BIOLOGICS

The FY 2009 program level budget request for the FDA Biologics Program is $245,421,000.

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

FDA Program Resources Table

	FY 2007 Actual	FY 2008 Enacted	FY 2009 Estimate	FY 2009 +/- FY 2008
Program Level	**$202,162,000**	**$235,891,000**	**$245,421,000**	**$9,530,000**
Center	*$172,045,000*	*$202,767,000*	*$211,821,000*	*$9,054,000*
FTE	827	879	905	26
Field	*$30,117,000*	*$33,124,000*	*$33,600,000*	*$476,000*
FTE	218	218	218	0
Program Level FTE	**1,045**	**1,097**	**1,123**	**26**
Budget Authority	**$146,328,000**	**$155,229,000**	**$158,175,000**	**$2,946,000**
Center	*$117,774,000*	*$125,834,000*	*$128,344,000*	*$2,510,000*
Field	*$28,554,000*	*$29,395,000*	*$29,831,000*	*$436,000*
Med. Prod. Safety & Devel. (non-add)	*$146,328,000*	*$155,229,000*	*$159,295,000*	*$4,066,000*
Admin. Savings & Man. Efficiencies (non-add)			*-$1,120,000*	*-$1,120,000*
Budget Authority FTE	**763**	**776**	**784**	**8**
User Fees	**$55,834,000**	**$80,662,000**	**$87,246,000**	**$6,584,000**
Center PDUFA	*$48,540,000*	*$66,824,000*	*$71,109,000*	*$4,285,000*
Field PDUFA	*$1,315,000*	*$3,262,000*	*$3,262,000*	*$0*
Center DTC			*$1,400,000*	*$1,400,000*
Center MDUFMA	*$5,731,000*	*$10,109,000*	*$10,968,000*	*$859,000*
Field MDUFMA	*$248,000*	*$467,000*	*$507,000*	*$40,000*
User Fee FTE	**282**	**321**	**336**	**15**
Mandatory User Fees:	**$0**	**$0**	**$434,000**	**$434,000**
Field Reinspection (non-add)			*$434,000*	*$434,000*
Mandatory User Fees FTE			**3**	**3**

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. Through our mission, the Biologics Program also helps to defend the public against the threats of emerging infectious diseases and bioterrorism.

The Biologics Program plays an important role in protecting America from terrorism and other emerging threats. Preparedness planning is imperative to lessen the impact of such a threat and a major focus for the Program is the expeditious development and licensing of products to diagnose, treat, or prevent disease resulting from exposure to the pathogens that have been identified as bioterrorist threats and by ensuring the availability of safe and effective medical countermeasures. In 2007, FDA licensed a second generation vaccine to protect against smallpox, a highly contagious disease with the potential to be used as a deadly bioterror weapon, and the first vaccine for H5N1 avian influenza virus which is an emerging threat.

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 the 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 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 and user fee dollars.

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. 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 became its own center within FDA. The program operates

* 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).

with both budget authority and user fee authorizations for prescription drug and medical device review.

The Prescription Drug User Fee Act (PDUFA) and Medical Device User Fee and Modernization Act (MDUFMA) programs 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 the latest completed performance period, FY 2006, the Biologics Program successfully achieved all seven performance targets. So far, the Biologics program successfully achieved the FY 2007 targets for which completed performance data is available. The Biologics program expects to continue to meet the other performance targets when data becomes available later in FY 2008.

The Biologics Program executes it regulatory responsibilities in three program areas: Blood and Blood Products; Vaccines and Allergenics; and Cells, Gene Therapies and Tissues.

Blood and Blood Products – Center Activities

FDA 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. This is especially important in the face of an emerging infectious disease, pandemic or terrorist event. FDA 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. FDA also establishes product standards and performs lot-release testing for these products and works closely with many partners, including, DHHS Office of the Secretary, CDC, and the American Association of Blood Banks (AABB) to ensure the safety and availability of blood products.

