency's review of new medical products, and some postmarket safety oversight activities.[23] PDUFA and MDUFMA user fee funding only partially covers FDA's costs for reviewing applications for certain new medical products and associated activities. FDA is also required to use a specified

[22]Pub. L. No. 107-250, 116 Stat. 1588. MDUFMA has been amended and reauthorized several times since enactment, most recently in 2007. References to MDUFMA in this report refer to MDUFMA as amended, except where otherwise indicated.

[23]The list of agency activities receiving, and excluded from receiving, user fee funding has changed over time. From fiscal years 1999 through 2002, medical product program activities funded with user fees included program activities related to the premarket review of new drugs and biologics as well as inspections of certain mammography facilities. Activities not funded by user fees during this period included, for example, the agency's oversight of the safety of transfusion-related blood products and human tissues; review of applications for generic drugs, over-the-counter drugs and new devices; inspections unrelated to the agency's review of an application for a new drug or new biologic; oversight of the advertising and promotion of medical products; oversight of the safety of marketed medical products, including the agency's review of adverse event reports; as well as agency research and policy development unrelated to the review of new drugs and new biologics. Beginning in fiscal year 2003, user fee activities also included those related to the review of device applications, including the evaluation of postmarket studies and safety and effectiveness information for certain devices, and the review of safety information, including adverse event reports, for drugs approved after October 1, 2002. And, beginning in fiscal year 2008, FDA is authorized to apply PDUFA user fee funding to more postmarket safety activities for drugs, including the agency's review of adverse event reports for these products, regardless of approval date. See 21 U.S.C. §§ 379g, 379h, 379i, 379j.

amount of its fiscal year appropriations to support its review of these applications.[24]

Within FDA, three centers have primary responsibility for ensuring the safety and effectiveness of medical products. The Center for Biologics Evaluation and Research (CBER) is responsible for overseeing biologics; the Center for Drug Evaluation and Research (CDER) is responsible for overseeing drugs and some therapeutic biologics;[25] and the Center for Devices and Radiological Health (CDRH) is responsible for overseeing devices and for ensuring that radiation-emitting products, such as microwaves and x-ray machines, meet radiation safety standards. Among other things, these centers evaluate the safety and effectiveness of new medical products prior to marketing, monitor the safety and effectiveness of marketed products, oversee the advertising and promotion of marketed products, formulate regulations and guidance, conduct research, communicate information to industry and the public, and set their respective medical product program's priorities. In addition to the work of the three centers, the Office of Regulatory Affairs (ORA) conducts field activities for all of FDA's product centers. Field activities include conducting inspections of domestic and foreign establishments involved in manufacturing medical products, examining medical products offered for import, and collecting and analyzing samples. Medical product program resources include funding for center activities and field activities. Center activity funding represents funding for the three centers—CDER, CBER, or CDRH—and field activity funding represents ORA funding for all medical product programs.

[24]Current law permits FDA to apply user fee funding only to defray increases in the costs of resources allocated to the process of reviewing new drug and new biologic applications over the costs for fiscal year 1997, adjusted for inflation, within certain limits; and current law permits FDA to apply user fee funding only to defray increases in the costs of resources allocated to the review of device applications over the costs for fiscal year 2002, adjusted for inflation. Unlike PDUFA and MDUFMA, user fees collected under the Mammography Quality Standards Act were designed to fully cover the cost of inspections conducted, and FDA is not required to use its fiscal year appropriations to support the cost of these inspections. See 21 U.S.C. §§ 379h(g)(2)(ii), 379j(h)(2)(ii); 42 U.S.C. § 263b.

[25]In fiscal year 2004, responsibility for overseeing some therapeutic biologics was transferred from CBER to CDER. Examples of products transferred to CDER include monoclonal antibodies and proteins intended for therapeutic use. CBER retained responsibility for other biologics including blood, vaccines, and human tissues.

FDA's Medical Product Oversight Responsibilities

As part of its oversight responsibilities, FDA reviews applications submitted by manufacturers for medical products they wish to market in the United States to ensure that new products are safe and effective, inspects establishments producing medical products to ensure manufacturing processes meet quality standards, reviews reports of adverse events to monitor the safety of marketed medical products, and examines advertising and other promotional materials to ensure they are not false and misleading.

Oversight of New Medical Products

FDA's oversight of medical product safety and effectiveness typically begins when medical product sponsors develop a new product, long before such products are marketed for sale. For example, FDA requires sponsors to submit an investigational new drug (IND) application before beginning clinical trials (studies in humans) of a new drug or new biologic. The IND application provides FDA with extensive information about the product, including safety and manufacturing information about the product, and outlines the sponsor's plans for clinical trials. FDA assesses this preliminary information to ensure that the product is reasonably safe to begin studying in humans. While FDA does not issue a formal approval to the sponsor regarding an IND application, it can prohibit the start of a clinical trial by placing it on hold if, for example, the agency determines that human volunteers would be exposed to an unreasonable and significant risk of illness or injury.[26]

Sponsors often request guidance and feedback from FDA during the process of drug and biologic development. Before and during clinical trials, FDA may meet with sponsors to provide guidance on the design of the clinical trial. In addition, FDA may issue a written evaluation of particular aspects of a clinical trial—known as a special protocol assessment. FDA may also meet with sponsors after the completion of a successful clinical trial to discuss the information the agency would expect to see submitted to the agency for marketing approval.

FDA's approval is required before new drugs and biologics can be marketed for sale in the United States.[27] To obtain FDA's approval, sponsors must submit an application containing data on the safety and

[26]Sponsors may provide additional information to FDA in reply to a clinical hold. FDA, in turn, is responsible for reviewing this information and issuing a written response, known as a response to a clinical hold.

[27]21 U.S.C. § 355.

effectiveness of their new medical product as determined through clinical trials and other research. For example, sponsors must request approval for a new drug or new biologic by submitting an NDA or BLA. FDA reviews data included in these applications to determine whether the product is safe and effective for its intended use. FDA also examines proposed product labeling to ensure that it clearly states the condition and population the product is intended to treat. After completing its assessment of the information in the application and any subsequent submissions of additional information, known as application resubmissions, FDA determines whether to approve the product for marketing. After FDA approves a product, manufacturers requesting changes to product labeling, manufacturing, dosing, or usage must submit an application supplement to obtain FDA approval.

In addition to its responsibility for approving new drugs prior to marketing, FDA approval is also required before generic drugs—drugs that are copies of already approved new drugs—can be marketed for sale in the United States. Sponsors of generic drugs may obtain FDA approval by submitting an abbreviated new drug application (ANDA) to the agency for review. The ANDA contains data showing, among other things, that the generic drug is bioequivalent to, or performs in the same manner as, a drug approved through the NDA process.[28] Similar to its review of NDAs, FDA reviews information submitted in the application, including proposed product labeling. To request FDA approval of proposed changes to product labeling, manufacturing, dosing, or usage after a generic drug is approved, sponsors must submit an ANDA supplement.

FDA is also responsible for overseeing the safety and effectiveness of devices. Devices are classified into one of three classes—class I, II, or III—based on the level of risk posed to the patient or user and the controls necessary to reasonably ensure safety and effectiveness. Class I devices are those that pose the lowest risk, and class III devices are those that pose the highest risk.[29] Some devices are subject to one of two types of

[28]21 C.F.R. § 355(j). The application for generic drugs is abbreviated because FDA does not require sponsors to conduct or provide evidence from clinical trials that are required of developers of new drugs.

[29]For example, class I (low-risk) devices include tongue depressors, elastic bandages, reading glasses, and forceps; class II (medium-risk) devices include electrocardiographs, powered bone drills, and mercury thermometers; and class III (high-risk) devices include pacemakers and replacement heart valves. See 21 U.S.C. § 360c.

FDA review before they may be marketed for sale in the United States.[30] Some class II devices are required to obtain FDA clearance through a premarket notification process, whereby a sponsor must demonstrate to FDA that the new device is substantially equivalent to a device that FDA previously approved or cleared for marketing. In contrast, class III devices are generally required to obtain FDA approval through a more stringent premarket approval process, whereby a sponsor must provide evidence, typically including clinical data, to demonstrate with reasonable assurance that the new device is safe and effective. As with new drugs and biologics, FDA's review of these applications includes an assessment of product labeling and usage.

FDA is required to review certain medical product applications within specified time frames. For example, FDA is generally required to review NDAs, BLAs, and ANDAs within 180 days of receipt.[31] PDUFA also established performance goals to speed up FDA's process for reviewing NDAs and certain BLAs. These performance goals can be grouped into three main categories—those related to the speed at which the agency (1) reviews applications and supplemental materials, (2) schedules and holds meetings with sponsors, and (3) issues written guidance as requested by sponsors.[32] Multiple performance goals exist within each of these broad categories. For example, one performance goal is that FDA review and act on 90 percent of certain NDAs and BLAs within 10 months of their receipt; another is that FDA schedule 90 percent of certain meetings with sponsors within 30 days of receiving the sponsor's meeting request. In addition, MDUFMA also established similar types of performance goals related to the timeliness of FDA's process for reviewing applications for new devices subject to the premarket approval and premarket notification process.

Inspections Conducted to Oversee Medical Product Research and Manufacturing

As part of its oversight responsibilities, FDA conducts inspections of domestic and foreign establishments. Specifically, FDA conducts inspections of clinical trial sites to ensure the protection of human subjects and the accuracy and validity of clinical trial data reported to the agency. FDA also inspects medical product manufacturing establishments

[30]21 U.S.C. § 360(k). Most class I devices are exempt from premarket review requirements. 21 U.S.C. § 360(l). Some class II devices are also in this exempt category.

[31]21 U.S.C. § 355.

[32]Each reauthorization of PDUFA was accompanied by new performance goals for various aspects of the drug review process, as set by the Secretary of HHS.

to ensure that manufacturing processes adhere to current good manufacturing practices requirements and regulations.[33] Inspections of manufacturing establishments may occur before medical products are marketed in the United States. To ensure continued adherence to current good manufacturing practices requirements, FDA may also inspect establishments after the product is on the market.

FDA is required to inspect certain types of establishments with a particular frequency; however, requirements governing the frequency of these inspections differ. For example, FDA is required to conduct inspections of certain types of establishments every 2 years—including domestic drug and device manufacturers, as well as domestic blood banks.[34] However, there are no comparable requirements regarding the frequency with which FDA should conduct inspections of other types of domestic establishments, such as domestic human tissue banks, or some foreign establishments, including those manufacturing drugs and devices marketed for sale in the United States. FDA does not have the authority to require foreign establishments to allow the agency to inspect their facilities. However, FDA has the authority to prevent the importation of products manufactured at establishments that refuse to allow an FDA inspection.[35]

Oversight of Adverse Event Reporting

Because no medical products are absolutely safe—there is always some risk of an adverse event—FDA continues to assess products' risks and benefits after the products are on the market by using multiple strategies. One such strategy is to collect and analyze adverse event reports related to the use of medical products and monitor them to identify potential safety issues associated with the use of a specific medical product. FDA receives adverse event reports from various sources, including medical product manufacturers, physicians, and the public. FDA requires medical product manufacturers and others to submit reports of adverse events associated with the use of a medical product to FDA at certain frequencies depending on the seriousness of the adverse event and the amount of time the

[33]These requirements relate to standards for storage of and manufacturing of medical products. See 21 C.F.R. pts. 210, 211, 606, 820, and 1271 (2008).

[34]21 U.S.C. § 360(h). FDA is required to inspect domestic establishments that manufacture class III and class II devices every 2 years. There is no comparable statutory requirement for the inspection of establishments manufacturing class I devices, and FDA does not routinely inspect them.

[35]21 U.S.C. § 381.

product has been on the market.[36] Physicians and the public may voluntarily submit reports of adverse events to FDA at any time. The agency's review of these reports helps to identify, among other things, unexpected adverse events, product quality problems, and product use errors related to marketed medical products. These reviews provide information that may lead FDA to require the product's sponsor to conduct a safety study, make changes to product labeling, or recall a product from the market.

Oversight of Advertising and Promotional Activities

FDA oversees the advertising and promotion of prescription drugs, biologics, and some devices to ensure that information disseminated about medical products is not false or misleading.[37] FDA regulations also require that product promotions include a balanced disclosure of side effects, contraindications, and warnings.[38] In addition, advertising and promotions may not recommend or suggest any use of a product that is not included in the product's approved labeling. FDA regulates the content of advertising and promotions regardless of whether they are directed toward consumers or medical professionals.

FDA regulations require manufacturers to submit to the agency all final advertising and promotional materials for drugs and biologics at the time the materials are first disseminated to the public.[39] In contrast, FDA does not require manufacturers to submit advertising and promotional materials for devices at the time of their initial dissemination. Companies may also voluntarily submit draft advertising and promotional materials to FDA prior to their public release in order to obtain advisory comments from the agency. Although FDA is not required to review all materials submitted, reviewing final and draft advertising and promotional materials is the

[36]See 21 C.F.R. §§ 310.305, 312.32, 314.80 (2008) (drugs); 21 C.F.R. §§ 312.32, 600.80, 1271.350 (2008) (biologics); 21 C.F.R. pt. 803 (2008) (devices).

[37]See 21 U.S.C. § 352(a), (n), (q), (r); 21 C.F.R. § 202.1(e)(5)(i) (2008). The Federal Trade Commission oversees the advertising and promotion of over-the-counter drugs and some devices. See 15 U.S.C. §§ 52-55. According to FDA, devices whose advertisements are regulated by the Federal Trade Commission include most class I and II devices, and some class III devices.

[38]21 C.F.R. § 202.1(e) (2008); see also 21 C.F.R. §§ 201.100(c)(1), 201.128 (2008). By law, advertisements for certain devices must include a brief statement of warnings, precautions, side effects, and contraindications. 21 U.S.C. § 352(r).

[39]21 C.F.R. §§ 314.81(b)(3)(i), 601.12(f)(4) (2008).

agency's primary mechanism for ensuring that information disseminated about drug and biologic products is not false or misleading.

To supplement its examination of submitted materials, FDA staff also monitor the content of disseminated advertising and promotional materials, for example, by attending medical conferences, reviewing company Web sites, and following up on complaints received.

Driven by User Fees, Funding and Staffing for Medical Product Programs Have Increased, Although FDA Is Concerned about Staffing Levels

Funding and staffing for FDA's medical product programs have increased mostly as a result of user fee funding, which is primarily directed toward the agency's review of new medical products. FDA is required to apply a certain amount of its fiscal year appropriations to support user fee activities, and agency officials said that this requirement limits the resources available for other medical product program activities that are not supported by user fee funding. In addition to their concerns about the sufficiency of their resources, FDA officials are concerned about the agency's ability to hire and retain staff in certain scientific occupations.

