

BIOLOGICS

The FY 2010 program level budget submission for the FDA Biologics Program is \$305,731,000.

The following table shows a three-year funding history for the Biologics Program.

FDA Program Resources Table

	FY 2008		FY 2009 Omnibus	FY 2010 President's Budget Request	FY 2010 +/- FY 2009 Omnibus
	Enacted	Actuals			
Program Level	\$248,627,000	\$233,508,000	\$271,490,000	\$305,731,000	\$34,241,000
Center	\$212,390,000	\$202,278,000	\$232,308,000	\$260,997,000	\$28,689,000
FTE	888	858	916	959	43
Field	\$36,237,000	\$31,230,000	\$39,182,000	\$44,734,000	\$5,552,000
FTE	228	209	230	238	8
Program Level FTE	1,116	1,066	1,146	1,197	51
Budget Authority	\$167,965,000	\$154,831,000	\$183,451,000	\$206,438,000	\$22,987,000
Center	\$135,457,000	\$125,383,000	\$148,134,000	\$166,182,000	\$18,048,000
Field	\$32,508,000	\$29,448,000	\$35,317,000	\$40,256,000	\$4,939,000
<i>Pay Increase (non add)</i>				\$2,803,000	\$2,803,000
<i>Safer Medical Products (non-add)</i>				\$20,184,000	\$20,184,000
Budget Authority FTE	795	725	810	836	26
Center	579	526	592	615	23
Field	216	199	218	221	3
User Fees	\$80,662,000	\$78,677,000	\$88,039,000	\$99,293,000	\$11,254,000
Center PDUFA	\$66,824,000	\$70,890,000	\$73,206,000	\$83,747,000	\$10,541,000
FTE	278	304	293	313	20
Field PDUFA	\$3,262,000	\$1,524,000	\$3,358,000	\$3,489,000	\$131,000
FTE	10	8	10	10	0
Center MDUFMA	\$10,109,000	\$6,005,000	\$10,968,000	\$11,068,000	\$100,000
FTE	31	28	31	31	0
Field MDUFMA	\$467,000	\$258,000	\$507,000	\$507,000	\$0
FTE	2	2	2	4	2
Proposed User Fees	\$0	\$0	\$0	\$482,000	\$482,000
Field Reinspection (non-add)				\$482,000	\$482,000
FTE				3	3
User Fees FTE	321	342	336	361	25

The FDA Biologics Program operates under the following legal authorities:

Public Health Service Act

Federal Food, Drug, and Cosmetic Act* (21 U.S.C. 321-399)

Medical Device Amendments of 1976*

Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 201)

Safe Medical Devices Act of 1990*

Medical Device Amendments of 1992*

Food and Drug Administration Modernization Act*

Medical Device User Fee and Modernization Act of 2002*

Public Health Security and Bioterrorism Preparedness Response Act of 2002*

Project BioShield Act of 2004 (21 U.S.C. 360bbb-3)

Medical Device User Fee Stabilization Act of 2005*
Food and Drug Administration Amendments Act of 2007*

Allocation Method: Direct Federal/Intramural

Program Description and Accomplishments

The FDA Biologics Program is responsible for ensuring the safety, purity, potency, and effectiveness of biological products, including vaccines and allergenics, blood and blood products, and cells, tissues, and gene therapies for the prevention, diagnosis, and treatment of human diseases, conditions, or injuries. The Biologics Program also helps to defend the public against the threats of emerging infectious diseases and bioterrorism through preparedness planning, development and licensing of medical countermeasures (that are used to diagnose, treat, or prevent disease from pathogen exposure), and ensuring the availability of safe and effective medical countermeasures.

The Biologics Program began in 1902 with the passage of the Biologics Control Act, which established the authority to regulate biological products and ensure their safety for the American public. This program was located in the Department of Treasury's Hygienic Laboratory, which in 1930 became the National Institutes of Health (NIH). In 1972, the Biologics Program was transferred from NIH to FDA and became the Bureau of Biologics. In 1988, the Center for Biologics Evaluation and Research (CBER) became its own center within FDA. The program operates with both budget authority appropriations and user fees to support prescription drug and medical device review.

CBER is committed to advancing the public health through innovative regulation that ensures the safety, effectiveness, and timely delivery of biological products to patients. CBER is responsible for ensuring the safety of the nation's blood supply and the products derived from blood, the production and approval of safe and effective adult and childhood vaccines, the oversight of human tissue for transplantation, and an adequate and safe supply of allergenic materials and anti-toxins.

The Office of Regulatory Affairs (ORA) provides FDA leadership on enforcement, import, inspection, and laboratory policies. Through its field offices nationwide, ORA supports the Biologics Program by conducting premarket activities such as bioresearch monitoring of clinical research, preapproval inspections and laboratory method validations needed for application decisions, and inspecting manufacturing facilities to ensure their ability to manufacture the product to the specifications stated in the application. ORA also conducts risk-based domestic and foreign postmarket inspections of medical products to assess their compliance with Good Manufacturing Practice requirements. In addition to overseeing regulated products on a surveillance or for cause basis, ORA responds to emergencies and investigates incidents of product tampering and natural or intentional disasters that may affect FDA-regulated goods. In

* Authorities under this act do not appear in sequence in the U.S. Code. The authorities are codified as amended in scattered sections of 21 U.S.C. or 42 U.S.C. (Public Health Service Act and Public Health Security and Bioterrorism Preparedness Response Act of 2002).

instances of criminal activity, ORA's Office of Criminal Investigations (OCI) complements the regular Field force. ORA's Field Biologics Program is funded by appropriated budget authority and user fee dollars that allow the Field to perform inspections.