Additionally, FDA regulates devices used to prepare blood products, including blood establishment computer software (BECS), cell separators, and blood collection containers, as well as tests to screen blood donors for human immunodeficiency virus-type 1 (HIV1) and other viruses, such as hepatitis B and C viruses (HBV and HCV), West Nile virus (WNV), human T-lymphotropic virus types I and II, and for syphilis. Testing of donors for infectious agents is a critical safeguard for blood safety. To further enhance blood safety, FDA facilitates the development and implementation of sensitive tests to detect infectious agents in blood, and questions to screen donors to reduce risk by identifying and deferring high risk donors. In the postmarket arena, the Agency develops and enforces quality standards, and monitors, analyzes, and acts on reports of biological product deviations and adverse clinical events.

In FY 2006, CBER exceeded all of its performance goals by completing review and action on 100 percent of all complete blood bank and source plasma BLA submissions, and BLA supplements within 12 months.

FDA facilitates the development and implementation of sensitive tests to detect infectious agents in blood and develops guidances and rules to help ensure the blood supply remains safe. Some FY 2007 highlights include the approval of screening tests for West Nile Virus, Chagas' Disease, and for early detection of antibodies to HCV (Hepatitis C virus) and HIV-1. Additionally, FDA

published a final rule and final guidance on "HCV Lookback" to require blood banks to identify and notify transfusion recipients if they received blood from donors later identified as infected with HCV and appropriate donor screening tests for Hepatitis B.

Blood and Blood Products – Field Activities

Under the provisions of both the Public Health Service Act and the Federal Food Drug and Cosmetic Act, investigators conduct inspections of blood establishments that manufacture or participate in the manufacture of blood and blood components for human use. Inspections are conducted to ensure that blood establishments manufacture biological products that are safe and that the establishment manufactures them according to 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's efforts are focused in two main areas which include 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 2007, ORA conducted 1,256 inspections of registered domestic blood banks, source plasma operations, and biologics manufacturing establishments.

Vaccines and Allergenics – Center Activities

FDA also regulates vaccine products. Many of these 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 are playing 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.

FDA reviews additional studies after some vaccines are approved to further evaluate their safety and effectiveness (e.g., 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 this also includes lot-release testing to ensure vaccines are potent, safe, and sterile before the manufacturer distributes the product through interstate commerce.

FDA also maintains reference standards for allergenics, used by physicians to detect allergies in patients, and distributes them to manufacturers and evaluates novel technological approaches for

improving allergenic product development, standardization, and characterizing these complex biological products.

In the postmarket area, the U.S. Centers for Disease Control and Prevention (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 (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, FDA uses VAERS to monitor vaccine adverse event reports for possible indicators of vaccine safety concerns.

The Agency also is engaged in a leadership role to prepare for and respond to the risks of a pandemic influenza outbreak with industry, agencies in the Department of Health and Human Services (DHHS), and global partners to facilitate 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. Some FY 2007 highlights include: the approval of the first vaccine in the United States for humans against the H5N1 influenza virus, commonly known as avian or bird flu; licensure of a second-generation smallpox vaccine; increased influenza vaccine diversity and availability by licensing a sixth manufacturer, thus allowing for an estimated 134 million doses (double what was available three years ago); licensure of the nasal vaccine, FluMist, to include children between the ages of 2 and 5 years; and finalization of two guidances that outline the regulatory pathways for the rapid development and approval of safe and effective influenza vaccines for both seasonal and pandemic uses.

Vaccines and Allergenics – Field Activities

ORA provides significant inspectional oversight, technical assistance, and outreach to manufacturers to help assure the adequate preparation and rapid availability of safe and effective influenza 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 bioresearch monitoring inspections in support of FDA's review of new applications submitted by flu vaccine manufacturers. ORA's Office of Criminal Investigations (OCI) targets individuals and Internet websites that promote the sale of counterfeit Tamiflu and fraudulent pandemic flu medications and products. ORA's vigilance is demonstrated by the recent arrest of a defendant in Hong Kong after attempting to sell several thousand counterfeit Tamiflu capsules manufactured in China.

Cells, Gene Therapies and Tissues – Center Activities

FDA is responsible for regulating many different types of human tissue and cells that are transplanted during various types of medical procedures, for example, skin replacement following severe burns, tendons and ligaments used to repair injuries, bone replacement, and corneas used to restore eyesight. Transplantation of human tissues presents unique safety challenges, in particular the risks of transmitting infectious diseases from donor to recipient and the contamination of tissues during processing. Since 1993, FDA 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, FDA 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.