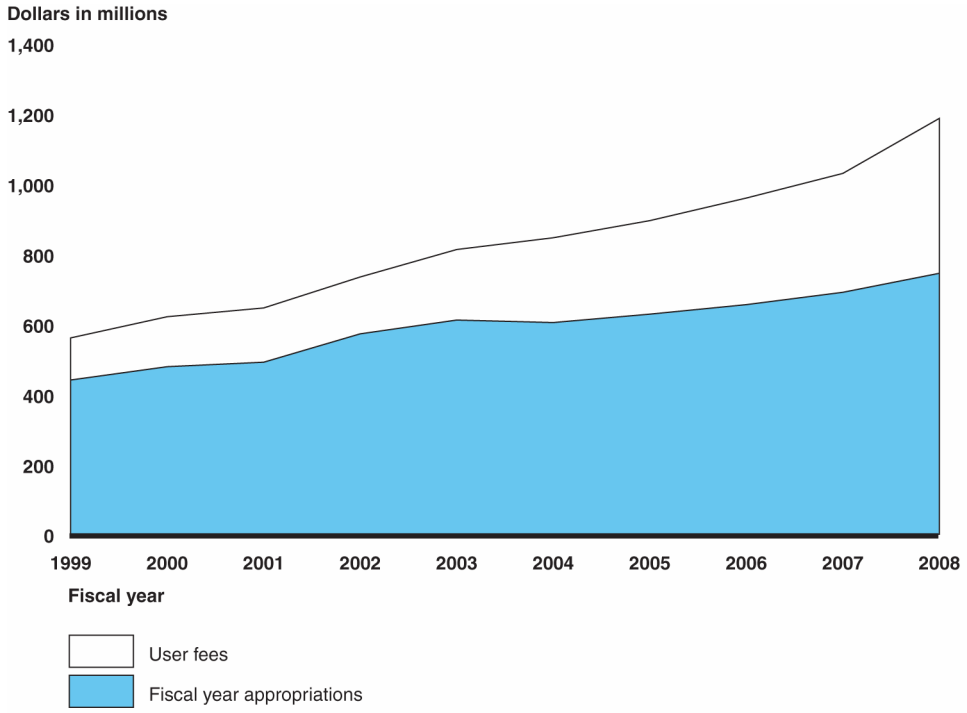
Medical Product Program Funding Has Increased, Largely Due to User Fees

Funding for FDA's medical product programs increased between fiscal year 1999 and fiscal year 2008, mostly due to increases in user fee funding. Medical product program funding increased 112 percent overall, from about $562 million in fiscal year 1999 to about $1.2 billion in fiscal year 2008.[40] (See fig. 2.) This funding increase was greater than the GDP rate of inflation across this time period—25 percent. Over half of the increase in medical product program funding was due to growth in user fee funding, which grew four times as fast as fiscal year appropriations during this 10-year period. Between fiscal years 1999 and 2008, user fee funding increased 268 percent from about $120 million to about $443 million, while fiscal year appropriations increased 69 percent from about $441 million to about $746 million. Over three-quarters of the increase in user fee funding over this period supported the drugs program, with the remaining portion supporting the biologics and devices programs. Appendix I provides

[40]For information on trends in FDA's food safety resources, see GAO, *Food Safety: Improvements Needed in FDA Oversight of Fresh Produce*, GAO-08-1047 (Washington, D.C.: Sept. 26, 2008). For information on trends in FDA's information technology resources, see GAO, *Information Technology: FDA Needs to Establish Key Plans and Processes for Guiding Systems Modernization Efforts*, GAO-09-523 (Washington, D.C.: June 2, 2009).

additional information on funding and staffing resources for FDA's medical product programs.

Figure 2: Annual Medical Product Program Funding from Fiscal Year Appropriations and User Fees, Fiscal Years 1999 through 2008



Source: GAO analysis of FDA data.

Between fiscal years 1999 and 2008, total funding for FDA's medical product programs—including fiscal year appropriations and user fee funding—grew 112 percent. This rate of growth was higher than the rates of growth in total funding for the rest of FDA (86 percent), as well as total funding for HHS (98 percent) and the federal government (87 percent).[41] The high rate of growth in total funding for FDA's medical product programs was due to large increases in FDA's user fee funding. Fiscal year appropriations for FDA's medical product programs grew at a slower rate than fiscal year appropriations for other FDA programs between fiscal years 1999 and 2008, as shown in table 1. Fiscal year appropriations for

[41]Our analysis of HHS and federal government funding reflects these entities' fiscal year 2008 funding, which includes funding for discretionary and mandatory programs.

FDA's medical product programs also grew at a slower rate (69 percent) than discretionary funding for HHS (74 percent) and the federal government (103 percent).

Table 1: Percentage Increase in Fiscal Year Appropriations, User Fee Funding, and Total Funding for FDA, Fiscal Years 1999 through 2008

	Percentage increase in		
	Fiscal year appropriations	User fee funding	Total funding
Medical product programs	69	268	**112**
Drugs program	77	320	**145**
Biologics program	63	168	**88**
Devices program	63	184	**73**
Other programs	79	234	**86**
FDA Total	**75**	**262**	**99**

Source: GAO analysis of FDA data.

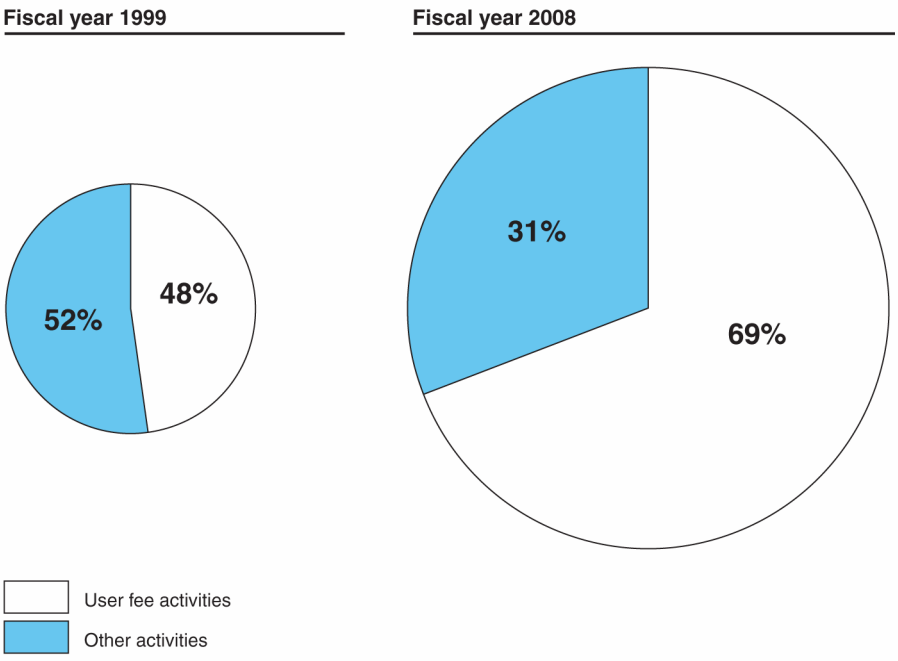
PDUFA and MDUFMA require the agency to apply all user fee funding, as well as a specified amount of fiscal year appropriations, to support user fee activities that are related to the agency's process for reviewing applications for new drugs, new biologics, and certain new devices. Taking this requirement into account, we found that total funding for the medical product programs' user fee activities increased eight times faster than funding for the programs' other activities between fiscal years 1999 and 2008.[42] Specifically, funding for user fee activities increased 207 percent over the 10-year period while total funding for the programs' other activities increased 25 percent—the same rate as inflation over this period as measured by the GDP price index.[43]

[42]In fiscal year 1999, because MDUFMA was not yet enacted, FDA's user fee activities were related to the agency's premarket review of new drugs and new biologics, as well as inspections of certain mammography facilities. By fiscal year 2008, FDA's user fee activities also included the agency's premarket review of certain devices, some postmarket activities for certain devices, and some postmarket activities for drugs.

[43]Between fiscal years 1999 and 2008, CDER, CBER, and CDRH funding for user fee activities grew 223 percent while the centers' funding for other center activities not funded with user fees grew 16 percent—less than the GDP inflation rate (25 percent) over this period. Medical product program field funding for user fee activities increased 69 percent over this period while funding for other field activities increased 41 percent.

As funding for user fee activities grew faster between fiscal year 1999 and 2008 than funding for other program activities not funded with user fees, a declining share of fiscal year appropriations was available to other program activities. In fiscal year 1999, the medical product programs allocated 48 percent of their total $562 million funding—including 33 percent of their fiscal year appropriations—to user fee activities. In fiscal year 2008, these programs allocated 69 percent of their total $1.2 billion funding—including 51 percent of their fiscal year appropriations—to user fee activities. In fiscal year 2008, the medical product programs allocated 31 percent of their total funding to other program activities not funded by user fees. (See fig. 3.)

Figure 3: Portion of Total Medical Product Program Funding Allocated to User Fee Activities and Other Program Activities, Fiscal Years 1999 and 2008



Funding for user fee activities and other activities (dollars in millions)

	Fiscal year 1999	Fiscal year 2008
User fee activities	$267.1	$820.4
Other agency activities not funded with user fees	294.6	369.4
Total	**$561.7**	**$1,189.7**

Source: GAO analysis of FDA data.

Note: In fiscal year 1999, FDA's user fee activities were related to the agency's premarket review of drugs and biologics, as well as inspections of certain mammography facilities. In fiscal year 2008, FDA's user fee activities also included the agency's premarket review of certain devices, postmarket activities for certain devices, and some postmarket activities for drugs. Other activities not funded with user fees included all other program activities, such as the agency's oversight of the safety of transfusion-related blood products and human tissues; review of applications for generic and over-the-counter drugs; inspections unrelated to an application for a new product; oversight of advertising and promotional activities for marketed products; activities related to the oversight of the safety of marketed biologics and devices; as well as agency research and policy development unrelated to the review of new medical products.

Although total funding increased, FDA officials reported that the decline in the portion of funding available to activities not funded by user fees has seriously limited the agency's ability to fulfill its oversight responsibilities in some areas.[44] FDA officials noted a disproportionate growth in funding available for the agency's user fee activities compared with other agency activities not funded with user fees, such as the agency's oversight of transfusion-related blood products, human tissues, device compliance and enforcement, and radiological health, as well as its work in reviewing ANDAs, examining drug-related advertising materials, and conducting inspections of establishments manufacturing approved drugs.

To supplement our analysis of trends in FDA resources from fiscal years 1999 through 2008, we analyzed how FDA's medical product programs allocated funding to center and field activities from fiscal years 2004 through 2008. We found that each of the medical product programs allocated most of their annual funding to activities conducted by the centers (CDER, CBER, and CDRH). The programs also provided some funding for field activities conducted by ORA. We found that funding for the medical product programs' center activities grew three times as fast as funding for the programs' field activities. We also noted that funding for field activities increased at about the same rate as the GDP inflation rate. (See app. II for additional information on trends in center and field funding and staffing resources for the medical product programs.)

Medical Product Program Staffing Resources Have Increased, but FDA Is Concerned about Hiring and Attrition

Staffing resources for FDA's medical product programs increased between fiscal year 1999 and fiscal year 2008. The number of FTEs[45] supporting FDA's medical product programs increased 14 percent from 4,925 FTEs in fiscal year 1999 to 5,626 FTEs in fiscal year 2008.[46] This increase was due solely to a growth in the number of FTEs funded by user fees—the number of FTEs funded by fiscal year appropriations declined. Specifically, the number of medical product program FTEs funded by user fees increased

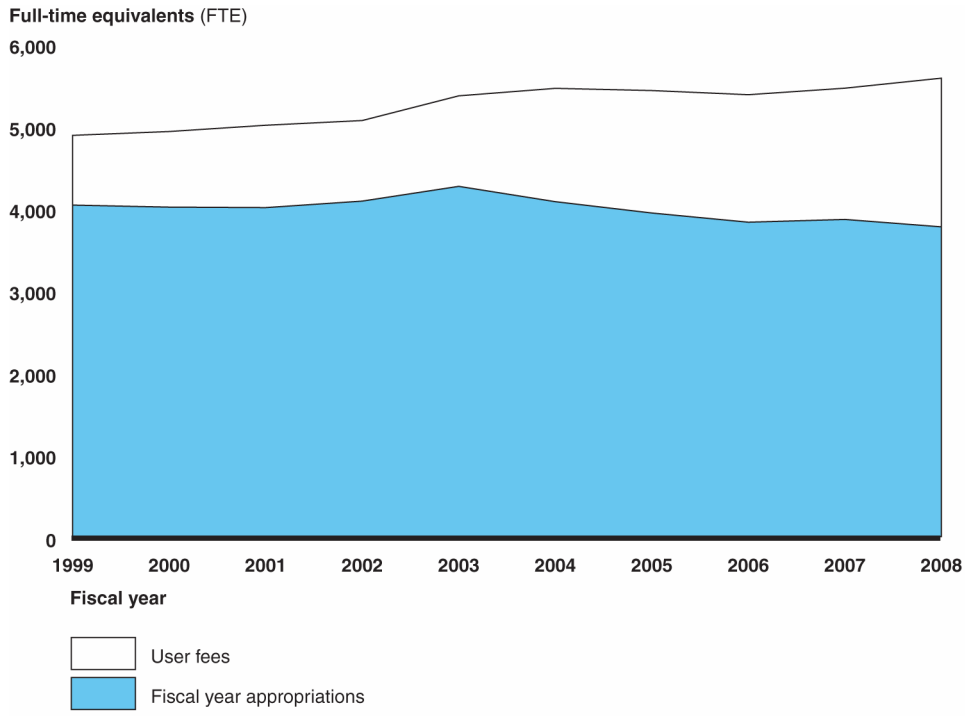
[44]We have previously reported that FDA's user fees have the effect of limiting the resources available to other activities not funded with user fees. See GAO, *Food and Drug Administration*: *Effect of User Fees on Drug Approval Times*, *Withdrawals*, *and Other Agency Activities*, GAO-02-958 (Washington, D.C.: Sept. 17, 2002).

[45]FTEs do not include contractors and therefore provide a partial measure of staffing resources.

[46]In late fiscal year 2008, FDA began a major multiyear initiative to hire individuals with science and medical backgrounds. Some of the increase in FTEs in fiscal year 2008 may be attributed to this initiative.

113 percent—from 856 FTEs in fiscal year 1999 to 1,825 FTEs in fiscal year 2008—while FTEs funded by fiscal year appropriations declined 7 percent, or from 4,069 FTEs in fiscal year 1999 to 3,802 FTEs in fiscal year 2008. FDA officials told us that they had to actively reduce the number of staff by offering buyouts to employees to leave the agency between fiscal years 2004 and 2006 because the agency did not receive enough fiscal year appropriations in these years to maintain staffing levels. According to FDA officials, FTE costs—salary and benefit costs—grew at a faster rate than fiscal year appropriations during this period. Figure 4 displays the number of FTEs from fiscal year appropriations and user fees for each year, fiscal years 1999 through 2008.

Figure 4: Annual Medical Product Program Staffing Resources from Fiscal Year Appropriations and User Fees, Fiscal Years 1999 through 2008



Source: GAO analysis of FDA data.

Note: FTEs do not include contractors and therefore provide a partial measure of total staffing resources.