The Office of Information Management (OIM) provides FDA's leadership in transforming and improving the systems and infrastructure needed to support critical agency operations. OIM works to align information technology (IT) investments to business goals that fully support core mission and business priorities and reduce costs of existing legacy systems while providing the platform required for FDA to meet Agency-wide IT initiatives and to move towards the Bioinformatics era of science-based decisions in the 21st Century. With the centralization of IT projects and resources in 2008, OIM supports the Biologics Program by maintaining its legacy systems and databases used for managing and tracking its premarket review programs, for monitoring and tracking adverse event activities, and for conducting various compliance activities. OIM also work with the Biologics Program through the FDA Bioinformatics Board to ensure that current and future IT enterprise and center investments continue to fulfill program requirements while meeting broader FDA objectives.

The Prescription Drug User Fee Act (PDUFA) and Medical Device User Fee and Modernization Act (MDUFMA) enable the Biologics Program to ensure the timeliness and predictability of FDA review of new products for sponsors and consumers. Under these user fee programs, FDA agreed to pursue a comprehensive set of application review performance goals. During FY 2007, the latest completed performance period, the Biologics Program met or exceeded all of its user fee performance commitments.

The Biologics Program has also continued to meet all of the targets in FY 2007 for all of the non-user fee Government Performance and Results Act (GPRA) goals. Thus far, CBER has successfully achieved the FY 2008 targets for which completed performance data is available and expects to continue to meet the performance targets when data becomes available in FY 2009. In FY 2008 CBER also achieved the 2003 Program Improvement Plan long-term outcome goal to reduce the approval time for the fastest 50 percent of standard New Molecular Entities/Biologics Licensing Applications for the FY 2005- 2007 cohort.

The Biologics Program executes its regulatory responsibilities in three major program areas: Blood and Blood Products, Vaccines and Allergenics, and Cell, Tissues and Gene Therapies. The activities conducted in these program areas are as follows:

Blood and Blood Products – Center Activities

CBER is responsible for ensuring the safety of the nation's blood supply by minimizing the risk of infectious disease transmission and other hazards while facilitating the maintenance of an adequate supply of blood and blood products. The scope of the blood program is far reaching, with over 14.4 million human whole blood and red blood cell components and over 15 million transfusions of other blood components transfused annually, according to *The 2007 National Blood Collection and Utilization Survey*. The responsibility to keep the blood supply safe is especially important in the face of an emerging infectious disease, pandemic or terrorist event. CBER regulates blood and blood components used for transfusion and for manufacture into products such as plasma derivatives and their resulting blood products, including clotting factors,

concentrates, immune globulins, albumin and protease inhibitors. CBER also establishes product standards and performs lot-release testing for products. CBER works closely with many partners, including the Department of Health and Human Services' (DHHS) Office of the Secretary, the Centers for Disease Control and Prevention (CDC), and industry to ensure the safety and availability of blood products.

CBER also regulates related products, including blood establishment computer software, cell separators, and blood collection containers, as well as tests to screen blood donors for human immunodeficiency virus-type 1 (HIV1) and other viruses, including hepatitis B and C viruses (HBV and HCV), West Nile virus (WNV), human T-lymphotropic virus types I and II, and for syphilis. The testing of donors for infectious agents is a critical safeguard for blood safety. To further enhance blood safety, CBER facilitates the development and implementation of sensitive tests to detect infectious agents in blood. CBER also continues the development of donor screening questionnaires to reduce risk by identifying and deferring high risk donors. In the postmarket arena, CBER develops and enforces quality standards, and monitors, analyzes, and acts on reports of errors, accidents and adverse clinical events.

In FY 2007, CBER exceeded all of its performance goals by completing review and action on at least 99 percent of all complete blood bank and source plasma Biologic License Application (BLA) submissions, and BLA supplements within 12 months. Some FY 2009 highlights include the approval of two orphan drugs for patients with potentially fatal, rare conditions to help prevent bleeding and the formation of blood clots, and the approval of the first nucleic acid test that screens for the presence of two divergent types of HIV in donated blood plasma and tissue.

Blood and Blood Products – Field Activities

Under the provisions of both the Public Health Service Act and the Federal Food Drug and Cosmetic Act, ORA field investigators conduct inspections of blood establishments that manufacture or participate in the manufacture of blood and blood components for human use. The Field conducts inspections to ensure that blood establishments manufacture biological products that are safe and are in accordance with current good manufacturing practices. FDA implemented the inspection of blood establishments in 1972.

The inspection of a blood establishment is based on a multi-layered set of safeguards related to blood and blood component collection, manufacturing, and distribution. Inspections verify that firms institute proper procedures to screen donors, test blood for required infectious diseases, and follow-up on blood donor and recipient adverse reactions.

Blood and blood products are vitally important products in medical treatment. ORA Field efforts focus on two main areas: performing inspections of blood establishments engaged in the collection, manufacturing, preparation or processing of human blood or blood products and inspecting laboratories that perform testing on blood products and donors to confirm donor screening for communicable disease agents. In FY 2008, ORA conducted 1,014 inspections of highest priority registered domestic blood banks, source plasma operations, and biologics manufacturing establishments, exceeding the FY 2008 GPRA performance target of 870 establishments.