FDA also regulates cellular and gene therapy products including therapeutic cancer vaccines. 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 including the development of a Web-accessible database on human gene transfer to enable faster reporting of adverse events in human gene transfer trials.

FDA has provided proactive scientific and regulatory advice 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, we are also committed to protecting human-study subjects. Our involvement in broad public interactions helps FDA and product developers address important issues involving the development of novel gene and cellular therapy products. Tissue transplantation is a rapidly growing industry. The number of musculoskeletal tissue transplants increased from approximately 350,000 in 1990, to more than 1.6 million in 2006.

Some FY 2007 highlights include the issuance of a final guidance on tissue donor eligibility, including screening and testing for relevant communicable disease agents and diseases for all donors of cells or tissue used in Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps). FDA also established a multidisciplinary task force on human cell and tissue safety to strengthen its comprehensive, risk-based system for regulating human cells and tissues. The Human Tissue Task Force (HTTF) recommended targeted inspections, or a "blitz," of U.S. companies that recover human tissues to look widespread problems in tissue recovery after FDA ordered two companies to cease manufacturing in 2006. While some deviations from the regulations were identified, no major inaccuracies or deficiencies were found that could put tissue recipients at risk.

Cell, Gene Therapy and Tissues – 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 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 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. In FY 2007, the field inspected 427 human tissue establishments.

In FY 2007, FDA conducted a blitz of U.S. companies that recover human tissues – including tendons, ligaments, bone and other musculoskeletal tissues. One goal of the blitz was to look for more widespread problems in tissue recovery after FDA ordered two companies to cease manufacturing in 2006. FDA had found that these companies were not following procedures intended to prevent infectious disease transmission. ORA investigators inspected 153 major human tissue recovery firms from October 2006 through March 2007. While some deviations from the regulations were identified, no major inaccuracies or deficiencies were found that could put tissue recipients at risk. Based on data from the blitz, nearly all tissue recovery firms were in substantial compliance with FDA's comprehensive risk-based tissue regulations.

Five-Year Funding Table with FTE Totals

Fiscal Year	Program Level	Budget Authority	User Fees	Program Level FTE
2005 Actual	$170,684,000	$123,109,000	$47,575,000	1,041
2006 Actual	$197,709,000	$138,518,000	$59,191,000	979
2007 Actual	$202,162,000	$146,328,000	$55,834,000	1,045
2008 Enacted	$235,891,000	$155,229,000	$80,662,000	1,097
2009 Estimate	$245,421,000	$158,175,000	$87,246,000	1,123

Budget Request

The FY 2009 President's Budget requests $245,421,000 in program level funding for the Biologics Program, including the support of 1,123 FTE. The field portion of this request is $33,600,000, supporting 218 FTE. The request represents an increase of $9,530,000 (or 4.percent) over the FY 2008 enacted level in budget authority and user fee amounts. The overall increase provides additional budget authority to cover blood and tissue safety and to help cover the mandatory cost of living pay increase for the entire Biologics Program.

Modernizing Medical Product Safety and Development Initiative

The FY 2009 budget requests $159,295,000 for the Medical Product Safety and Development Initiative, an increase of $4,066,000 over the FY 2008 enacted level. Base funding for medical product review and safety encompasses all of the Biologics program and its goals for ensuring the safety and effectiveness of biological products, including, blood, blood products, vaccines, cellular and gene therapies, tissues, xenotransplantation, biological-related devices and allergenics.

The FY 2009 budget requests $159,295,000 for the Medical Product Safety and Development Initiative. Of this amount, $2,566,000 is for the pay raise and $1,500,000 is the Biologics portion of the initiative that will fund enhancements to the human tissue and blood safety programs. The CBER portion of the pay raise is $1,958,000 and the Field portion of the pay

raise is $608,000. The cost of living pay raise will contribute to maintaining the Results Act performance targets and other workload outputs at the FY 2008 levels.