While our analysis of FDA data shows that the number of medical product program FTEs increased between fiscal year 1999 and 2008, FTEs do not include contractors and therefore provide a partial measure of total staffing resources. FDA could not provide data showing the total number of contractors it used or the total amount of funding it spent on contractors to support its medical product programs over this period. As a result, we could not fully assess the medical product programs' staffing resources. FDA officials estimated that the agency used an increasing number of contractors to fulfill its medical product responsibilities between fiscal years 1999 and 2008.[47] However, agency officials were unable to provide us with data to corroborate this estimate.[48]

According to FDA officials, the decline in the number of FTEs funded by FDA's fiscal year appropriations limited the agency's ability to fulfill its medical product oversight responsibilities. FDA officials noted that they do not have enough staff to adequately perform duties that do not receive user fee funding, such as the agency's review of ANDAs, oversight of product advertising and promotion, and inspections of establishments manufacturing marketed products. As a result, FDA officials noted that the agency's work in these areas is increasingly backlogged.

In addition to their concerns about the adequacy of the agency's fiscal year appropriations, FDA officials are also concerned about the agency's ability to hire staff, particularly those in certain scientific occupations. For example, FDA officials noted that the agency is facing challenges hiring biologists, chemists, computer programmers, consumer safety officers, engineers, epidemiologists, mathematical statisticians, medical officers, and pharmacologists, among other occupations. FDA officials noted that the lack of sufficient numbers of staff and extended vacancies in specific occupations resulted in higher workloads and longer hours for current staff, as well as postponed or reduced work in some areas.

[47]In particular, CDRH and ORA estimated that their use of contractors increased over the time period, while CDER and CBER estimated that their use of contractors remained steady.

[48]To obtain an estimate of the number of contractors working with FDA's medical product programs, we reviewed HHS' online employee directory. As of March 2009, this directory listed over 700 contractors as working with CDER, CBER, CDRH, and ORA. However, one contractor is not comparable to one FTE because each contractor may not work the equivalent of 40 hours each week over the course of 1 year, which is the definition of an FTE. In addition, the HHS directory may not include a current or complete list of contractors and does not provide a list of contractors from prior years. We did not verify the accuracy of information provided by the directory.

FDA officials also noted concerns about the agency's ability to retain staff, particularly those in certain scientific occupations. FDA officials said that a high percentage of staff from the medical product centers and ORA leave their positions—including those who move within FDA, leave the agency, and retire. Specifically, FDA data show that between 2000 and 2007, the average annual percent of staff who left their positions at CDER, CBER, and CDRH ranged from 11 to 13 percent, and at ORA headquarters and regional offices ranged from 6 to 23 percent. However, a portion of these staff stayed within FDA and HHS. FDA officials told us that the loss of any staff from their centers presents challenges as it takes time for the centers to hire and train new staff. For example, FDA officials noted that it takes about 2 years to effectively train new staff who review applications for new medical products.

FDA Faced Challenges Fulfilling and Managing Its Growing Medical Product Oversight Responsibilities, Citing Resource Constraints

New laws and a growing workload increased FDA's medical product oversight responsibilities. FDA did not fulfill its oversight responsibilities between fiscal years 2004 and 2008 in some areas, which agency officials attributed to resource constraints.

FDA's Medical Product Oversight Responsibilities Expanded Due to the Enactment of New Laws

Laws enacted since 1999 added new requirements that expanded FDA's medical product oversight responsibilities. On the basis of our review, we found 11 laws that specifically added to FDA's medical product oversight

responsibilities. These 11 laws were enacted between 2002 and 2007.[49] (See fig. 5.)

Figure 5: Timeline of 11 Laws Enacted between 2002 and 2007 That Increased FDA's Medical Product Oversight Responsibilities

Source: GAO analysis of FDA documents and CRS reports.

These 11 laws added many additional requirements and authorities to FDA, increasing the agency's oversight responsibilities ranging from premarket review of medical products to the agency's oversight of the safety of marketed medical products. These additional oversight responsibilities included an expansion in FDA's authority to regulate devices, an increase in the amount of information that the agency needs to review before deciding whether to approve new drugs and biologics, and greater authority to monitor the safety of approved products. To implement these new requirements and authorities, FDA, for example, needed to issue new guidance for industry and new operating procedures for staff, and established new committees that the agency needed to consult with to fulfill its oversight responsibilities.

[49]FDA officials confirmed that these 11 laws increased the agency's medical product oversight responsibilities. While these laws imposed requirements on FDA expressly, other laws enacted between fiscal years 1999 and 2008 also added to FDA's medical product responsibilities. For example, the Pandemic and All-Hazards Preparedness Act was enacted in December 2006 to improve the nation's public health and medical preparedness and response capabilities for emergencies. While not expressly directed at FDA, agency officials noted that this act included provisions that added to their medical product responsibilities. Our review did not identify any laws enacted in 1999, 2000, 2001, or 2008 that specifically affected FDA's medical product responsibilities.

One of the many new oversight responsibilities that FDA was charged with was added by MDUFMA.[50] In 2002, MDUFMA instituted a regulatory oversight function for reprocessed single-use devices.[51] MDUFMA required manufacturers of certain devices to submit additional information to the agency validating that reprocessed single-use devices are substantially equivalent to current or previously marketed single-use devices. The law also created a new application for the approval of reprocessed high-risk devices. As a result of these new authorities, FDA created new guidance documents and conducted presentations with industry and healthcare professionals related to the agency's oversight of these products. According to agency officials, the implementation of this expanded authority resulted in a significant increase in FDA's workload, particularly in 2002 when FDA officials estimated that about 17 FTEs were dedicated to implementing this authority and developing guidance documents.

Another law, the Pediatric Research Equity Act of 2003 (PREA), increased the amount of information that FDA must review to approve a new drug or new biologic.[52] FDA became responsible for reviewing more materials to assess the products' safety and effectiveness for children, including appropriate information to include on product labeling. Specifically, PREA required sponsors to submit a pediatric assessment containing additional information about the pediatric use of a drug or biologic at the time they submit an application or supplement. As a result of the reviews of these required pediatric assessments, FDA issued 86 PREA-related labeling changes for drugs and biologics between December 2003 and December 2008.

A more recent example of a law increasing FDA's medical product responsibilities is the Food and Drug Administration Amendments Act of 2007 (FDAAA).[53] FDAAA increased FDA's postmarket oversight responsibilities for medical products by giving FDA authority to require sponsors to conduct studies or clinical trials for approved drugs in cases

[50]Pub. L. No. 107-250, 116 Stat. 1588.

[51]The term reprocessed, with respect to a single-use device, means an original single-use device that has previously been used on a patient and has been subjected to additional processing and manufacturing for the purpose of an additional single use on a patient. 21 U.S.C. § 321(ll)(2).

[52]Pub. L. No. 108-155, 117 Stat. 1936.

[53]Pub. L. No. 110-85, 121 Stat. 823.

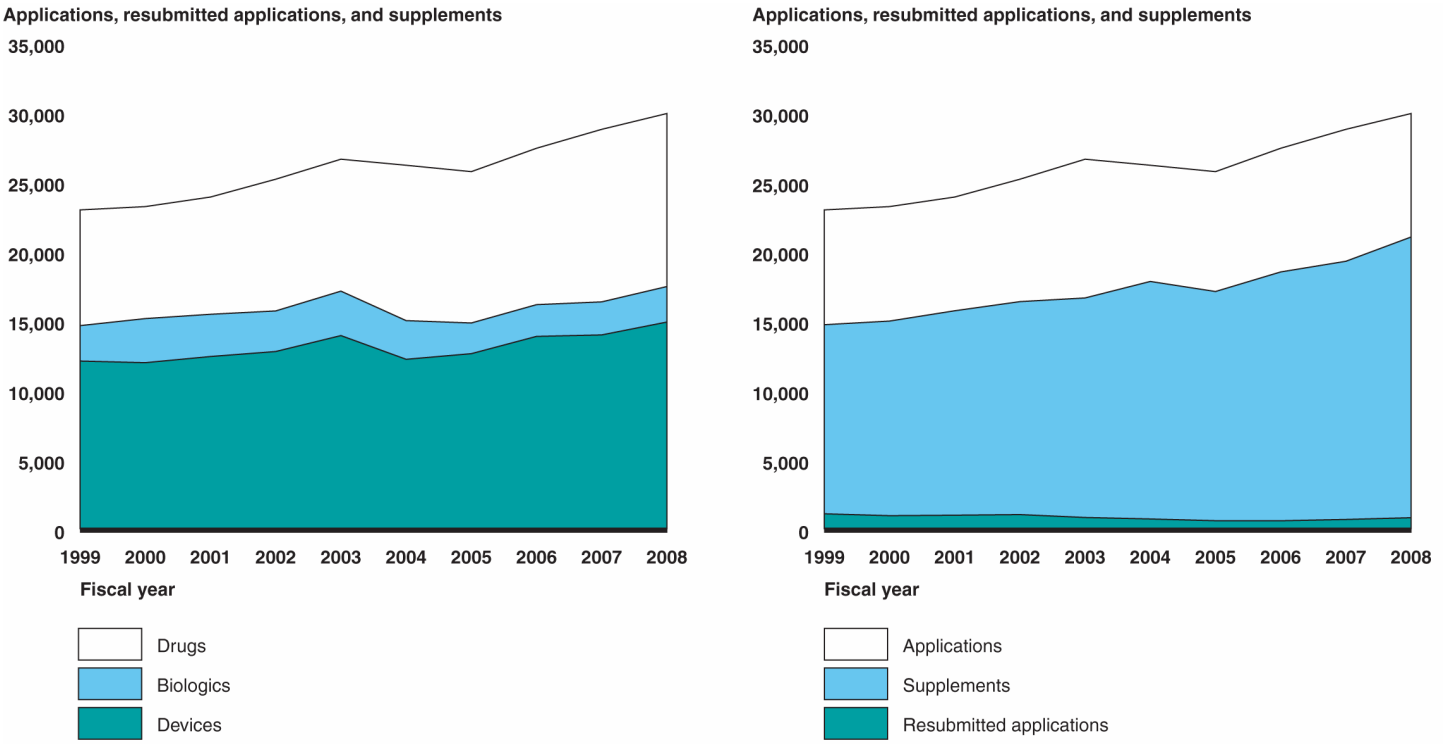
where FDA has identified new safety concerns.[54] To require such a study, FDA officials said that they document their rationale in a legally enforceable contract with a sponsor. These contracts may outline specific elements of the study design. FDA officials stated that the process of developing such contracts results in additional work for the agency. From the enactment of FDAAA in September 2007 through January 2009, FDA required drug sponsors to conduct 45 postmarket studies for NDAs and biologics sponsors to conduct 15 postmarket studies for BLAs, for drugs and biologics approved before and after the implementation of FDAAA.

FDA Faced a Growing Workload

FDA also faced a growing workload and was responsible for overseeing increasing numbers of marketed products and establishments. FDA's medical product workload grew between fiscal years 1999 and 2008 in part due to the receipt of an increasing number of applications and application supplements. The number of drug, biologic, and device application materials submitted to FDA grew 30 percent over this period, from 23,079 in fiscal year 1999 to 30,060 in fiscal year 2008. In particular, the number of application supplements grew 48 percent (from 13,694 application supplements in fiscal year 1999 to 20,329 application supplements in fiscal year 2008). The number of medical product applications also increased during this time period by 8 percent, or from 8,313 applications to 8,943 applications. At the same time, the number of applications resubmitted for medical product approval decreased 26 percent from 1,072 to 788 (see fig. 6).

[54]Prior to the enactment of FDAAA, FDA only had the authority in limited circumstances to require sponsors to conduct a study once a drug or biologic had been approved for marketing in the United States.

Figure 6: Trends in Medical Product Applications, Resubmitted Applications, and Application Supplements Submitted to FDA, Fiscal Years 1999 through 2008



Source: GAO analysis of FDA data.

Note: In fiscal year 2004, FDA transferred oversight responsibilities for certain biological products from the biologics program to the drugs program.

In addition to receiving an increasing number of applications and application supplements, FDA's workload also grew due to an increase in other demands placed on the agency. For example, FDA received 797,889 more reports of adverse events related to medical products in fiscal year 2008 than in fiscal year 1999, an increase of 228 percent. FDA also received 40,193 more drug- and biologic-related advertising and promotional materials to examine (an increase of 115 percent),[55] and 885 more meeting

[55]According to FDA officials, the agency does not maintain information on the number of advertising and promotional materials that it receives for devices. FDA does not require manufacturers to submit advertising and promotional materials for devices at the time of initial dissemination.

requests from sponsors regarding drug and biologic products in development during this time period (an increase of 56 percent).[56]

The complexity of products subject to FDA oversight has also grown, thus increasing the agency's workload. FDA officials, as well as FDA's Science Board, reported that rapid advances in science and technology, including the fields of genomics and nanotechnology, have increased the complexity of the medical products submitted to FDA for premarket approval. FDA officials told us that the agency seeks and provides training for its reviewers so they can more effectively review the safety and effectiveness of these increasingly complex products. However, agency officials said that this training results in less time available for staff to perform their routine duties. In addition, FDA officials also increasingly seek the advice of scientific experts from outside the agency, including advisory committee members, to assist in the review of applications for new drugs and new biologics. Similarly, seeking the advice of experts requires additional staff time to obtain and weigh these perspectives.

In addition to facing a growing workload, the total number of medical products and establishments FDA oversees also increased between fiscal years 1999 and 2008. FDA is responsible for monitoring the safety of marketed medical products, and as the number of these products and manufacturing establishments has grown, so have the agency's oversight responsibilities. The number of medical products approved or cleared for marketing has grown 55 percent, or by 41,203 medical products, during this time period. In addition, the total number of establishments registered to produce medical products marketed for sale in the United States—a proxy for the number of establishments subject to FDA oversight and inspection—grew over this time period, due to increases in the number of foreign establishments. However, from fiscal years 1999 to 2008, FDA saw a decrease—2 percent or 311 establishments—in the number of domestic

[56]Data for the number of meeting requests from industry officials regarding devices was not available from FDA for fiscal years 1999 through 2004. From fiscal years 2005 to 2008, FDA saw a 28 percent increase in the number of meetings requested from device sponsors, or 144 more meeting requests.

establishments registered to produce medical products.[57] Over the same time period, the number of foreign establishments registered to produce medical products increased by 23 percent or 1,921 establishments. See table 2 for trends in domestic and foreign establishments registered to produce medical products.

Table 2: Number of Domestic and Foreign Establishments Registered to Produce Medical Products for the U.S. Market, Fiscal Years 1999 and 2008

	Fiscal year	
	1999	**2008**
Domestic establishments		
Drugs	3,715	5,074
Biologics	1,601	2,571
Devices	10,179	7,539
Total domestic establishments	**15,495**	**15,184**
Foreign establishments		
Drugs	857	3,035
Biologics	7	57
Devices	7,399	7,092
Total foreign establishments	**8,263**	**10,184**
Total domestic and foreign establishments	**23,731**	**25,368**

Source: GAO analysis of FDA data.

Notes: In prior reports we found that FDA's establishment registration databases contain inaccurate information on the number of establishments manufacturing drugs and devices. However, these data represent the best information available and are what FDA relies on to manage its inspection activities. In fiscal year 2004, FDA transferred oversight responsibilities for certain biological products from CBER to CDER. The number of establishments registered to produce biologics and drugs reflects agency oversight responsibilities in fiscal years 1999 and 2008.

[57]This decrease was mostly due to a decrease in the number of domestic establishments registered to produce devices. FDA officials told us that the number of domestic establishments manufacturing devices in fiscal year 1999 may have been inflated, and that the lower number of such establishments reported for fiscal year 2008 may be related to changes FDA made to its device establishment registration system during that time. FDA officials found that the changes resulted in a smaller, more accurate listing of establishments manufacturing devices in fiscal year 2008. See GAO-08-780T.