Vaccines and Allergens – Center Activities

CBER regulates vaccine and allergenic products. Many vaccine products are pediatric vaccines that have contributed to the dramatic reduction or elimination of life-threatening childhood diseases in the U.S., such as diphtheria, measles, and polio. Newer vaccines play an increasing role in protecting and improving the lives of adolescents and adults and include vaccines to prevent meningococcal disease, shingles, and cervical cancer. In addition, there are vaccines under development that offer the promise of preventing serious infectious diseases, such as pandemic influenza viruses and severe acute respiratory syndrome (SARS), HIV-1, and malaria. As with all medical products, highly-trained scientists and clinicians rigorously review laboratory and clinical data in assessing the safety, effectiveness, and quality of vaccines.

CBER reviews additional studies after some vaccines are approved to further evaluate their safety and effectiveness (for example, in broader population groups). Both before and after a vaccine is licensed, FDA inspects vaccine manufacturing facilities to help ensure continued high quality and safe production. Due to the complexity of the manufacturing process, CBER activities also include lot-release testing to ensure vaccines are potent, safe, and sterile before the manufacturer distributes the product in interstate commerce.

CBER regulates allergenic products: patch tests and extracts. Allergen patch tests are diagnostic tests applied to the surface of the skin that are used by physicians to determine the specific causes of contact dermatitis. Allergenic extracts are used for the diagnosis and treatment of allergic diseases such as allergic rhinitis ("hay fever"), allergic sinusitis, allergic conjunctivitis, bee venom allergy and food allergy. CBER maintains reference standards for allergenics, used by physicians to detect allergies in patients. CBER distributes the reference standards to manufacturers and evaluates novel technological approaches to improve allergenic product development, standardization, and characterization of these complex biological products.

In the postmarket area, the CDC and FDA jointly manage the Vaccine Adverse Event Reporting System (VAERS), a cooperative program for vaccine safety. VAERS is a postmarketing safety surveillance program that collects information about adverse events (also known as side effects) potentially related to vaccination and reported after the administration of U.S. licensed vaccines. In collaboration with CDC, state health departments, and other partners, CBER uses VAERS to monitor vaccine adverse event reports for possible indicators of vaccine safety concerns.

CBER plays a leadership role to prepare for and respond to the risks of a pandemic influenza outbreak. Working with industry, agencies in DHHS, and global partners, CBER facilitates the development and availability of pandemic influenza vaccines in the shortest time possible to protect the largest number of people using a vaccine that is safe, effective, and easy to deliver.

CBER accomplished its annual performance targets under its performance goal for increasing manufacturing diversity and capacity for pandemic influenza vaccine production in FY 2008. These targets included ensuring all six influenza vaccine producers were licensed before the start of the influenza season, creating an influenza A reference strain for manufacturers to make an effective vaccine, and engaging in pre-BLA discussions with a manufacturer on a pandemic vaccine, and holding workshops with the World Health Organization (WHO) to develop and post guidelines for regulatory preparedness regarding pandemic influenza vaccines on the web. Additionally, CBER approved the first vaccine available in the United States to protect against

Japanese encephalitis virus which is transmitted to people by mosquitoes, and is evaluating vaccine postmarket safety information from a large managed care organization.

Vaccines and Allergens – Field Activities

ORA provides significant inspection oversight, technical assistance, and outreach to manufacturers to help assure the adequate preparation and rapid availability of safe and effective vaccines. ORA's activities include annual inspections of influenza virus vaccine manufacturing facilities and appropriate compliance follow-up with manufacturers when inspections reveal issues that could compromise a safe, plentiful supply of influenza vaccine, and bioresarch monitoring inspections in support of FDA's review of new applications submitted by flu vaccine manufacturers. ORA also provides technical support to CBER, HHS agencies and flu vaccine manufacturers during product development.

Cell, Tissue and Gene Therapy – Center Activities

CBER is responsible for regulating many different types of human tissue and cells that are transplanted during various types of medical procedures, including skin replacement following severe burns, tendons and ligaments used to repair injuries, bone replacement, and corneas used to restore eyesight. Tissue transplantation is a rapidly growing industry. The number of musculoskeletal tissue transplants increased from approximately 350,000 in 1990, to more than 1.5 million transplants annually.

Transplantation of human tissues presents unique safety challenges in light of the risks of transmitting infectious diseases from donor to recipient and the contamination of tissues during processing. Since 1993, CBER has required tissue establishments to screen and test donors, and since 1997 required tissue establishments to prepare, validate, and follow written procedures to prevent contamination and cross-contamination during processing. In response to the increased use, role, and complexity of tissue transplants, CBER developed a comprehensive regulatory framework, which went into effect in May 2005, for the regulation of human cells, tissues, and cellular- and tissue-based products. The new framework promotes the use of the most up-to-date tools and methods to reduce risks of infectious disease transmission and contamination.

CBER also regulates cellular and gene therapy products. Somatic cells, vectors expressing certain gene products, and genetically manipulated cells offer the promise of harnessing the power of different cell types to fight disease, restore normal function, repair injuries, replace lost cells, or regenerate failing organs. CBER is aware of both the promise of gene therapy and its potential to cause serious adverse events, and works closely with NIH, academia, and industry on these products. For example, CBER and NIH have collaboratively developed a Web-accessible database on human gene transfer to enable faster reporting of adverse events in human gene transfer trials.