The Modernizing Medical Product Safety and Development initiative will move FDA closer to realizing the promise of personalized medicine while improving the safety of blood and tissue safety. Base funding for medical product review and safety encompasses all of the Biologics program and its goals for ensuring the safety and effectiveness of biological products, including, blood, blood products, vaccines, cellular and gene therapies, tissues, xenotransplantation, biological-related devices and allergenics. The requested increase will allow CBER to support development of needed review expertise and laboratory capacity, by developing assays, standards, methods, and technologies to support collaborative activities to provide early detection and respond to emerging safety threats. CBER will also provide needed medical and microbiologic review and epidemiologic capacity to evaluate adverse events and conduct safety investigations. CBER will sponsor workshops on tissue processing and other tissue safety topics to share information on existing and new technologies and methods to make tissues safer.

Administrative Savings and Management Efficiencies

The Biologics Program will achieve -$1,120,000 in administrative management efficiencies by implementing new business processes that streamline current practices, and new information technology standard operating procedures to eliminate redundancy in technical equipment and systems.

User Fee Increases

The request also includes a total of $87,246,000 in user fees for the Biologics Program, an increase of $6,584,000 over the FY 2008 Enacted level. The Biologics program receives increases for human drug review (PDUFA) and medical device review (MDUFMA). FDA is requesting an increase in PDUFA user fee collection authority that will provide an additional $5,685,000 and 18 FTE for CBER's human drug review program, including $1,400,000 and 3 FTE for review of direct-to-consumer television advertisements. The PDUFA increase includes expanded postmarket safety activities, an update in the workload adjuster to better reflect the IND workload, an adjustment for rent activities, and an inflation factor to reflect the five-year average of FDA's salary and benefit costs. These increases will help FDA meet the agreed upon performance goals negotiated with industry when PDUFA IV was passed in FY 2007.

This request also includes an increase in MDUFMA user fee collection authority that will provide an additional $859,000 for CBER's medical device review program and $40,000 for Biologics Field activities pertaining to device review. The MDUFMA increase includes the addition of an establishment fee to provide more revenue stability and an inflation factor that reflects the five-year average of FDA's salary and benefit costs. These increases will help FDA meet the agreed upon performance goals negotiated with industry in MDUFMA II.

Additionally, FDA is proposing a mandatory Reinspection User Fee which is funded out of FDA's budget authority resources. 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. The FY 2009 budget includes $434,000 and 3 FTE for reinspection related activities.

Biologics Outputs / Outcomes Table

#	Key Outcomes/Outputs	FY 2004 Actual	FY 2005 Actual	FY 2006 Target	FY 2006 Actual	FY 2007 Target	FY 2007 Actual	FY 2008 Target	FY 2009 Target
Long-Term Objective 1: Increase the number of safe and effective new products available to patients, including products for unmet medical and public health needs, emerging infections diseases.									
1	Complete review and action on standard original PDUFA NDA/BLA submissions within 10 months of receipt. (233201) (Output)	100% of 6	100% of 3	90%	100% of 2	90%	11/08	90%	90%
2	Complete review and action on priority original PDUFA NDA/BLA submissions within 6 months of receipt. (233202) (Output)	100% of 1	100% of 3	90%	100% of 3	90%	4/08	90%	90%
3	Complete review and action on standard PDUFA efficacy supplements within 10 months of receipt. (233203) (Output)	100% of 7	100% of 10	90%	100% of 9	90%	11/08	90%	90%
4	Complete review and action on complete blood bank and source plasma BLA submissions within 12 months after submission date. (233205) (Output)	100% of 1	100% of 4	90%	100% of 2	90%	11/08	90%[†]	90%
5	Complete review and action on complete blood bank and source plasma BLA supplements within 12 months after submission date. (233206) (Output)	100% of 542	100% of 401	90%	100% of 326	90%	11/08	90%[‡]	90%
Long-Term Objective 2: Prevent safety problems by modernizing science-based standards and tools to ensure high-quality manufacturing, processing, and distribution.									
6	Increase manufacturing diversity and capacity for pandemic influenza vaccine production. (234101) (Output)	NA	NA	See goal-by goal section, below.	Accom-plished targets. See goal-by goal section, below.	See goal-by-goal section, below.	Accom-plished targets. See goal-by goal section, below.	See goal-by-goal section below.	See goal-by-goal section below.
Long-Term Objective 3: Detect safety problems earlier and better target interventions to prevent harm to consumers.									
7	Number of high risk registered domestic blood bank and biologics manufacturing inspections. (234202) (output)	NA	NA	NA	NA	NA	NA	870[§]	870
8	Number of highest priority human tissue establishment inspections. (234203) (output)	NA	NA	250	354	325	427	325	370