FDA Officials Cited Resource Constraints as Hindering the Agency's Ability to Fulfill Its Oversight Responsibilities in Some Areas between Fiscal Years 2004 and 2008

FDA officials told us that resource constraints hindered the agency's ability to fulfill all of its medical product oversight responsibilities between fiscal years 2004 and 2008, but the agency also lacked information to manage some of these oversight responsibilities and estimate current and future resource needs. For the two key areas we reviewed where statutory requirements and performance goals set expectations for the agency's work during this period—review of applications for generic drugs, new drugs, and new biologics, and medical product inspections—FDA did not meet all of its medical product oversight responsibilities. In the other two key areas we reviewed—examination of advertising and promotional materials and review of adverse event reports—we found that while FDA faced an increasing workload, it could not always provide data on the work it performed to fulfill these responsibilities.

FDA did not meet all of its medical product oversight responsibilities where requirements and performance goals set expectations for the agency's work from fiscal years 2004 through 2008. For example, FDA did not meet the requirement to complete its first review of ANDAs within 180 days of receipt during this period. We found that the percent of ANDAs that FDA reviewed within this 180 day requirement declined from 87 percent in fiscal year 2004 to 32 percent in fiscal year 2008.[58] FDA received an increasing number of ANDAs during this time period, and agency officials explained that they were unable to review all applications submitted within the 180 day requirement because they did not have sufficient resources to conduct these reviews. As a result, an increasing number of ANDAs were pending review, creating a backlog.[59]

While FDA met most of its PDUFA performance goals related to the speed at which it reviewed NDAs and BLAs and related application supplements, the agency did not meet most PDUFA performance goals related to the speed at which it scheduled and held meetings with sponsors and responded to sponsor requests for information between fiscal years 2004 and 2008. FDA officials explained that they were unable to meet all of these performance goals due to inadequate resources. FDA officials

[58]Fiscal year 2008 data are as of November 2008.

[59]FDA has requested authorization to collect user fees from industry and use the amounts collected to support its review of ANDAs. In its fiscal year 2009 budget justification, FDA explained it would need an additional $15 million and 34 FTEs from user fees to support its review of these applications, noting that these resources would enable the agency to reduce the time it takes to review ANDAs and respond to the growing number of applications submitted.

explained that they placed a higher priority on reviewing applications and therefore had fewer resources to schedule and hold meetings or respond to sponsors' requests for information.

FDA also did not meet all of its inspection requirements and requested additional funding to begin conducting more inspections. FDA did not conduct inspections every 2 years as required for two of three types of establishments we reviewed. FDA officials estimated that the agency, on average, conducts inspections of domestic drug manufacturers every 3 years, domestic device manufacturers every 3 or 5 years, and domestic blood banks every 2 years. FDA officials estimated that the agency conducts inspections less frequently for other types of establishments that do not have required time frames for the frequency of inspections—domestic human tissue banks, foreign drug manufacturers, and foreign device manufacturers. (See table 3.) In fiscal year 2008, FDA requested and received additional funding to strengthen field operations and conduct more domestic and foreign inspections of medical product establishments.

Table 3: FDA's Estimated Frequency of Inspections for Selected Establishment Types

Establishment type	Frequency of inspection
Establishment types with a biennial inspection requirement	
Domestic drug manufacturing[a]	3 years
Domestic blood banks	2 years
Domestic device manufacturing[b]	Class III (high-risk) devices: 3 years
	Class II (medium-risk) devices: 5 years
Establishment types without a requirement for inspection frequency	
Foreign drug manufacturing[a]	12 years
Domestic human tissue banks	4-5 years
Foreign device manufacturing[b]	Class III (high-risk) devices: 6 years
	Class II (medium-risk) devices: 27 years

Source: FDA.

Notes: We provide FDA's estimated inspection frequency because FDA does not know how many establishments are subject to inspection and therefore the percentage of those inspected cannot always be calculated with certainty.

[a]FDA primarily conducts inspections of establishments manufacturing prescription drugs, as opposed to over-the-counter drugs, because FDA generally considers establishments manufacturing over-the-counter drugs to have a lower inspection priority.

[b]FDA classifies devices into one of three categories: class III (high-risk) devices include devices such as heart valves, pacemakers, and defibrillators; class II (medium-risk) devices include mercury thermometers, hearing aids, and electrocardiograph machines; and class I (low-risk) devices include tongue depressors, elastic bandages, and bedpans. There is no requirement for the frequency of FDA inspection of manufacturers of class I devices and FDA does not routinely inspect them. See 21 U.S.C. §§ 360(h), 360c.

FDA faced an increasing workload in the other two areas we reviewed—review of adverse event reports and examination of advertising and promotional materials. Agency officials said they lacked sufficient resources in these areas. Similar to what we reported in 1989, we found that FDA lacks information to manage these responsibilities and estimate current and future resource needs. Although adverse event monitoring is a key mechanism for FDA to identify postmarket safety risks related to the use of marketed medical products, agency officials told us that they receive substantially more drug-, biologic-, and device-related adverse event reports than staff can review. Between fiscal years 2004 and 2008, FDA received an increasing number of adverse event reports for medical products, from 635,035 reports in fiscal year 2004 to 1,147,442 reports in fiscal year 2008. However, FDA officials could not provide data showing how many adverse event reports staff review. FDA officials told us that they place the highest priority on reviewing reports of serious adverse events, such as those involving death or severe injury, and unexpected adverse events—those not noted on approved product labeling. Yet, FDA officials were unable to provide data to corroborate their reviews of these reports of serious and unexpected events. In addition, while FDA receives relatively few promotional materials for biologics and devices, the agency receives substantially more drug-related promotional materials than staff can review, according to agency officials. Between fiscal years 2004 and 2008, FDA received a steadily increasing number of final promotional materials—from 45,394 in fiscal year 2004 to 70,509 in fiscal year 2008. Again, FDA could not provide data showing how many drug-related advertising and promotional materials staff review. Although FDA officials told us that they place a high priority on reviewing materials that have the greatest potential to affect public health, they were unable to provide data to corroborate their reviews of these materials. FDA officials have told us that collecting data on the work staff performed would be time-consuming and detract from resources needed to devote to conducting these reviews.[60]

While FDA officials noted the agency's inability to fulfill all of its responsibilities due to resource constraints, FDA does not have the data to develop a complete and reliable estimate of the resources it needs to conduct all of its responsibilities. Specifically, we found that FDA lacked

[60]We also previously reported that FDA cannot be certain that it is reviewing the highest-priority materials or that violative materials are not being circulated. See GAO, *Prescription Drugs: FDA's Oversight of the Promotion of Drugs for Off-Label Uses*, GAO-08-835 (Washington, D.C.: July 28, 2008).

information about its current resources, workload, and performance in some areas, such as with the review of adverse event reports and promotional materials. This basic management information is critical to the development of a complete and reliable resource estimate. FDA officials also told us that the funding amounts requested for FDA and provided by Congress during the past 2 years will permit the agency to respond to its most urgent needs and priorities, although officials also noted that they did not receive enough resources to meet some statutory requirements. For example, agency officials noted that they were unable to inspect certain manufacturing establishments at prescribed intervals due to resource constraints. Furthermore, FDA officials also noted that the agency continues to face significant challenges fulfilling its mission.

For more information on the trends in FDA's workload and resources for the four key areas that we reviewed, see appendix III for FDA's review of generic drug, new drug, and new biologic applications, appendix IV for inspections of medical product research activities and manufacturing establishments, appendix V for the review of adverse event reports, and appendix VI for the examination of advertising and promotional materials.

Conclusions

The growth in the complexity and number of new medical products and the establishments manufacturing them, increasing globalization, and added statutory requirements and responsibilities have translated into mounting and competing demands for FDA's resources. Concerns regarding the adequacy of these resources are not new, but as demands on the agency have soared in recent years, these concerns have intensified. Earlier this year, we included FDA's oversight of medical products in our High-Risk Series. Our current examination of FDA's resources confirms that the agency's ability to protect Americans from unsafe and ineffective medical products is compromised. The structure of the agency's funding—its reliance on user fees to fund certain activities, particularly those related to the review of new products—is a driving force behind which responsibilities FDA does and does not fulfill. The approval of new products has increasingly become the beneficiary of the agency's budget, without parallel increases in funding for activities designed to ensure the continuing safety of products, once they are on the market. The enactment of FDAAA in 2007 gave FDA the ability to apply user fee funding to more postmarket activities for some types of medical products, providing the agency more flexibility in its use of funding.

FDA reports that it cannot do all that is asked of it and our analysis of the agency's activities confirms this. However, as FDA officials told us, the agency's requests for resources do not reflect all the resources it needs to fulfill its mission, including meeting its statutory requirements. FDA could not provide data showing its workload and accomplishments in some areas. Furthermore, it lacks other basic management information, such as the size of its contractor workforce. Without this information, FDA does not have data to reliably estimate its resource needs—a problem we reported 20 years ago and which served as the basis of our recommendation that FDA collect such data. Since then we have made similar recommendations that the agency improve its management and tracking of its resources and workload. FDA has disagreed with these recommendations, claiming that it lacks the resources to devote to this data collection and that it would detract from its oversight responsibilities. We acknowledge that FDA is facing significant challenges in fulfilling its responsibilities, but continue to believe that developing such information is an essential component of ultimately enhancing the agency's ability to adequately fulfill its mission. Without such basic data needed for managing its programs, FDA cannot develop sound and justifiable budget requests that reflect all the work that is vital to fulfilling its mission, including meeting its performance goals and its statutory requirements. It is also difficult for others to independently verify the extent to which FDA receives sufficient resources and whether the agency is appropriately utilizing and prioritizing the resources it receives.

Recommendations for Executive Action

We recommend that the Commissioner of FDA establish a comprehensive and reliable basis to substantiate the agency's estimates of its current and future resource needs in a manner consistent with the principles contained in our cost estimating and assessment guide. To do so, we recommend that the Commissioner of FDA take the following four actions:

1. Conduct a comprehensive assessment of the agency's staffing resources, including its contractor workforce.
2. Gather data on the work the agency conducts to fulfill its responsibilities.
3. Assess the extent to which the agency is meeting its responsibilities.
4. Develop an evidence-based estimate of the resources needed to fulfill all of its responsibilities.

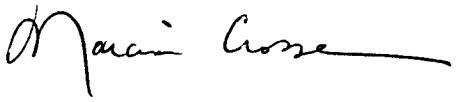
Agency Comments

We provided a draft of this report to HHS for review. HHS provided comments from FDA. In its comments, FDA agreed with our four recommendations and described the steps it would take to implement them. FDA's comments are reprinted in appendix VII. FDA also provided technical comments, which we incorporated as appropriate.

In its comments, FDA acknowledged that we identified some important issues regarding the challenges the agency faces in meeting its medical product responsibilities. It highlighted the President's requested increase in the agency's medical product program funding for fiscal year 2010, which it said would support a life-cycle approach to safety, provide for increased inspections, and support the implementation of requirements included in FDAAA. Specifically, regarding our recommendations, FDA said that a comprehensive assessment of its staffing resources would provide useful information and that it will expand its current staffing assessment process to include its contractor workforce. The agency also said it will conduct a complete inventory of all regulatory work products by FDA center and that it would identify and implement measures to determine how effectively the agency is meeting its responsibilities. Finally, FDA said that it plans to link these measures to its budget and funding allocation. FDA said that this approach will inform the agency about how well it is allocating its resources and help identify what additional resources it needs to fulfill its responsibilities. We believe that the agency's completion of the activities described, as well as other necessary and related actions to implement our recommendations, should assist FDA in developing a comprehensive and reliable basis for substantiating the agency's resource needs and help it better manage its medical product programs.

As agreed with your offices, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time, we will send copies to the Commissioner of FDA and appropriate congressional committees. The report also will be available at no charge on the GAO Web site at http://www.gao.gov.

If you or your staff have any questions about this report, please contact me at (202) 512-7114 or crossem@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made major contributions to this report are listed in appendix VIII.



Marcia Crosse
Director, Health Care

List of Requesters

The Honorable Edward M. Kennedy
Chairman
Committee on Health, Education, Labor, and Pensions
United States Senate

The Honorable Charles E. Grassley
Ranking Member
Committee on Finance
United States Senate

The Honorable Henry A. Waxman
Chairman
The Honorable John D. Dingell
Chairman Emeritus
The Honorable Joe Barton
Ranking Member
Committee on Energy and Commerce
House of Representatives

The Honorable Bart Stupak
Chairman
The Honorable Greg Walden
Ranking Member
Subcommittee on Oversight and Investigations
Committee on Energy and Commerce
House of Representatives

Appendix I: Funding and Staffing Resources for FDA Medical Product Programs, Fiscal Years 1999 through 2008

Funding resources for the Food and Drug Administration's (FDA) medical product programs increased 112 percent between fiscal years 1999 and 2008. Of the medical product programs

- drugs program funding increased 145 percent, from $278.3 million in fiscal year 1999 to $680.9 million in fiscal year 2008;
- biologics program funding increased 88 percent, from $124.4 million in fiscal year 1999 to $233.5 million in fiscal year 2008; and
- devices program funding increased 73 percent, from $159.0 million in fiscal year 1999 to $275.3 million in fiscal year 2008.

Table 4 displays funding resources for FDA programs for fiscal years 1999 through 2008.

Table 4: Funding Resources for FDA Programs, Fiscal Years 1999 through 2008

Dollars in millions

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Drugs program	**$278.3**	**$311.2**	**$322.5**	**$364.3**	**$403.8**	**$459.6**	**$482.1**	**$508.9**	**$543.6**	**$680.9**
Fiscal year appropriations	200.4	215.5	218.5	254.7	274.1	292.1	291.5	297.7	315.1	353.9
User fees	77.9	95.7	104.0	109.6	129.8	167.5	190.7	211.2	228.4	327.0
Biologics program[a]	**124.4**	**140.7**	**147.2**	**177.8**	**193.4**	**167.0**	**170.7**	**197.7**	**202.2**	**233.5**
Fiscal year appropriations	95.0	106.1	108.3	138.6	145.3	122.4	123.1	138.5	146.3	154.8
User fees	29.3	34.6	38.9	39.2	48.1	44.7	47.6	59.2	55.8	78.7
Devices program	**159.0**	**170.3**	**177.6**	**193.7**	**217.3**	**221.5**	**244.3**	**255.0**	**267.5**	**275.3**
Fiscal year appropriations	145.8	157.7	165.3	180.0	193.4	191.1	215.0	220.6	230.7	237.7
User fees	13.2	12.6	12.3	13.7	23.9	30.4	29.3	34.5	36.9	37.6
Medical product programs[b]	**561.7**	**622.2**	**647.3**	**735.8**	**814.6**	**848.1**	**897.1**	**961.7**	**1,013.3**	**1,189.7**
Fiscal year appropriations	441.2	479.3	492.1	573.3	612.7	605.6	629.6	656.8	692.1	746.5
User fees	120.4	142.9	155.2	162.6	201.8	242.5	267.5	304.9	321.1	443.2
Other programs[c]	**568.3**	**591.8**	**630.9**	**801.1**	**813.1**	**830.8**	**880.4**	**901.0**	**960.8**	**1,055.3**
Fiscal year appropriations	544.0	569.1	607.2	781.1	777.3	795.6	822.7	836.8	890.5	974.2
User fees	24.3	23.0	23.7	20.0	35.8	35.2	57.7	64.3	70.3	81.1
FDA total	**$1,130.0**	**$1,214.0**	**$1,278.1**	**$1,537.0**	**$1,627.7**	**$1,678.9**	**$1,777.5**	**$1,862.7**	**$1,974.1**	**$2,245.0**
Fiscal year appropriations	985.3	1,048.4	1,099.3	1,354.4	1,390.1	1,401.2	1,452.3	1,493.6	1,582.7	1,720.6
User fees	144.7	165.8	178.8	182.6	237.6	277.7	325.2	369.1	391.4	524.4

Source: GAO analysis of FDA data.