CBER has provided proactive scientific and regulatory advice through meetings, guidance and regulations to biologic manufacturers in areas of novel product development. Focusing on how best to evaluate essential issues of safety and efficacy while facilitating product development, CBER is also committed to protecting human-study subjects. CBER's involvement in broad public interactions helps CBER and product developers address important issues involving the development of novel gene and cellular therapy products.

Some FY 2009 accomplishments include issuing recommendations for developing tests to measure potency of therapies, participation in many outreach activities such as workshops, and the issuance of draft guidance on Current Good Tissue Practices for Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/P) manufacturing establishments to help prevent the introduction, transmission, or spread of communicable disease during the manufacturing process.

Cell, Tissue and Gene Therapy – Field Activities

FDA’s risk-based approach to assure the safety of HCT/Ps is being implemented to prevent infectious disease transmission and contamination and to increase the quality and consistency of products. ORA’s efforts are concentrated in two main areas. The first area includes ensuring that tissues are recovered, processed, stored and distributed in a manner that reduces the risks of serious infectious diseases and contamination with infectious agents. The second area includes performing inspections to monitor the recovery and processing of HCT/Ps and the testing and screening of donors, and assuring that HCT/Ps do not contain communicable disease agents, that they are not contaminated, and that they do not become contaminated during manufacturing. During FY 2008, ORA inspected 383 highest priority human tissue establishments, exceeding the FY 2008 performance target of 325 establishments.

Five-Year Funding Table with FTE Totals

The following table shows a five-year funding history for the Biologics Program’s program level, budget authority, and user fee resources.

Fiscal Year	Program Level	Budget Authority	User Fees	Program Level FTE
FY 2006 Actual	\$197,709,000	\$138,518,000	\$59,191,000	979
FY 2007 Actual	\$202,162,000	\$146,328,000	\$55,834,000	1,045
FY 2008 Actual	\$233,508,000	\$154,831,000	\$78,677,000	1,066
FY 2009 Omnibus	\$271,490,000	\$183,451,000	\$88,039,000	1,146
FY 2010 Estimate	\$305,731,000	\$206,438,000	\$99,293,000	1,197

Budget Overview and Supported Activities

The FY 2010 President’s Budget requests \$305,731,000 in program level funding for the Biologics program, including the support of 1,197 FTE. The Field portion of this request is \$44,734,000, supporting 238 FTE.

The request represents an increase of \$34,241,000 (or 12.6 percent) over the FY 2009 FDA appropriation level in the Omnibus Appropriations Act, 2009 in budget authority and user fee amounts. The overall increase provides additional resources for pay increases, strengthening the information technology systems, increasing safety of blood and tissues, maintaining user fee goals and strengthening the science behind CBER's regulatory decisions.

The budget authority for the FY 2010 President's Budget is \$206,438,000, an increase of \$22,987,000 over the FY 2009 FDA appropriation in the Omnibus Appropriations Act, 2009. The CBER portion of the submission is \$166,182,000 and the Field amount is \$40,256,000.

The user fee collection authority includes a total of \$99,293,000 for the Biologics Program, an increase of \$11,254,000 over the FY 2009 FDA appropriation in the Omnibus Appropriations Act. The Biologics program collects user fees for human drug review (PDUFA) and medical device review (MDUFMA). The CBER portion of the current law user fees is \$94,815,000 and the Field amount is \$3,996,000. The proposed user fee for the Field to conduct additional reinspections and export certification is \$482,000 in new fees.

Safer Biologics Initiative

The FY 2010 budget requests an increase over the FY 2009 FDA appropriation level in the Omnibus Appropriations Act, 2009 of \$22,987,000 for the safer biologics initiative. Of this amount, \$2,803,000 is for the pay raise and \$20,184,000 is the Biologics portion of the initiative that will fund enhancements to the biologics safety programs, including information technology. The CBER portion of the pay raise is \$2,041,000 and the Field portion of the pay raise is \$762,000. The cost of living pay raise will contribute towards allowing the Biologics program to maintain their GPRA performance targets and other workload outputs at the FY 2009 levels.

Base funding for this initiative encompasses the entire Biologics program. This increase along with the base funding will work to ensure the safety and effectiveness of biological products, including the nation's blood supply and the products derived from it. It will contribute to the production and approval of safe and effective adult and childhood vaccines, the oversight of human tissue for transplantation, cell and gene therapies, biological related devices, and an adequate and safe supply of allergenic materials and anti-toxins. It will also continue to ensure preparedness to help defend against the threats of emerging infectious disease and bioterrorism.

With the requested increases, CBER will continue to implement the pediatric and postmarket safety requirements of the 2007 Food and Drug Administration Amendments Act (FDAAA). To improve safety in the pediatrics arena, CBER will review pediatric plans, assessments, waivers, and deferrals and conduct a retrospective review. In the postmarket safety arena, CBER will develop a system and standards to track and review safety information for prescription biologics to help report regularly on potential risks identified through the system.

The requested increase will continue enhancements to modernize the human tissue, blood safety, and vaccine programs, including the supply, quality, and availability of these products, and innovative technologies to deal with terrorism and emerging public health threats. Enhancements will include conducting safety investigations, modernizing tissue, blood and vaccine standards, testing assays, disease models, methods, sample panels, and review capacity.