[†] FY 2008 target increased to 90% due to the revised FY 07 funding levels.
[‡] FY 2008 target increased to 90% due to the revised FY 07 funding levels.
[§] This new FY 2008 goal is the result of a concerted effort to develop a better high risk measure for Biologics. While the overall number of inspections in this program are not decreasing, this goal guarantees that the riskiest establishments are inspected, better protecting the public health.

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 2009, 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 is not available until the prescribed review time, i.e., 10 months after receipt, is expired, making the FY 2007 data unavailable until November of 2008. In FY 2006, CBER exceeded its goal by completing review and action on 100 percent of 2 standard applications within 10 months of receipt and has met or exceeded this performance goal since 1994.

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

Context: The Prescription Drug User Fee Act 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 2009, 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 is not available until the prescribed review time, i.e., 6 months after receipt, is expired, making the FY 2007 data unavailable until April of 2008. In FY 2006, CBER exceeded its goal by completing review and action on 100 percent of 3 priority applications within 6 months of receipt and has met or exceeded this performance goal since 1994.

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

Context: The 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 2009, 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 is not available until the prescribed review time, i.e., 10

months after receipt, is expired, making the FY 2007 data unavailable until November of 2008. In FY 2006, CBER exceeded its goal by completing review and action on 100% of 9 standard PDUFA efficacy supplements within 10 months of receipt has met or exceeded most of these performance goals since 1994.

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

Context: In FY 2009 CBER will work to complete review and action on 90 percent of the complete blood bank and source plasma BLA submissions within 12 months. Since so few complete blood bank and source plasma submissions are received by FDA, the actual performance may be significantly different than the target. User fee resources are not available for blood bank and source plasma BLA supplements.

Performance: CBER tracks performance by year-of-receipt, which FDA calls the cohort year and complete performance data is not available until the prescribed review time, i.e., 12 months after receipt, is expired, making the FY 2007 data unavailable until November of 2008. In FY 2006, CBER exceeded its goal by reviewing and acting on 100% of 2 submissions within 12 months of receipt.

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

Context: In FY 2009 CBER will work to complete review and action on 90 percent of the complete blood bank and source plasma BLA submissions within 12 months. FDA does not expect to exceed the target, as we have in past years, since user fees are not available for blood bank and source plasma BLA supplements.

Performance: CBER tracks performance by year-of-receipt, which FDA calls the cohort year and complete performance data is not available until the prescribed review time, i.e., 12 months after receipt, is expired, making the FY 2007 data unavailable until November of 2008. In FY 2006, CBER exceeded its goal by reviewing and acting on 100% of 326 supplements within 12 months of receipt.

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

Context: The Biologics Program has received appropriated funding 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 and current vaccines will not provide protection. Industry will need to produce vaccines for pandemic influenza 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 include: 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; 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 target is to: facilitate rapid development, evaluation and availability of at least one new pandemic influenza vaccine, and one new trivalent 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 2009 pandemic target is to begin to develop a pilot program that utilizes a national healthcare database to evaluate the safety of potential pandemic vaccines and participate in at least one international workshop or conference.

Performance: In FY 2006, CBER accomplished all of it targets for this goal. The targets included: developing a concept paper on clinical data needed to support license of new trivalent vaccines and of pandemic vaccines; draft a guidance on cell substrates to facilitate development on non-egg based influenza vaccines and co-sponsor two workshops with WHO an pandemic vaccines. In FY 2007, CBER met all of its pandemic targets. This included: issuing the guidance "Clinical Data Needed to Support the Licensure of Pandemic Influenza Vaccines" to facilitate development of non-egg-based influenza vaccines; evaluated the potency of five influenza vaccines (four inactivated and one live) using quality systems guidelines; demonstrated 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 and recombination on the backbone of A/Puerto Rico/8/34 virus.

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. There are currently an estimated 2,450 establishments in the Biologics program inventory covered under the cGMP regulation. 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.