Notes: We use the terms "user fee funding" to describe amounts derived from user fee collections and "fiscal year appropriations" to describe amounts derived from the General Fund of the Treasury. Both user fee funding and fiscal year appropriations are made available through the annual appropriations process. FDA uses the term "budget authority" to refer to its fiscal year appropriations. Fiscal year appropriations and user fees may not sum to totals due to rounding.

[a]In fiscal year 2004, FDA transferred oversight responsibilities for certain biological products from the biologics program to the drugs program.

[b]Medical product program resources reflect the sum of resources for drugs, biologics, and devices.

[c]Other program resources reflect the sum of resources for all nonmedical product programs, including those for FDA's Foods Program, Animal Drugs and Feeds Program, the National Center for Toxicological Research, the Office of the Commissioner, and rent and facilities.

Staffing resources supporting FDA's medical product programs—as measured by the number of full-time equivalent (FTE) staff—varied from year to year, and increased 14 percent between fiscal year 1999 and fiscal year 2008.[1] Specifically,

- drugs program FTEs increased 22 percent from 2,456 FTEs in fiscal year 1999 to 2,996 FTEs in fiscal year 2008;
- biologics program FTEs increased 8 percent from 989 FTEs in fiscal year 1999 to 1,066 in fiscal year 2008; and
- devices program FTEs increased 6 percent from 1,480 FTEs in fiscal year 1999 to 1,564 FTEs in fiscal year 2008.

Table 5 displays staffing resources for FDA programs from fiscal years 1999 through 2008.

[1]One FTE represents 40 hours of work per week conducted by a federal government employee over the course of 1 year, and does not include contractors.

Table 5: Staffing Resources for FDA Programs, Fiscal Years 1999 through 2008

Full-time equivalents (FTE)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Drugs program	**2,456**	**2,509**	**2,535**	**2,517**	**2,696**	**2,949**	**2,918**	**2,947**	**2,915**	**2,996**
Fiscal year appropriations	1,846	1,838	1,824	1,817	1,920	1,943	1,837	1,801	1,772	1,712
User fees	610	671	711	700	776	1,006	1,081	1,146	1,143	1,284
Biologics program[a]	**989**	**991**	**1,041**	**1,136**	**1,229**	**1,038**	**1,041**	**979**	**1,045**	**1,066**
Fiscal year appropriations	791	780	786	894	947	792	768	730	763	725
User fees	198	211	255	242	282	246	273	249	282	342
Devices program	**1,480**	**1,472**	**1,473**	**1,454**	**1,485**	**1,515**	**1,516**	**1,498**	**1,544**	**1,564**
Fiscal year appropriations	1,432	1,426	1,428	1,407	1,432	1,376	1,367	1,328	1,358	1,365
User fees	48	46	45	47	53	139	149	170	186	199
Medical product programs[b]	**4,925**	**4,972**	**5,049**	**5,107**	**5,410**	**5,502**	**5,475**	**5,424**	**5,504**	**5,626**
Fiscal year appropriations	4,069	4,044	4,038	4,118	4,299	4,111	3,972	3,859	3,893	3,802
User fees	856	928	1,011	989	1,111	1,391	1,503	1,565	1,611	1,825
Other programs[c]	**3,985**	**3,858**	**3,940**	**4,361**	**4,847**	**4,639**	**4,435**	**4,274**	**4,065**	**4,185**
Fiscal year appropriations	3,782	3,684	3,767	4,193	4,641	4,456	4,209	4,034	3,812	3,876
User fees	203	174	173	168	206	183	226	240	253	308
FDA total	**8,910**	**8,830**	**8,989**	**9,468**	**10,257**	**10,141**	**9,910**	**9,698**	**9,569**	**9,811**
Fiscal year appropriations	7,851	7,728	7,805	8,311	8,940	8,567	8,181	7,893	7,705	7,678
User fees	1,059	1,102	1,184	1,157	1,317	1,574	1,729	1,805	1,864	2,133

Source: GAO analysis of FDA data.

Notes: We use the terms “user fee funding” to describe amounts derived from user fee collections and “fiscal year appropriations” to describe amounts derived from the General Fund of the Treasury. Both user fee funding and fiscal year appropriations are made available through the annual appropriations process. FDA uses the term “budget authority” to refer to its fiscal year appropriations. One FTE represents 40 hours of work per week conducted by a federal government employee over the course of 1 year and does not include contractors. Fiscal year appropriations and user fees may not sum to totals due to rounding.

[a]In fiscal year 2004, FDA transferred oversight responsibilities for certain biological products from the biologics program to the drugs program.

[b]Medical product program resources reflect the sum of resources for drugs, biologics, and devices.

[c]Other program resources reflect the sum of resources for all nonmedical product programs, including those for FDA’s Foods Program, Animal Drugs and Feeds Program, the National Center for Toxicological Research, the Office of the Commissioner, and rent and facilities.

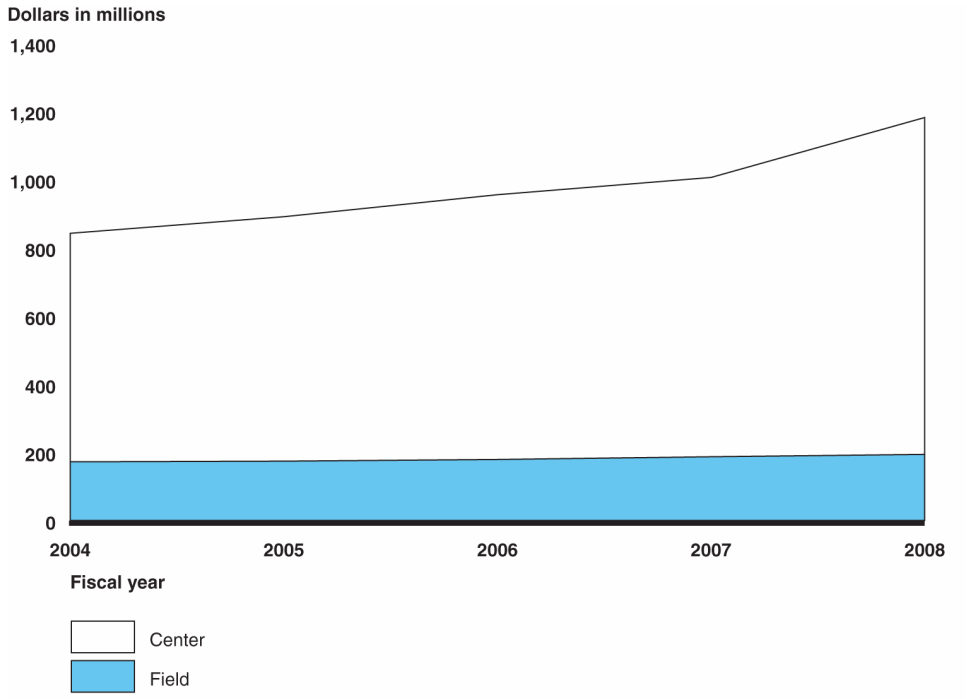
Appendix II: Trends in Center and Field Resources for the Drugs, Biologics, and Devices Programs

Between fiscal years 2004 and 2008, the drugs, biologics, and devices programs allocated most of their funding and staffing to center activities, leaving a smaller share of resources for field activities. Funding for center activities grew faster than funding for field activities, which increased at nearly the same rate as inflation, as measured by the gross domestic product (GDP) price index. During the same period, staffing resources for center activities increased while staffing resources for field activities decreased.

Trends in Funding Resources for Center and Field Activities

Funding for center activities grew more than three times as fast as funding for field activities between fiscal years 2004 and 2008. Specifically, center funding for all medical product programs combined grew from $675 million to $995 million over this period, an increase of 47 percent, while field funding for all medical programs increased from $173 million to $195 million, an increase of 13 percent. (See fig. 7.) While increases in total center funding outpaced the GDP inflation rate of 12 percent during this period, the rate of increase in total field funding remained close to the GDP inflation rate.

Figure 7: Annual Medical Product Program Funding for Center and Field Activities, Fiscal Years 2004 through 2008



Source: GAO analysis of FDA data.

- Drugs program funding for center activities conducted by the Center for Drug Evaluation and Research (CDER) increased 57 percent from about $373 million in fiscal year 2004 to about $588 million in fiscal year 2008, while funding for field activities conducted by the Office of Regulatory Affairs (ORA) rose 8 percent from about $86 million to about $93 million over this period. The increase in field funding for this program was less than the rate of GDP inflation (12 percent) over this period.

- Biologics program funding for center activities conducted by the Center for Biologics Evaluation and Research (CBER) increased 45 percent from about $140 million in fiscal year 2004 to about $202 million in fiscal year 2008, while funding for biologics field activities conducted by ORA increased 15 percent over this period, from about $27 million to about $31 million.

- Devices program funding for center activities conducted by the Center for Devices and Radiological Health (CDRH) increased 26 percent from about $162 million in fiscal year 2004 to about $205 million in fiscal years 2008,

while funding for field activities conducted by ORA increased 18 percent, from about $60 million to about $70 million.

Over two-thirds of each of the medical product centers' funding supported their user fee activities in fiscal year 2008. Specifically, CDER, CBER and CDRH each allocated about 78 percent of their centers' total funding—including an average of 61 percent of the centers' total fiscal year appropriations—to user fee activities in fiscal year 2008, leaving 22 percent of funding to support the centers' other activities. In contrast, 23 percent of the medical product programs' total field funding supported user fee activities, with 77 percent of field funding supporting other activities not funded with user fees. Table 6 displays how the medical product programs allocated funding resources to specific center and field activities.

Table 6: Medical Product Program Funding Resources for Center and Field Activities, Fiscal Years 2004 through 2008

Dollars in millions

	Fiscal year				
Activity	**2004**	**2005**	**2006**	**2007**	**2008**
Drugs program					
Center for Drug Evaluation and Research (CDER) activities					
Generic drug review	$34.0	$43.1	$44.4	$52.8	$64.6
New drug safety and effectiveness	292.8	302.0	324.8	321.4	384.2
Postmarket safety and surveillance	46.7	51.0	53.8	80.0	138.7
CDER activities subtotal	**373.5**	**396.0**	**423.1**	**454.2**	**587.6**
Office of Regulatory Affairs (ORA) field activities					
Bioresearch monitoring	14.0	13.3	14.1	16.3	17.6
Generic drug evaluation	5.4	4.7	4.0	5.0	5.0
New drug evaluation	5.9	5.1	4.5	5.8	6.7
Over-the-counter drug evaluation	0.1	0.1	0.1	0.0	0.2
Postmarket surveillance and epidemiology	1.1	1.6	1.6	1.3	1.8
Prescription drug advertising and labeling	0.1	0.0	0.0	0.1	0.0
Quality assurance	58.3	59.9	59.9	59.0	58.7
Unapproved and misbranded drugs	1.4	1.3	1.6	1.8	3.4
Field activities subtotal	**86.1**	**86.1**	**85.8**	**89.3**	**93.4**
Drugs program total	**$459.6**	**$482.1**	**$508.9**	**$543.6**	**$680.9**
Biologics Program					
Center for Biologics Evaluation and Research (CBER) activities					
Blood and blood products	$50.2	$51.3	$64.3	$62.7	$72.9
Cell, gene therapy, and tissues	22.4	22.0	25.8	28.9	32.8
Vaccines and allergenic products	67.3	69.7	78.7	80.5	96.5
CBER activities subtotal	**139.9**	**143.0**	**168.9**	**172.0**	**202.3**
ORA field activities					
Blood and blood products	22.1	21.8	20.2	20.0	22.1
Cell, gene therapy, and tissues	3.7	3.2	6.2	7.5	5.8
Vaccines and allergenic products	1.4	2.6	2.4	2.6	3.3
Field activities subtotal	**27.1**	**27.7**	**28.8**	**30.1**	**31.2**
Biologics program total	**$167.0**	**$170.7**	**$197.7**	**$202.2**	**$233.5**

Dollars in millions

	Fiscal year				
Activity	**2004**	**2005**	**2006**	**2007**	**2008**
Devices Program					
Center for Devices and Radiological Health (CDRH) activities					
Premarket applied research	$9.3	$10.2	$9.1	$8.9	$10.9
Premarket outreach and coordination	6.2	6.8	10.5	8.4	9.2
Premarket review	73.5	89.8	118.1	119.2	101.1
Postmarket applied research	2.9	2.2	0.9	1.2	1.3
Postmarket laboratory analysis	8.5	13.8	5.8	6.7	11.1
Postmarket outreach, coordination, and compliance	61.5	60.4	45.4	54.4	71.2
CDRH activities subtotal	**161.9**	**183.2**	**189.8**	**198.7**	**204.8**
ORA field activities					
Compliance	38.8	42.4	45.4	47.6	49.0
Mammography Quality Standards Act Authority	2.1	2.4	2.4	2.7	2.7
Postmarket assurance	1.9	2.5	2.6	2.8	3.5
Product Evaluation	10.0	8.0	9.2	10.2	10.2
Radiation Control for Health and Safety Act Authority	5.8	5.1	5.0	4.9	4.8
Science	1.0	0.8	0.7	0.7	0.3
Field activities subtotal	**59.6**	**61.1**	**65.2**	**68.8**	**70.5**
Devices program total	**$221.5**	**$244.3**	**$255.0**	**$267.5**	**$275.3**

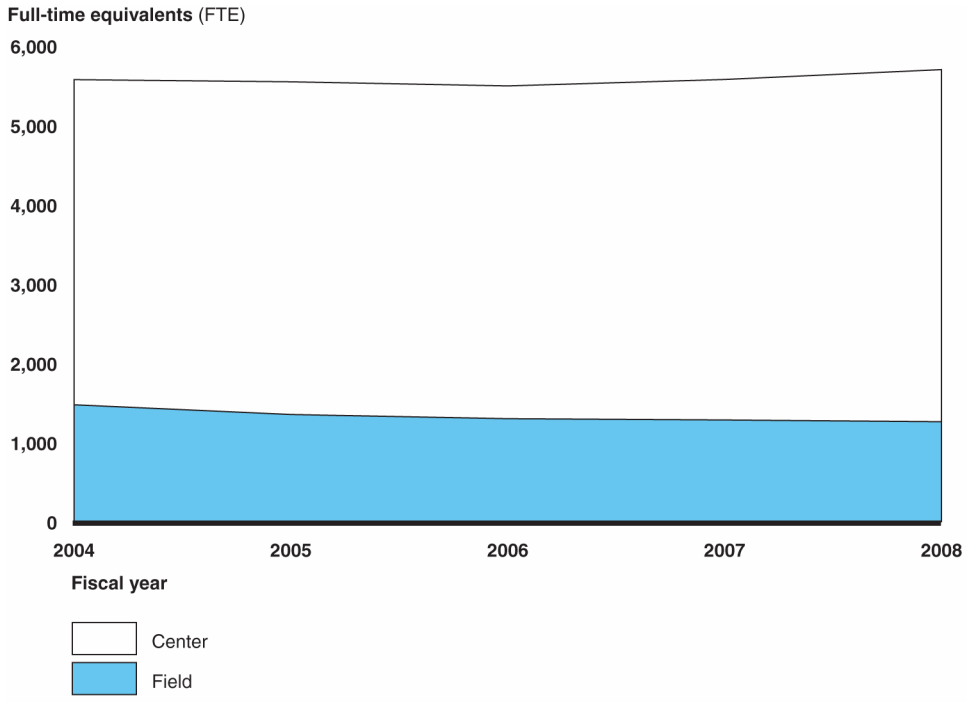
Source: FDA.