CBER will increase the capacity and expertise of their blood, tissue and vaccine safety teams to proactively monitor and analyze outcomes and potential adverse events, including data gained through increased partnerships with healthcare organizations and other federal agencies. Additionally, CBER will develop enhanced guidance for evolving technologies and provide early interactions, outreach and training on product development and safety. Support for inspections, the enhancement of risk analysis tools and help for manufacturers to implement and expand a quality systems approach that will contribute to safer biologic products.

CBER plans to meet its pandemic influenza vaccine production performance goal by completing an evaluation of a pilot vaccine adverse-effects program. This includes developing and evaluating new methods to detect possible adverse effects of newly licensed vaccines and to participate in at least one international workshop or conference.

In FY 2010, ORA is continuing to progress towards the GPRA goal to increase tissue inspections to 518. Additionally, ORA will continue to establish its workforce for inspections and import exams and to increase laboratory capacity with the FY 2010 Budget Request. Specifically, ORA will increase inspections for the Biologics Program:

- to 25 domestic tissue inspections above the FY 2010 levels by the end of 2012
- to 23 foreign tissue inspections above the FY 2010 levels by the end of 2013.

These inspections are planned to for 2012 and 2013 because it will take two years to hire and train new field staff so they can conduct inspections.

User Fees Authority and Increases

The current law and proposed user fees will provide an increase of \$11,254,000 for the Biologics Program. This amount includes increases for the current PDUFA and MDUFMA user fees and a proposed user fee for reinspection. The base funding for the current user fees is \$88,039,000.

The Biologics Program is submitting an increase in PDUFA user fee collection authority that will provide an additional \$10,672,000. Of this amount, CBER will receive an increase of \$10,541,000 and the Field portion will be \$131,000. The PDUFA increase provides for inflation and workload adjustments. These increases will help FDA meet the agreed upon performance goals negotiated with industry when PDUFA IV was passed in FY 2007. For the FY 2010 performance, the Biologics Program will maintain or exceed performance targets to review and complete action on standard and priority original PDUFA NDA/BLA submissions within 10 months and 6 months respectively. It will also maintain or exceed performance targets to review and complete action on standard PDUFA efficacy supplements within 10 months.

This submission also includes an increase in MDUFMA user fee collection authority that will provide CBER an additional \$100,000 for Biologics medical device review program. The MDUFMA increase provides for inflation and workload adjustments. These increases will help FDA meet the agreed upon performance goals negotiated with industry in MDUFMA.

Proposed User Fees

The FY 2010 request also includes \$482,000 for a proposed mandatory reinspection user fee.

The Reinspection User Fees supports reinspection costs incurred when FDA conducts follow-up inspections to verify that a firm implements action to correct violations discovered during an inspection or stemming from a warning letter. This new user fee will amend the Food, Drug, and Cosmetic Act to permit FDA to collect and retain fees to recover from the inspected firm the full cost of reinspections that FDA performs to ensure that their products and facilities comply with current FDA regulations.

Biologics Performance Measures Table

Long Term Objective: Increase the number of safe and effective new medical products available to patients

Measure	FY	Target	Result
<u>233201</u> : Complete review and action on standard original PDUFA NDA/BLA submissions within 10 months of receipt. <i>(Output)</i>	2010	90%	Nov 30, 2011
	2009	90%	Nov 30, 2010
	2008	90%	Nov 30, 2009
	2007	90%	100% (Target Exceeded)
	2006	90%	100% (Target Exceeded)
	2005	90%	100% (Target Exceeded)
<u>233202</u> : Complete review and action on priority original PDUFA NDA/BLA submissions within 6 months of receipt. <i>(Output)</i>	2010	90%	Apr 30, 2011
	2009	90%	Apr 30, 2010
	2008	90%	Apr 30, 2009
	2007	90%	100% (Target Exceeded)
	2006	90%	100% (Target Exceeded)
	2005	90%	100% (Target Exceeded)
<u>233203</u> : Complete review and action on standard PDUFA efficacy supplements within 10 months of receipt. <i>(Output)</i>	2010	90%	Nov 30, 2011
	2009	90%	Nov 30, 2010
	2008	90%	Nov 30, 2009
	2007	90%	100% (Target Exceeded)
	2006	90%	100% (Target Exceeded)
	2005	90%	100% (Target Exceeded)
<u>233205</u> : Complete review and action on complete blood bank and source plasma BLA submissions within 12 months after submission date. <i>(Output)</i>	2010	90%	Nov 30, 2011
	2009	90%	Nov 30, 2010
	2008	90%	Nov 30, 2009
	2007	90%	100% (Target Exceeded)
	2006	N/A	100% (Target Not In Place)
	2005	N/A	100% (Target Not In Place)

Measure	FY	Target	Result
<u>233206</u> : Complete review and action on complete blood bank and source plasma BLA supplements within 12 months after submission date. <i>(Output)</i>	2010	90%	Nov 30, 2011
	2009	90%	Nov 30, 2010
	2008	90%	Nov 30, 2009
	2007	90%	99% (Target Exceeded)
	2006	N/A	100% (Target Not In Place)
	2005	N/A	100% (Target Not In Place)

Long Term Objective: Prevent safety problems by modernizing science-based standards and tools to ensure high-quality manufacturing, processing, and distribution.