Performance: In FY 2007, FDA exceeded the previous statutory inspection goal of 1,138 by inspecting 1,256 blood banks, source plasma and biologics manufacturing establishments. The FY 2008 target reflects the new high-risk prioritized goal for which accomplishment data will not be available until the end of FY 2008.

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 will increase this goal by 45 additional tissue inspections in order to cover more of the firms that registered as a result of the new regulations. However, the FY 2008 and 2009 targets are lower than the FY 2007 actuals because the FY 2007 actuals reflect a one-time Agency blitz of US companies to look for problems related to tissue recovery issues uncovered in FY 2006.

Performance: In FY 2007, FDA exceeded the human tissue goal of 325 by conducting 427 inspections under new regulations.

CBER Program Activity Data (PAD)

Workload and Outputs for Premarket Review Applications	FY 2007 Actuals	FY 2008 Estimate	FY 2009 Estimate
NDA/BLA Submissions			
Applications received			
Standard:	19	21	21
Priority:	6	7	7
Applications completed [1/]			
Standard:	80	88	88
Priority:	2	3	3
Applications approved [2/]			
Standard:	26	29	29
Priority:	6	7	7
Applications pending [3/]			
Standard:	82	90	90
Priority:	3	4	4
Efficacy Supplements			
Applications received			
Standard:	9	10	10
Priority:	0	1	1
Applications completed [1/]			
Standard:	6	7	7
Priority:	0	1	1
Application approved [2/]			
Standard:	13	14	14
Priority:	0	1	1
Applications pending [3/]			
Standard:	12	13	13
Priority:	0	1	1
Original Manufacturing Supplement			
Applications received	1,507	1,658	1,658
Applications completed [1/]	290	319	319
Applications approved [2/]	1,530	1,683	1,683
Applications pending [3/]	882	970	970
Device Premarket Applications	FY 2007 Actuals	FY 2008 Estimate	FY 2009 Estimate
Applications received	0	1	1
Supplements received	30	33	33
Applications completed [1/]	7	8	8
Supplements completed [1/]	6	7	7
Applications approved [2/]	3	4	4
Supplements approved [2/]	25	28	28
Applications pending [3/]	1	2	2

Supplements pending [3/]	7	8	8
Device 510(k)s			
Applications received	58	64	64
Applications completed [1/]	57	63	63
Applications approved [2/]	53	58	58
Applications pending [3/]	24	26	26
Investigational Applications			
Commercial IND/IDE Receipts [4/]	147	162	162
IND/IDE Amendment Receipts [4/]	10,223	11,245	11,245
Active INDs/IDEs [4/]	2,968	3,265	3,265
Other Activities			
Patient Safety			
Adverse Event Reports Received [5/]	28,255	30,000	30,000
Biological Product Deviation Report Received	43,345	41,000	41,000
Sponsor Assistance/Outreach			
Meetings	357	393	393
Final Guidance Documents	25	25	25
Admin/Management Support			
Advisory Committee meetings held	11	12	13
FOI requests processed	415	425	425

1/ Completed means complete action letter was sent to sponsor. Includes withdrawn, denied, not substantially equivalent (NSE), and exempts.
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.

Field Biologics Program Activity Data (PAD)

Field Biologics Program Workload and Outputs	FY 2007 Actual	FY 2008 Estimate	FY 2009 Estimate
DOMESTIC INSPECTIONS			
Bioresearch Monitoring Program Inspections	116	175	175
Blood Bank Inspections	1,082	1,071	1,082
Source Plasma Inspections	168	182	182
Pre-License, Pre-Approval (Pre-Market) Inspections	23	11	22
GMP Inspections	33	32	32
GMP (Device) Inspections	12	11	13
Human Tissue Inspections	426	517	562
Total Above Domestic Inspections	1,860	1,999	2,068
PROGRAM OUTPUTS-			
IMPORT/FOREIGN INSPECTIONS			
Blood Bank Inspections	9	13	15
Pre-License Inspections	1	0	0
GMP Inspections	20	17	17
Total Above Foreign FDA Inspections	30	30	32
Import Field Exams/Tests	46	100	100
Import Line Decisions	48,949	53,942	59,445
Percent of Import Lines Physically Examined	0.09%	0.19%	0.17%