Note: Totals may not sum due to rounding.

Trends in Center and Field Staffing Resources

The number of full-time equivalent (FTE) staff supporting center activities grew 8 percent from 4,048 FTEs in fiscal year 2004 to 4,384 in fiscal year 2008, while the number of FTEs supporting field activities conducted by ORA decreased 15 percent from 1,454 FTEs in fiscal year 2004 to 1,243 FTEs in fiscal year 2008. (See fig. 8.) Because counts of FTEs do not include contractors, these data do not fully represent FDA's staffing resources for these activities.

Figure 8: Annual Medical Product Program Staffing Resources for Center and Field Activities, Fiscal Years 2004 through 2008



Source: GAO analysis of FDA data.

Note: One FTE represents 40 hours of work per week conducted by a federal government employee over the course of 1 year and does not include contractors.

- Drugs program staffing resources for CDER activities grew 9 percent from 2,190 FTEs in fiscal year 2004 to 2,396 FTEs in fiscal year 2008, while staffing resources for drugs field activities declined 21 percent from 759 FTEs in fiscal year 2004 to 600 FTEs in fiscal year 2008.
- Biologics program staffing resources for CBER activities grew 8 percent from 797 FTEs to 858 FTEs, while FTEs supporting biologics field activities declined 13 percent from 241 FTEs to 209 FTEs.
- Devices program staffing resources for CDRH activities grew 7 percent from 1,061 FTEs to 1,130 FTEs, while staffing resources for devices field activities declined 4 percent from 454 FTEs to 434 FTEs.

Table 7 shows how FDA's medical product programs allocated FTE resources to various center and field activities.

Table 7: Medical Product Program Staffing Resources for Center and Field Activities, Fiscal Years 2004 through 2008

Full-time equivalents (FTE)

	Fiscal year				
Activity	**2004**	**2005**	**2006**	**2007**	**2008**
Drugs program					
Center for Drug Evaluation and Research (CDER) activities					
Generic drug review	260	257	250	248	287
New drug safety and effectiveness	1,673	1,683	1,767	1,583	1,608
Postmarket safety and surveillance	257	280	269	457	501
CDER activities subtotal	**2,190**	**2,220**	**2,286**	**2,288**	**2,396**
Office of Regulatory Affairs (ORA) field activities					
Bioresearch monitoring	123	108	108	115	113
Generic drug evaluation	47	38	31	35	32
New drug evaluation	52	41	35	41	43
Over-the-counter drug evaluation	1	1	1	0	1
Postmarket surveillance and epidemiology	9	13	13	9	12
Prescription drug advertising and labeling	0	0	0	1	0
Quality assurance	514	485	461	414	377
Unapproved and misbranded drugs	12	11	13	12	22
Field activities subtotal	**759**	**698**	**661**	**627**	**600**
Drugs program total	**2,949**	**2,918**	**2,947**	**2,915**	**2,996**
Biologics program					
Center for Biologics Evaluation and Research (CBER) activities					
Blood and blood products	286	294	294	301	309
Cell, gene therapy, and tissues	128	126	119	138	139
Vaccines and allergenic products	383	398	359	388	409
CBER activities subtotal	**797**	**818**	**772**	**827**	**858**
ORA field activities					
Blood and blood products	196	176	146	145	148
Cell, gene therapy, and tissues	32	26	44	54	39
Vaccines and allergenic products	13	21	17	19	22
Field activities subtotal	**241**	**223**	**207**	**218**	**209**
Biologics program total	**1,038**	**1,041**	**979**	**1,045**	**1,066**

Full-time equivalents (FTE)

	Fiscal year				
Activity	**2004**	**2005**	**2006**	**2007**	**2008**
Devices program					
Center for Devices and Radiological Health (CDRH) activities					
Premarket applied research	59	58	54	54	51
Premarket outreach and coordination	42	46	51	43	68
Premarket review	516	566	578	634	618
Postmarket applied research	19	15	7	9	7
Postmarket laboratory analysis	57	82	54	51	48
Postmarket outreach, coordination, and compliance	368	337	341	333	338
CDRH activities subtotal	**1,061**	**1,104**	**1,085**	**1,124**	**1,130**
ORA field activities					
Compliance	296	286	287	290	301
Mammography Quality Standards Act Authority	16	16	15	16	16
Postmarket assurance	15	17	16	17	22
Product Evaluation	76	54	58	62	63
Radiation Control for Health and Safety Act Authority	44	34	31	30	30
Science	7	5	5	4	2
Field activities subtotal	**454**	**412**	**413**	**420**	**434**
Devices program total	**1,515**	**1,516**	**1,498**	**1,544**	**1,564**

Source: FDA.

Notes: One FTE represents 40 hours of work per week conducted by a federal government employee over the course of 1 year and does not include contractors. Totals may not sum due to rounding.

Appendix III: Trends in FDA's Review of Generic Drug, New Drug and New Biologic Applications

The Food and Drug Administration (FDA) faced an increasing workload related to the process for reviewing generic drug, new drug, and new biologic applications between fiscal year 2004 and fiscal year 2008. For example, FDA received 47 percent more applications for generic drugs in fiscal year 2008 than in fiscal year 2004. Even though FDA funding for the review of these applications grew 53 percent over this time period, agency officials said that resource constraints precluded them from reviewing all applications submitted, resulting in a growing number of applications pending review.

Trends in Reviewing Generic Drug, New Drug, and New Biologic Applications

FDA reviewed an increasing number of abbreviated new drug applications (ANDA) for generic drugs between fiscal years 2004 and 2008. However, FDA received a greater number of applications each year than it was able to review. The number of original ANDAs received for review increased by 47 percent—from 563 in fiscal year 2004 to 830 in fiscal year 2008. During this time period, FDA reviewed an increasing number of ANDAs each year. In fiscal year 2004, FDA reviewed 1,357 ANDAs and in fiscal year 2008 the agency reviewed 1,933 ANDAs—an increase of 42 percent.[1] While the number of ANDAs the agency reviewed each year increased, FDA was not able to review them all. As a result, the number of applications pending review increased 123 percent over the period. (See table 8.) FDA officials told us that they were unable to review all ANDAs because they did not have enough resources to conduct these reviews.

[1]The number of ANDAs FDA reviewed exceeds the number of original ANDAs received in a particular year because FDA may have completed its review of original ANDAs submitted during prior years, or may have reviewed resubmitted applications.

Table 8: Elements of FDA's Oversight Work Related to the Process of Reviewing ANDAs, Fiscal Years 2004 through 2008

	Fiscal year				
	2004	2005	2006	2007	2008
Original ANDAs received	563	766	793	880	830
ANDAs reviewed	1,357	1,496	1,456	1,779	1,933
ANDA supplements reviewed (manufacturing and labeling)	4,630	4,566	4,577	3,720	3,516
ANDAs pending review	646	891	1,216	1,344	1,441

Source: FDA.

Note: The number of ANDAs FDA reviewed exceeds the number received in a particular year because FDA may have completed its review of original ANDAs submitted during prior years, or may have reviewed resubmitted applications.

Between fiscal year 2004 and fiscal year 2008, FDA conducted an increased amount of work related to the review of new drug and new biologic applications. In particular, FDA was increasingly involved in the process of new drug and new biologic development, which typically occurs years before sponsors submit a new drug application (NDA) or biologics license application (BLA) to FDA for approval. FDA reported that sponsors' early consultation with the agency generally results in improvements in the safety and effectiveness of the clinical trials. In addition, FDA indicated that the agency's increased involvement generally improves the quality of information submitted in an application for marketing approval and increases the likelihood that the resulting application will gain faster approval.

The number of active investigational new drugs (IND)—representing new drugs and new biologics in development—grew from 12,523 in fiscal year 2004 to 15,020 in fiscal year 2008. To guide the development of these new products, FDA issued an increasing number of written guidance documents to sponsors between fiscal year 2004 and fiscal year 2008. For example, FDA issued 135 responses to clinical holds in fiscal year 2004 and 213 such responses in fiscal year 2008. In addition, while the number of meetings FDA conducted with sponsors regarding new drug development varied from year to year, between fiscal year 2004 and fiscal year 2008 FDA scheduled over 10,000 meetings with sponsors, with between 1,900 and 2,300 such meetings each year. (See table 9.) FDA officials stated that drafting written responses and preparing for and documenting the results of meetings with sponsors requires a substantial amount of staff time. In particular, FDA noted that each meeting typically requires the involvement of at least 15 FDA staff and can require between 120 to 540 hours of staff time.

Table 9: Elements of FDA's Oversight Work Related to the Process of New Drug Development and Application Review, Fiscal Years 2004 through 2008

	Fiscal year				
	2004	2005	2006	2007	2008
New drug development					
Active INDs	12,523	13,106	13,881	14,820	15,020[a]
Responses to clinical holds	135	130	145	175	213
Special protocol assessments	346	396	406	459	354
Responses to sponsor appeals of a decision (major dispute resolutions)	10	9	9	22	14
Meetings scheduled	2,125	2,230	2,273	2,151	1,903
Applications					
Original NDAs and BLAs received and filed	129	111	124	123	143
Resubmitted NDAs and BLAs	85	59	61	73	54
Total number of original and resubmitted NDAs and BLAs	214	170	185	196	197
NDAs and BLAs reviewed	206	192	177	184	161
NDA and BLA supplements (efficacy, labeling and manufacturing) reviewed	3,918	3,725	3,822	4,045	3,721

Source: FDA.

Note: Our examination of FDA's review of BLAs was restricted to those subject to certain performance goals. The total number of applications FDA reviewed may exceed the number FDA received in a particular year because FDA may have completed its review of applications submitted during prior years, or may have reviewed resubmitted applications.

[a]FDA estimate.

Although FDA was increasingly involved in the process of new drug and new biologic development between fiscal year 2004 and fiscal year 2008, the agency's review of NDAs and BLAs decreased slightly over the time period, following trends in the number of applications the agency received. As shown in table 9, the total number of original and resubmitted NDAs and BLAs FDA received decreased from 214 applications in fiscal year 2004 to 197 applications in fiscal year 2008.[2] FDA also reviewed a decreasing number of NDAs and BLAs—in fiscal year 2004 FDA reviewed 206 original and resubmitted NDAs and BLAs and in fiscal year 2008 FDA reviewed 161 such applications. FDA also reviewed between about 3,700

[2]The number of NDAs and BLAs submitted to FDA is significantly less than the number of active INDs. We previously reported data from the Pharmaceutical Research and Manufacturers of America showing that only one of every five new drugs successfully completes clinical testing. See GAO, *New Drug Development: Science, Business, Regulatory, and Intellectual Property Issues Cited as Hampering Drug Development Efforts*, GAO-07-49 (Washington, D.C.: Nov. 17, 2006).

and 4,000 efficacy, labeling, and manufacturing NDA and BLA supplements each year during this period.

FDA has many performance goals related to its process for reviewing new drug applications. According to FDA officials, the agency places a higher priority on the speed with which it reviews applications for new drugs and biologics, compared to the speed with which the agency responds to sponsor requests for information and scheduling and holding meetings with sponsors. As a result of this prioritization, FDA focused its resources on its review of applications—and we found FDA generally met its performance goals in this area. However, agency officials noted that the agency did not have sufficient resources to meet performance goals related to responding to sponsor requests for information and scheduling and holding meetings.

Trends in Resources for Reviewing Generic Drug, New Drug, and New Biologic Applications

Between fiscal year 2004 and fiscal year 2008, funding for FDA's review of ANDAs—which is provided solely through FDA's fiscal year appropriations—increased 53 percent from about $53 million in fiscal year 2004 to about $82 million in fiscal year 2008. Over the same period, funding resources for FDA's process for reviewing NDAs and BLAs, an activity that receives both user fee funding and fiscal year appropriations, increased 58 percent. Specifically, funding increased from $437 million in fiscal year 2004 to $691 million in fiscal year 2008.

During the same period, the number of full-time equivalent (FTE) staff supporting the agency's review of ANDAs decreased 12 percent from 427 FTEs in fiscal year 2004 to 376 FTEs in fiscal year 2008. In contrast, the number of FTEs supporting the agency's review of new drug and new biologic applications increased from 2,561 FTEs in fiscal year 2004 to 2,780 FTEs in fiscal year 2008. This increase in FTEs was solely due to an increase in the number of FTEs funded by user fees. Because counts of FTEs do not include contractors, these data do not fully represent FDA's staffing resources for these activities.

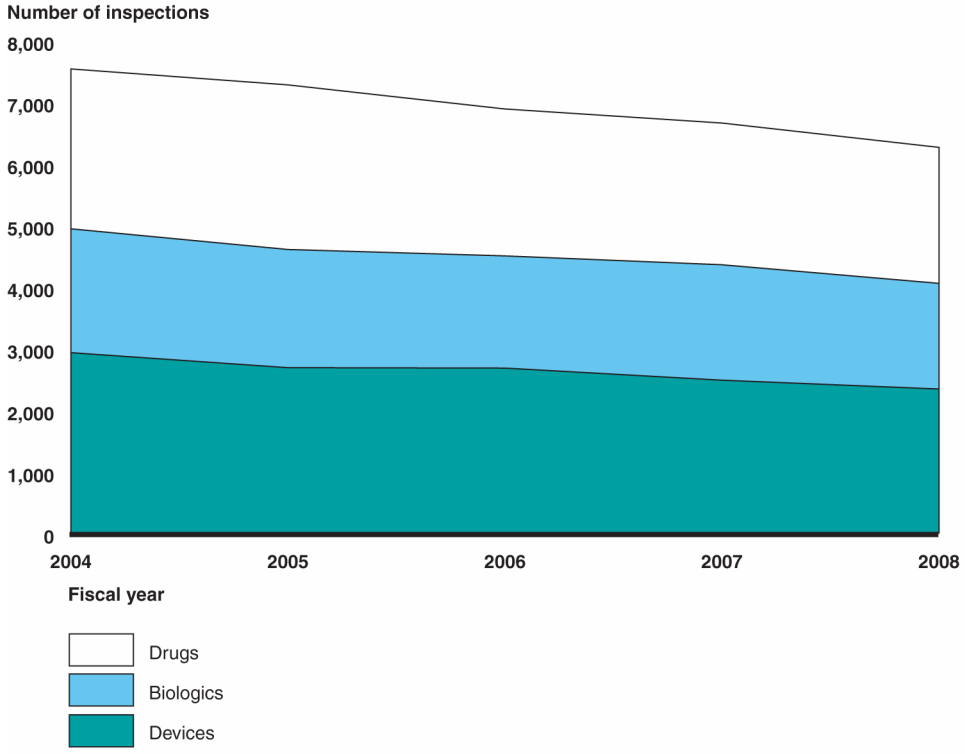
Appendix IV: Trends in FDA Inspections Conducted to Oversee Medical Product Research and Manufacturing

Between fiscal years 2004 and 2008, the number of medical product inspections the Food and Drug Administration (FDA) conducted decreased 17 percent—primarily due to a 19 percent decrease in the number of domestic inspections. Although the total number of inspections decreased, funding for inspections grew 16 percent overall, and the rate of funding increases for drugs and biologics inspections did not keep pace with inflation, as measured by the gross domestic product (GDP) price index. The agency conducted an increasing number of foreign inspections, which on average cost more than twice as much as each domestic inspection, and may explain why increased inspection funding supported a fewer number of total inspections.