Measure	FY	Target	Result
<u>234101</u> : Increase manufacturing diversity and capacity for pandemic influenza vaccine production. <i>(Output)</i>	2010	See goal-by-goal section below.	Nov 30, 2010
	2009	See goal-by-goal section below.	Nov 30, 2009
	2008	See goal-by goal section, below.	Accomplished targets. See goal-by-goal section below. (Target Met)
	2007	See goal-by goal section, below.	Accomplished targets. See goal-by-goal section, below. (Target Met)
	2006	N/A	Accomplished targets. See goal-by goal section, below. (Target Met)
	2005	N/A	N/A

Long Term Objective: Detect safety problems earlier and better target interventions to prevent harm to consumers.

Measure	FY	Target	Result
<u>234202</u> : Number of high risk registered domestic blood bank and biologics manufacturing inspections. <i>(Output)</i>	2010	1,000	December, 2010
	2009	870	December, 2009
	2008	870	1,014 (Target Exceeded)
<u>234203</u> : Number of highest priority human tissue establishment inspections. <i>(Output)</i>	2010	518	December, 2010
	2009	380	December, 2009
	2008	325	383 (Target Exceeded)
	2007	325	427 (Target Exceeded)

Measure	FY	Target	Result
	2006	N/A	354 (Historical Actual)

1. Complete review and action on standard original PDUFA NDA and BLA submissions within 10 months of receipt. (233201)

Context: The Prescription Drug User Fee Act (PDUFA) authorizes the FDA to collect fees from the prescription drug and biologic drug industries to expedite the review of human drugs and biologics so they can reach the market more quickly. Standard original BLAs are license applications for biological products, not intended as therapies for serious or life-threatening diseases. In FY 2010, FDA continues to maintain the target set for this goal in the PDUFA legislation.

Performance: FDA tracks PDUFA performance by year-of-receipt, which FDA calls the cohort year, and complete performance data are not available until the prescribed review time, i.e., 10 months after receipt, is expired. In FY 2007, CBER exceeded its goal by completing review and action on 100 percent of 9 standard applications within 10 months of receipt, and has met or exceeded this performance goal since 1994. The FY 2008 performance data for this goal will not be available until November 2009.

2. Complete review and act on priority original PDUFA NDA/BLA submissions within 6 months of receipt. (233202)

Context: PDUFA authorizes the FDA to collect fees from the prescription drug and biologic drug industries to expedite the review of human drugs and biologics so they can reach the market more quickly. A BLA will receive priority review if the product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis or prevention of a serious or life-threatening disease. In FY 2010, FDA continues to maintain the target set for this goal in the PDUFA legislation.

Performance: FDA tracks PDUFA performance by year-of-receipt, which FDA calls the cohort year and complete performance data are not available until the prescribed review time, i.e., 6 months after receipt, is expired. In FY 2007, CBER exceeded its goal by completing review and action on 100 percent of 6 priority applications within 6 months of receipt, and has met or exceeded this performance goal since 1994. The FY 2008 performance data for this goal will not be available until April 2009.

3. Complete review and action on standard PDUFA efficacy supplements within 10 months of receipt. (233203)

Context: PDUFA authorizes the FDA to collect fees from the prescription drug and biologic industries to expedite the review of human drugs and biologics so they can reach the market more quickly. An efficacy supplement is a change to an approved licensed product to modify the “approved effectiveness” of a product such as a new indication, and normally requires clinical data. In FY 2010, FDA continues to maintain the target set for this goal in the PDUFA legislation.

Performance: FDA tracks PDUFA performance by year-of-receipt, which FDA calls the cohort year and complete performance data are not available until the prescribed review time, i.e., 10 months after receipt, is expired. In FY 2007, CBER exceeded its goal by completing review and action on 100 percent of 9 standard PDUFA efficacy supplements within 10 months of receipt, and has met or exceeded most of these performance goals since 1994. The FY 2008 performance data for this goal will not be available until November 2009.

4. Complete review and action on complete blood bank and source plasma BLA submissions within 12 months after submission date. (233205)

Context: In FY 2010, CBER has established the goal of reviewing and acting upon complete blood bank and source plasma BLA submissions within 12 months after submission. Since so few complete blood bank and source plasma submissions are received by CBER, the actual performance may be significantly different than the target. User fee resources are not available for blood bank and source plasma application review.

Performance: CBER tracks performance by year-of-receipt, which FDA calls the cohort year and complete performance data are not available until the prescribed review time, i.e., 12 months after receipt, is expired. In FY 2007, CBER exceeded its goal by reviewing and acting on 100 percent of 5 submissions within 12 months of receipt. The FY 2008 performance data for this goal will not be available until November 2009.

5. Complete review and action on complete blood bank and source plasma BLA supplements within 12 months after submission date. (233206)

Context: In FY 2010, CBER has established the performance goal of reviewing and acting upon complete blood bank and source plasma BLA supplement submissions within 12 months after submission. User fee resources are not available for blood bank and source plasma application review.

Performance: CBER tracks performance by year-of-receipt, which FDA calls the cohort year and complete performance data are not available until the prescribed review time, i.e., 12 months after receipt. In FY 2007, CBER exceeded its goal by reviewing and acting on 99 percent of 371 supplements within 12 months of receipt. The FY 2008 performance data for this goal will not be available until November 2009.

6. Increase manufacturing diversity and capacity for pandemic influenza vaccine production. (234101)

Context: During FY 2006, the Biologics Program received appropriated funding under P.L. 109-148 to establish the infrastructure and surge capability to react to a potential disease pandemic. Influenza pandemics are explosive global events in which most, if not all, persons worldwide are at risk for infection and illness. Pandemic influenza strains, such as avian influenza, can rapidly change. Vaccines will need to be produced for pandemic influenza strains on a short notice, and FDA needs to provide new and accelerated pathways to facilitate their rapid production and evaluation. This goal changes on a yearly basis to ensure continued progress in preparation for a pandemic outbreak. In FY 2007, the targets included: Issue one guidance or concept paper to

facilitate development of non-egg-based influenza vaccines; evaluate the potency of monovalent influenza vaccines from at least three manufacturers by using quality systems guidelines; demonstrate two new or improved methods for improved influenza vaccine manufacture; and develop at least four influenza virus vaccine strains optimized for growth in non-egg culture systems by using quality systems guidelines.

In FY 2008, the pandemic preparedness targets were to: facilitate rapid development, evaluation and availability of at least one new pandemic influenza vaccine and one new trivalent (seasonal influenza) vaccine; demonstrate one improved method for evaluating the safety, potency or immunogenicity of influenza vaccines; and establish international regulatory cooperation, harmonization and information sharing in vaccine evaluation and safety activities by participating in one international workshop or conference. The FY 2009 pandemic preparedness targets include: starting a pilot program to develop and evaluate new methods to detect possible adverse effects, both pre-specified and non-pre-specified, of newly licensed vaccines, including pandemic influenza vaccines, in large population databases and participating in at least one international workshop or conference. The FY 2010 pandemic preparedness targets will be to complete and evaluate the pilot vaccine adverse-effects program and to participate in at least one international workshop or conference.

Performance: In FY 2006, CBER accomplished all of its targets for this goal. The targets include: developing a concept paper on clinical data needed to support license of new trivalent vaccines and of pandemic vaccines; drafting a guidance on cell substrates to facilitate development on non-egg based influenza vaccines and co-sponsoring two workshops with WHO on pandemic vaccines. In FY 2007, CBER met all of its pandemic targets. The targets include: issuing the guidance “Clinical Data Needed to Support the Licensure of Pandemic Influenza Vaccines” to facilitate development of non-egg-based influenza vaccines; evaluating the potency of five influenza vaccines (four inactivated and one live) using quality systems guidelines; and demonstrating four methods for improved influenza manufacture and develop four influenza virus vaccine strains optimized for growth in non-egg culture systems by using reverse genetics to rescue reassortants based on the A/Puerto Rico/8/34 virus backbone.

In FY 2008, CBER accomplished all of its targets for this goal. CBER facilitated rapid development and evaluation of a new pandemic vaccine through multiple activities including:

- ◆ Completing production of an H5 reassortant, "Influenza A virus reassortant A/Duck/Laos/3295/2006 (H5N1), DUCK/LAOS-PR8/CBER-RG1 reference strain" and distributing it to the recipients including the National Institute for Biological Standards and Control (NIBSC) in the UK and Taiwan-CDC in China;
- ◆ Characterizing attenuated reassortant of A/duck/Laos/3295/06 with modified internal gene;
- ◆ Completing collaborative calibration (with National Biological Standards Board-UK) for A/Anhui/2/2005

CBER posted guidelines on the WHO website of The WHO Guidelines on regulatory preparedness for pandemic influenza vaccines. The guidelines, co-authored by WHO, FDA and Health Canada, resulted from three technical workshops that were convened with representation of national regulatory authorities (NRAs) from a broad range of countries. The goals of these

workshops were to build a global network of key regulatory authorities engaged in and responsible for pandemic influenza vaccine regulation and to develop regulatory guidelines for preparedness of human pandemic influenza vaccines. The guidelines are intended to provide, both NRAs and vaccine manufacturers, state-of-the-art advice concerning regulatory pathways for human pandemic influenza vaccines; regulatory considerations to take into account in evaluating the quality, safety and efficacy of vaccine candidates; and requirements for effective postmarketing surveillance of human pandemic influenza vaccines.

7. Number of high risk registered domestic blood bank and biologics manufacturing inspections. (234202)

Context: FDA will increase risk-based compliance and enforcement activities by inspecting the highest priority registered manufacturers of biological products. The highest priority firms will be those whose operations are determined to be the highest risk, new product types in need of an inspectional history to evaluate and stratify risk, and emergency response situations. Inspections for the goal are conducted to ensure compliance with Current Good Manufacturing Practices (CGMPs), and to ensure, as appropriate, the safety, purity and potency of biological products. The biologics inventory includes high-risk establishments such as blood collection facilities, plasma fractionator establishments, and vaccine manufacturing establishments, especially seasonal and pandemic influenza vaccines. In FY 2010, the target has been increased to 1,000 inspections to reflect historical accomplishments.

Performance: In FY 2008, FDA exceeded the high risk inspection goal of 870 by inspecting 1,014 blood banks and biologics manufacturing establishments.