Trends in Conducting Inspections

The total number of inspections FDA conducted for its medical product programs decreased from 7,589 inspections in fiscal year 2004 to 6,306 inspections in fiscal year 2008, a decline of 1,283 inspections or 17 percent. The total number of inspections conducted for each program decreased over the time period. (See fig. 9.)

Figure 9: Medical Product Program Inspections, Fiscal Years 2004 through 2008



Source: FDA.

Between fiscal years 2004 and 2008, FDA decreased the number of domestic medical product program inspections conducted each year. FDA conducted 6,849 domestic inspections in fiscal year 2004 and 5,543 domestic inspections in fiscal year 2008—a decline of 19 percent or 1,306 inspections over the 5-year time period. FDA reduced the number of domestic inspections it conducted for each of the medical product programs between fiscal years 2004 and 2008.

- For the drugs program, FDA conducted 2,241 domestic inspections in fiscal year 2004 and 1,772 such inspections in fiscal year 2008—a decrease of 469 inspections or 21 percent.
- For the biologics program, FDA conducted 2,009 domestic inspections in fiscal year 2004 and 1,678 domestic inspections in fiscal year 2008, a decrease of 331 inspections or 16 percent.

- For the devices program, FDA conducted 2,599 domestic inspections in fiscal year 2004 and 2,093 domestic inspections in fiscal year 2008, a decline of 506 inspections or 19 percent.

FDA conducted fewer domestic medical product inspections overall, although the agency increased the number of certain types of domestic inspections.[1] For example, within the biologics program, FDA increased the number of domestic inspections of human cellular, tissue, and gene therapy products, and vaccines and allergenic products between fiscal years 2004 and 2008. In addition, FDA increased the number of domestic postmarket assurance device inspections it conducted over the 5 year period. (See table 10.)

[1]FDA tracks inspections in categories that reflect either inspection type or product type. For the drugs and devices programs, FDA tracks the number of inspections conducted based on inspection type. The types of inspections conducted for the drugs program include bioresearch monitoring, new drug evaluation, and postmarket surveillance, and the types of inspections conducted for the devices program include product evaluation, compliance, and postmarket assurance. FDA does not track biologics program inspections based on inspection type. Instead, the agency tracks the number of inspections conducted for the biologics program by product type—for example, blood and blood products, and vaccines and allergenic products.

Table 10: Number of Domestic and Foreign Inspections for the Drugs, Biologics, and Devices Programs, Fiscal Years 2004 through 2008

	Fiscal year									
	2004		2005		2006		2007		2008	
	Dom.	For.	Dom.	For.	Dom.	For.	Dom.	For.	Dom.	For.
Drugs Program										
Bioresearch monitoring	599	105	567	93	508	122	495	155	531	129
Generic drug evaluation	82	87	90	79	82	78	84	141	101	117
New drug evaluation	196	156	152	166	139	123	135	169	139	174
Over-the-counter drug evaluation	19	0	12	1	2	0	1	0		0
Postmarket surveillance and epidemiology	78	11	105	11	105	10	89	9	89	6
Prescription drug advertising and labeling	2	0	1	0	0	0	1	0	0	0
Quality assurance	1,524	201	1,619	217	1,447	164	1,233	283	1,135	268
Unapproved and misbranded drugs	38	0	54	0	47	0	34	0	49	0
Drugs program total	**2,241**	**374**	**2,322**	**370**	**2,061**	**342**	**1,817**	**501**	**1,772**	**452**
Biologics program										
Blood and blood products	1,706	8	1,613	25	1,462	8	1,398	21	1,314	22
Human cellular, tissue and gene therapies	351	3	305	1	402	1	458	6	407	5
Vaccines and allergenic products	38	6	70	14	52	13	79	13	66	23
Biologics program total	**2,009**	**17**	**1,893**	**40**	**1,813**	**22**	**1,848**	**40**	**1,678**	**50**
Devices program										
Compliance	1,645	293	1,486	225	1,530	209	1,318	268	1,303	208
Mammography Quality Standards Act Authority	444	18	489	16	473	5	417	19	406	14
Postmarket assurance	628	131	642	83	686	82	696	115	749	77
Product evaluation	489	61	448	49	443	74	430	67	373	61
Radiation Control for Health Safety Act Authority	119	24	107	9	85	24	86	10	90	11
Devices program total	**2,599**	**349**	**2,434**	**269**	**2,430**	**266**	**2,170**	**328**	**2,093**	**261**
Medical product programs total	**6,849**	**740**	**6,649**	**679**	**6,304**	**630**	**5,835**	**869**	**5,543**	**763**

Source: FDA.

Legend: Dom. = domestic inspection; For. = foreign inspection.

Note: Individual entries may not sum to program totals because FDA may conduct more than one type of inspection on the same occasion.

While the number of domestic inspections declined for medical product programs overall between fiscal year 2004 and fiscal year 2008, FDA increased the number of foreign inspections it conducted for the drugs and biologics programs. The total number of foreign inspections fluctuated from year to year, and in fiscal year 2008, FDA conducted a total of 763 foreign inspections—23 more than it did in 2004.

- For the drugs program, FDA conducted 374 foreign inspections in fiscal year 2004 and 452 such inspections in fiscal year 2008—an increase of 78 inspections.
- For the biologics program, FDA conducted 17 foreign inspections in fiscal year 2004 and 50 such inspections in fiscal year 2008—an increase of 33 inspections.
- For the devices program, FDA conducted 349 foreign inspections in fiscal year 2004 and 261 such inspections in fiscal year 2008—a decrease of 88 inspections.

Despite increases in the total number of foreign inspections conducted over this time period, they constituted a small share—12 percent—of the total number of medical product program inspections in fiscal year 2008. In addition, FDA is only able to reach a small share of the total number of foreign establishments producing medical products for the U.S. market. In fiscal year 2008, FDA conducted inspections at 749 foreign establishments, which represented about 7 percent of the 10,158 total foreign medical product establishments registered with the agency that year.

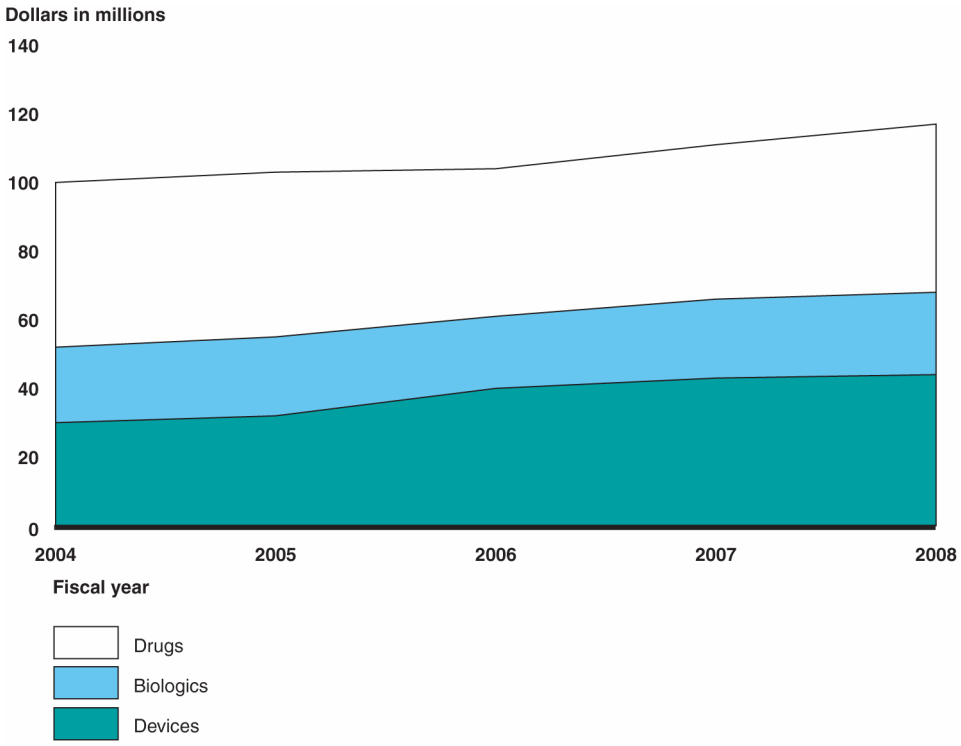
Trends in Inspection Resources

FDA conducted 17 percent fewer medical product inspections in fiscal year 2008 than it did in fiscal year 2004, although Office of Regulatory Affairs (ORA) funding for these inspections increased 16 percent during this period—from about $101 million to about $117 million. While the total number of medical product inspections FDA conducted decreased, the agency conducted more foreign inspections over this time period. FDA estimates that, on average, the cost of a foreign inspection is more than twice the cost of a domestic inspection. The agency's increase in foreign inspections may explain why increased inspection funding supported fewer total inspections.

Although funding for inspections was greater in fiscal year 2008 than in fiscal year 2004, it did not increase in each of these 5 years for each medical product program. Funding for the drugs and biologics program

inspections remained relatively constant between fiscal years 2004 and 2005, decreased in fiscal year 2006, and increased in fiscal years 2007 and 2008. In fiscal year 2008, funding for drugs program inspections was 1 percent greater than it was in fiscal year 2004, and funding for biologics program inspections was 8 percent greater than it was in fiscal year 2004. These rates of increase in funding were substantially lower than the GDP rate of inflation between fiscal years 2004 and 2008 of 12 percent. For the devices program, funding remained relatively constant between fiscal years 2004 and 2005, increased in fiscal years 2006 and 2007, and remained relatively constant between fiscal years 2007 and 2008. Over this period, funding for devices program inspections increased 46 percent. (See fig. 10.)

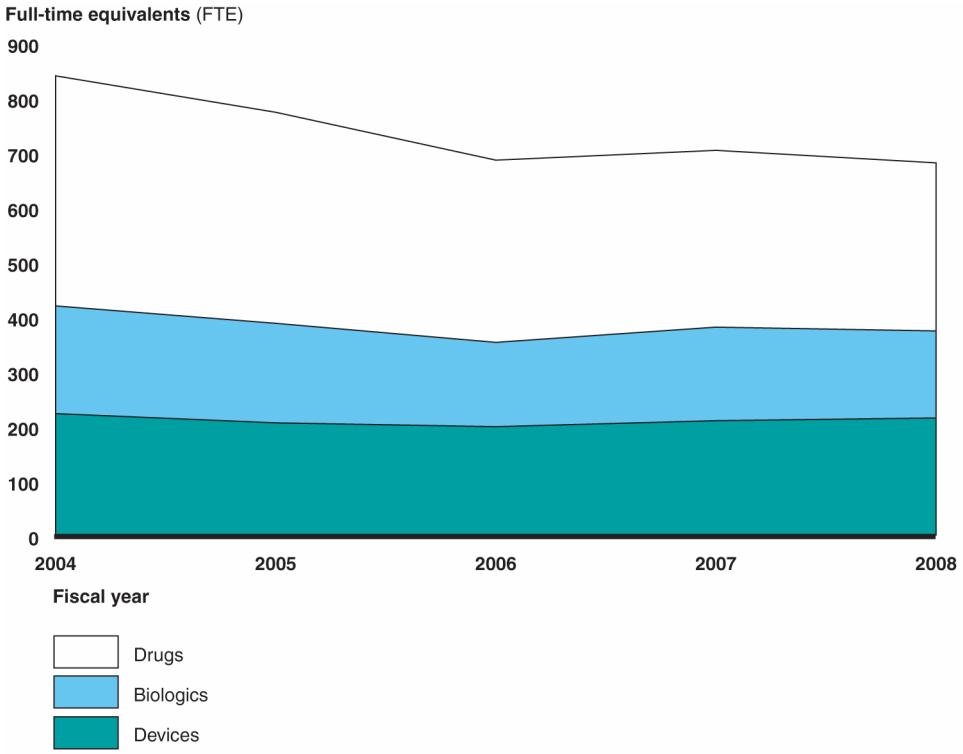
Figure 10: Annual Funding Resources for Medical Product Program Inspections, Fiscal Years 2004 through 2008



Source: FDA.

Although ORA funding for inspection activities increased between fiscal year 2004 and fiscal year 2008, the number of ORA full-time equivalent (FTE) staff devoted to medical product inspections declined 19 percent during this time period, from 844 FTEs in fiscal year 2004 to 684 FTEs in fiscal year 2008. Each of the medical product programs experienced a decline in FTEs conducting inspections during this time period. Compared to fiscal year 2004 FTE levels, in fiscal year 2008 there were 114 fewer FTEs devoted to drug inspections (a decline of 27 percent), 38 fewer FTEs devoted to biologics inspections (a decline of 19 percent), and 8 fewer FTEs devoted to device inspections (a decline of 4 percent). Most of the decreases in FTEs occurred between fiscal year 2004 and fiscal year 2006. (See fig. 11.) Although contractors do not perform establishment inspections, they may conduct activities that facilitate these inspections. Because counts of FTEs do not include contractors, these data do not fully represent FDA's staffing resources for these activities.

Figure 11: Annual Staffing Resources for Medical Product Program Inspections, Fiscal Years 2004 through 2008



Source: FDA.

Note: One FTE represents 40 hours of work per week conducted by a federal government employee over the course of 1 year, and does not include contractors.

Appendix V: Trends in FDA's Review of Adverse Event Reports

From fiscal years 2004 to 2008, the Food and Drug Administration (FDA) received an increasing number of adverse event reports for marketed medical products—substantially more reports than staff could review, according to FDA officials. While the total number of adverse event reports FDA received increased 81 percent over this time period, funding increased 154 percent and staffing resources increased 100 percent. Although FDA officials told us they received more adverse event reports than staff could review, the agency could not provide data showing the number of adverse event reports staff reviewed during this time period.