8. Number of highest priority human tissue establishment inspections. (234203)

Context: Beginning in FY 2006 as a result of new regulations, the human tissue inspection goal was created. FDA's responsibility for enforcing the new regulations and the need to quickly assess compliance makes tissues one of the highest priorities. Two new rules took effect regarding human tissue: one requiring tissue facilities to register with FDA became effective January 2004; while the "Donor Eligibility Rule" became effective May 2005. The Field conducts tissue inspections to determine if human tissues for transplantation are in compliance with FDA tissue regulations and to assure consumer protection from unsuitable tissue products and disease transmission which may endanger public health. In FY 2009, FDA increased this goal by 55 additional tissue inspections, over the FY 2008 target, in order to cover more of the firms that registered as a result of the new regulations. In FY 2010, the target was increased by 138 inspections.

Performance: In FY 2008, FDA exceeded the human tissue goal of 325 by conducting 383 inspections under new regulations.

BIOLOGICS PROGRAM ACTIVITY DATA (PAD)

<i>Premarket Review Applications</i>	FY 2008 Actual	FY 2009 Estimate	FY 2010 Estimate
NDA/BLA Submissions			
Applications received			
Standard:	26	29	29
Priority:	4	5	5
Applications completed ^{1/}			
Standard:	82	82	82
Priority:	2	3	4
Applications approved ^{2/}			
Standard:	59	35	37
Priority:	0	1	2
Applications pending ^{3/}			
Standard:	46	51	50
Priority:	7	8	6
Efficacy Supplements			
Applications received			
Standard:	7	8	8
Priority:	2	3	3
Applications completed ^{1/}			
Standard:	4	5	7
Priority:	1	2	3
Application approved ^{2/}			
Standard:	8	9	10
Priority:	1	2	3
Applications pending ^{3/}			
Standard:	15	17	15
Priority:	1	2	1
Original Manufacturing Supplement			
Applications received	1,689	1,858	1,860
Applications completed ^{1/}	528	581	585
Applications approved ^{2/}	1,458	1,604	1,610
Applications pending ^{3/}	1,031	1,134	1,100

Device Premarket Applications – PMAs	FY 2008 Actual	FY 2009 Estimate	FY 2010 Estimate
Applications received	0	1	1
Supplements received	33	36	40
Applications completed ^{1/}	0	1	1
Supplements completed ^{1/}	5	6	6
Applications approved ^{2/}	1	1	1
Supplements approved ^{2/}	30	33	33
Applications pending ^{3/}	0	1	1
Supplements pending ^{3/}	5	6	6
Device 510(k)s			
Applications received	53	58	60
Applications completed ^{1/}	43	47	50
Applications approved ^{2/}	45	50	55
Applications pending ^{3/}	23	25	20
Investigational Applications			
Commercial IND/IDE Receipts ^{4/}	137	151	151
IND/IDE Amendment Receipts ^{4/}	10,779	11,857	11,860
Active INDs/IDEs ^{4/}	2,894	3,183	3,190

Other Activities	FY 2008 Actual	FY 2009 Estimate	FY 2010 Estimate
Patient Safety			
Adverse Event Report Received ^{5/}	36,410	40,000	44,000
Biological Product Deviation Report Received	44,723	44,000	44,000
Sponsor Assistance/Outreach			
Meetings	408	450	455
Final Guidance Documents	30	28	28
Admin/Management Support			
Advisory Committee meetings held	7	9	14
FOI requests processed	562 ^{6/}	401	425

1/ Completed means complete action letter was sent to sponsor. Includes withdrawn, denied, NSE, and exemptions.

2/ Approved includes all applications approved during the fiscal year, regardless of year of receipt.

3/ Pending includes applications for which complete action has not been achieved at the end of the fiscal year. It does not mean the application is overdue.

4/ Includes IND, IDE, Master File and license master file receipts.

5/ Includes MedWatch, Foreign reports and VAERS reports. Does not include Fatality Reports or Medical Device Reports for CBER-regulated medical devices.

6/ Increase due to an Agency-wide effort to reduce the FOI backlog.

Field Biologics Program Activity Data (PAD)

Field Biologics Program Workload and Outputs	FY 2008 Actual	FY 2009 Estimate	FY 2010 Estimate
<i>FDA WORK</i>			
DOMESTIC INSPECTIONS			
<i>UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS</i>	<i>1,678</i>	<i>2,010</i>	<i>2,034</i>
Bioresearch Monitoring Program Inspections	104	183	183
Blood Bank Inspections	991	1,093	1,093
Source Plasma Inspections	149	205	205
Pre-License, Pre-Approval (Pre-Market) Inspections	38	24	24
GMP Inspections	25	17	17
GMP (Device) Inspections	3	10	10
Human Tissue Inspections	381	494	518
FOREIGN INSPECTIONS			
<i>UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS</i>	<i>50</i>	<i>52</i>	<i>66</i>
Bioresearch Monitoring Program Inspections	6	6	6
Foreign Human Tissue Inspections	2	0	13
Blood Bank Inspections	8	12	12
Pre-License Inspections	7	10	10
GMP Inspections	23	20	20
IMPORTS			
Import Field Exams/Tests	36	100	100
Import Line Decisions	63,302	81,864	105,868
Percent of Import Lines Physically Examined	0.06%	0.12%	0.09%
TOTAL BIOLOGICS INSPECTIONS (FOREIGN AND DOMESTIC/FDA AND STATE)			
<i>GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS</i>	<i>1,728</i>	<i>2,062</i>	<i>2,100</i>