Trends in Reviewing Adverse Event Reports

From fiscal years 2004 to 2008, FDA received an increasing number of adverse event reports for marketed medical products. During this time period the number of drug-related adverse event reports FDA received increased 23 percent, from 426,016 reports in fiscal year 2004 to 522,871 reports in fiscal year 2008. An even bigger increase occurred in the receipt of biologic adverse event reports, which increased 86 percent, from 19,569 reports in fiscal year 2004 to 36,410 reports in fiscal year 2008. FDA saw the highest growth—210 percent—in device-related adverse event reports, with 189,450 reports received in fiscal year 2004 and 588,161 reports received in fiscal year 2008. As the number of adverse event reports for drugs, biologics, and devices grew between fiscal years 2004 and 2008, the number of reports that FDA considers to be serious increased 72 percent.

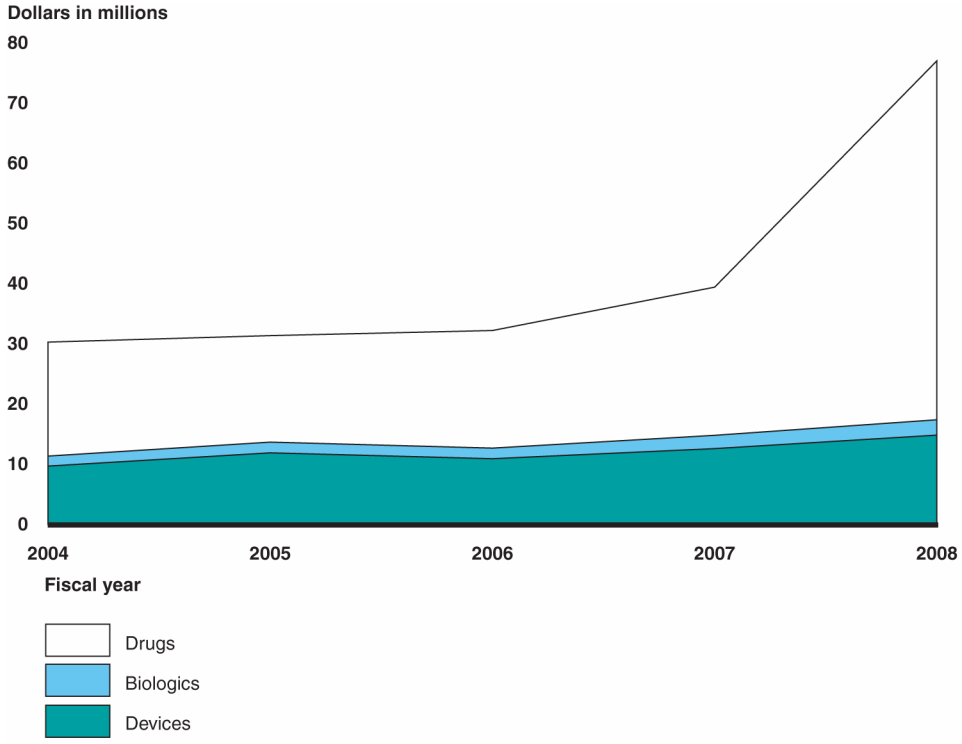
Although FDA officials told us that they place the highest priority in reviewing serious adverse event reports, agency officials reported that they receive substantially more adverse event reports than staff can review. However, FDA could not provide data showing how many adverse event reports staff have reviewed. According to agency officials, the drug, biologic, and device adverse event reporting systems used by FDA do not allow the agency to accurately determine if an individual adverse event report has been reviewed by staff.

Trends in Resources for Reviewing Adverse Event Reports

FDA's financial and staffing resources for the review of adverse event reports associated with the use of marketed medical products have grown from fiscal years 2004 to 2008. Overall, funding for adverse event reviews has increased 154 percent during this time period from about $31 million in fiscal year 2004 to about $78 million in fiscal year 2008. FDA experienced the greatest growth in financial resources for the review of drug-related adverse event reports with a 215 percent increase or from about $19 million in fiscal year 2004 to about $60 million in fiscal year 2008. Meanwhile, FDA saw the lowest increase in funding—53 percent—

for the review of device-related adverse event reports, or from about $10 million in fiscal year 2004 to about $15 million in fiscal year 2008. Funding for adverse event reviews—in total, and for each program—grew at a rate faster than inflation over this time period as measured by the gross domestic product (GDP) price index. See figure 12 for trends in FDA funding for the review of adverse events related to drugs, biologics, and devices.

Figure 12: Funding for Adverse Event Reviews Related to Drugs, Biologics, and Devices, Fiscal Years 2004 through 2008



Source: FDA.

Similar to the increase in funding for reviews related to drugs, biologics, and devices, the number of full-time equivalent (FTE) staff supporting the review of adverse event reports also increased from fiscal years 2004 through 2008. The largest growth in FTEs—248 percent or from 31 FTEs in fiscal year 2004 to 108 FTEs in fiscal year 2008—was for the review of drug-related adverse event reports. Over the same period, the number of FTEs for the review of adverse event reports related to biologics grew 17 percent, from 12 FTEs to 14 FTEs, while the number of FTEs for the

review of device-related adverse event reports grew 9 percent, from about 40 FTEs to about 43 FTEs. Because counts of FTEs do not include contractors, these data do not fully represent FDA's staffing resources for these activities.

With the enactment of the Food and Drug Administration Amendments Act of 2007 (FDAAA), FDA was able to apply user fees collected through the Prescription Drug User Fee Act of 1992 (PDUFA), as amended, to support more postmarket safety activities for drugs, such as the review of adverse event reports.[1] FDA attributes about two-thirds of the increase in funding and FTEs between fiscal years 2007 and 2008—142 percent and 40 percent respectively—for the review of drug-related adverse events to user fee funds.[2]

[1]FDA's authority to apply user fees collected under the Medical Device User Fee and Modernization Act of 2002, as amended, to postmarket safety activities for devices is limited to the evaluation of postmarket studies and safety and effectiveness information for certain devices.

[2]Along with authorizing FDA to use PDUFA funding for more postmarket safety activities, FDAAA also increased the actions FDA must take to meet its responsibility to ensure the safety of marketed drugs by requiring FDA to biweekly screen its system for adverse events and issue quarterly reports of new safety information or potential signals of serious risk associated with the use of a drug.

Appendix VI: Trends in FDA's Examination of Advertising and Promotional Materials

The Food and Drug Administration (FDA) faced an increasing workload related to its examination of advertising and promotional materials between fiscal years 2004 and 2008, particularly for drug-related promotions. Such promotions constitute the majority of advertising and promotional materials submitted. While the total number of final drug-related promotional materials FDA received increased 55 percent over the period, agency funding for the examination of these materials increased 167 percent and staff resources increased 26 percent. Although FDA officials noted that the agency did not have sufficient resources to examine all drug-related promotional materials submitted for review, FDA also could not provide information on the number of such materials staff reviewed.

Trends in Examining Advertising and Promotional Materials

During fiscal years 2004 through 2008, FDA received an increasing number of advertising and promotional materials for examination from manufacturers; however, the agency did not track all of the drug- and device-related materials that it received or reviewed during this period. According to FDA officials, the agency was unable to examine all materials promoting drugs, although we found it did examine nearly all such materials for biologics. FDA officials also told us that they review all device-related promotional materials that are submitted.

- *Drugs*. FDA received an increasing number of advertising and promotional materials for examination between fiscal year 2004 and fiscal year 2008, but agency officials told us that staff were unable to review all materials submitted. FDA received an increasing number of voluntary draft submissions each year, with 429 submissions in fiscal year 2004 and 634 submissions in fiscal year 2008.[1] In addition to receiving these voluntary draft submissions, FDA received a substantially greater and increasing number of final materials that manufacturers were required to submit. FDA received 45,394 final materials in fiscal year 2004 and 70,509 final materials in fiscal year 2008—an increase of 55 percent over the time period.[2] FDA officials told us that the agency was unable to examine all of

[1]FDA received a total of 2,709 draft submissions over the 5-year period. Draft submissions may be comprised of many submitted materials—for example, one submission may include multiple brochures. As we previously reported, FDA does not maintain data on the number of materials received. See GAO, *Prescription Drugs: FDA's Oversight of the Promotion of Drugs for Off-Label Uses*, GAO-08-835 (Washington, D.C.: July 28, 2008).

[2]FDA received a total of nearly 300,000 final drug-related promotional materials between fiscal year 2004 and fiscal year 2008.

the promotional materials for drugs it received between fiscal year 2004 and fiscal year 2008 because it lacked the resources to do so. However, FDA could not provide data on the number of draft or final materials staff examined during this time.[3]

- *Biologics*. We found that FDA received and examined an increasing number of draft and final advertising and promotional materials for biologics products between fiscal year 2006—the first year of available data—and fiscal year 2008. Specifically, our review of FDA data showed that the agency examined all 2,929 draft and final promotional materials submitted in fiscal year 2006, all 3,256 materials submitted in fiscal year 2007, and all but 17 of 4,480 materials submitted in fiscal year 2008. Most—over 90 percent—of the total number of materials submitted in each of these years were final promotional materials.

- *Devices*. An FDA official told us that the agency received very few promotional materials for devices between fiscal year 2004 and fiscal year 2008—device manufacturers are not required to submit these materials. The official also explained that although all materials received are examined, FDA could not provide data on the number of advertising and promotional materials submitted or examined during this period.

Trends in Resources for Examining Advertising and Promotional Materials

Funding for FDA's oversight of drug advertising and promotion increased 167 percent from about $4 million in fiscal year 2004 to about $10 million in fiscal year 2008. Funding for FDA's oversight of biologics advertising and promotion also increased from $546,000 in fiscal year 2004 to $925,000 in fiscal year 2008. In contrast, funding for the agency's oversight of devices advertising and promotion decreased from $590,000 in fiscal year 2004 to $452,000 in fiscal year 2008.

The number of full-time equivalent (FTE) staff supporting FDA's oversight of drug promotions grew 26 percent from 35 FTEs in fiscal year 2004 to 44 FTEs in fiscal year 2008. Over this period, the number of FTEs supporting the agency's oversight of biologics promotions increased from 4 FTEs to 6 FTEs, while the number of FTEs supporting the agency's review of devices

[3]FDA does track the number of letters it issues in response to the draft promotional materials that staff examined. However, these letters may encompass issues from multiple submitted materials, and the agency does not issue a letter for every draft promotional material examined. Between fiscal year 2004 and fiscal year 2008, FDA sent a total of 2,262 letters in response to its examination of draft promotional materials, and the number of letters issued decreased 44 percent during this period.

promotions decreased from 5 FTEs to 4 FTEs. Because counts of FTEs do not include contractors, these data do not fully represent FDA's staffing resources for these activities.

Appendix VII: Comments from the Department of Health and Human Services

DEPARTMENT OF HEALTH & HUMAN SERVICES

OFFICE OF THE SECRETARY

Assistant Secretary for Legislation
Washington, DC 20201

JUN 8 2009

Marcia Cross
Director, Health Care
U.S. Government Accountability Office
441 G Street N.W.
Washington, DC 20548

Dear Ms. Cross:

Enclosed are comments on the U.S. Government Accountability Office's (GAO) report entitled: "FOOD AND DRUG ADMINISTRATION: FDA Faced Challenges Meeting its Growing Medical Product Responsibilities, and Should Develop Complete Estimates of its Resource Needs (GAO-09-581).

The Department appreciates the opportunity to review this report before its publication.

Sincerely,

Barbara Pisaro Clark

Barbara Pisaro Clark
Acting Assistant Secretary for Legislation

Attachment

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

Date: June 5, 2009

To: Acting Assistant Secretary for Legislation

From: Principal Deputy Commissioner

Subject: FDA's General Comments to GAO's Draft Report Entitled, *Food and Drug Administration: FDA Faced Challenges Meeting its Growing Medical Product Responsibilities, and Should Develop Complete Estimates of its Resource Needs (GAO-09-581)*

FDA is providing the attached general comments to the U.S. Government Accountability Office's draft report entitled, *Food and Drug Administration: FDA Faced Challenges Meeting its Growing Medical Product Responsibilities, and Should Develop Complete Estimates of its Resource Needs (GAO-09-581).*

FDA appreciates the opportunity to review and comment on this draft report before it is published.

Joshua M. Sharfstein, M.D.

Attachment

FDA's General Comments on the U.S. Government Accountability Office (GAO) Draft Report entitled: *Food and Drug Administration: FDA Faced Challenges Meeting its Growing Medical Product Responsibilities, and Should Develop Complete Estimates of its Resource Needs (GAO-09-581)*

The Food and Drug Administration (FDA) appreciates the opportunity to review and comment on the Government Accountability Office's (GAO) draft report. GAO has raised some important issues regarding FDA's challenges in meeting its medical product responsibilities. The FY 2010 President's Budget for FDA includes an overall increase of $240 million for FDA's medical product activities. Nearly $120 million of that is in increased budget authority for safer medical products, including human and veterinary drug safety, the safety of medical devices, and biological products including blood, tissue and vaccine safety. The budget also proposes new user fees for generic drugs (+$36 million) and for reinspection fees (+10.6 million). These user fees are in addition to a $74.3 million increase in current law user fees supporting FDA medical product programs.

The increases will support a life-cycle approach to safety, which starts at product development and pre-approval testing, through approval, and post-approval safety surveillance. The additional funding also provides for increased inspections to improve the safety of the supply chain, and supports implementation of requirements included in the FDA Amendments Act.

FDA offers the following responses to the GAO recommendations:

Recommendation 1
Conduct a comprehensive assessment of the Agency's staffing resources, including its contractor workforce.

FDA Response
The FDA agrees that a comprehensive assessment of its staffing resources would provide useful information. The agency has in place a staffing assessment process that has been used for assessing needs for new staffing and backfills. This assessment has been conducted over the last 18 months for FDA's Hiring Surges (Phase I and II). FDA will expand this process to include both contractor workforce and existing staff. FDA will also utilize this process to plan and assess future agency staffing needs.

Recommendation 2
Gather data on the work the agency conducts to fulfill its responsibilities.

FDA Response
The FDA plans to conduct a complete inventory of all regulatory work products by Center.

Recommendation 3
Assess the extent to which the agency is meeting its responsibilities.

FDA Response
Along with the inventory of work products generated in response to recommendation 2 above, FDA will identify and implement relevant measures for agency programs and offices which will allow FDA to determine how effectively the agency is meeting its responsibilities. Many measures of productivity are already in place in conjunction with user fees and related performance indicators. The data collected and analyzed for these metrics will be used to inform FDA management about the effectiveness of specific programs in meeting the agency's responsibilities and inform management about whether or not changes to specific programs should be made.

Recommendation 4
Develop an evidence-based estimate of the resources needed to fulfill all of its responsibilities.

FDA Response
In addition to implementing performance management through the use of metrics across agency offices and programs the agency plans to link these metrics to its budget and funding allocation. This approach will inform the agency about how well it is allocating its resources and what additional resources it needs to fulfill its responsibilities.

Appendix VIII: GAO Contact and Staff Acknowledgments

GAO Contact

Marcia Crosse, (202) 512-7114, crossem@gao.gov

Staff Acknowledgments

In addition to the contact named above, Geri Redican-Bigott, Assistant Director; Kye Briesath; Cathy Hamann; Rebecca Hendrickson; Richard Lipinski; Emily Loriso; Kevin Milne; Lisa Motley; and Patricia Roy made key contributions to this report.

Related GAO Products

Information Technology: FDA Needs to Establish Key Plans and Processes for Guiding Systems Modernization Efforts. GAO-09-523. June 2, 2009.

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