BIOLOGICS

Introduction

FDA's Biologics Program summarizes the budget program requirements that justify a $215,835,000 request for FY 2008. The Biologics program narrative has four sections:

- summary of FDA's program resources, historical funding and FTE levels
- description of program functions of the Center for Biologics and related Field support from the Office of Regulatory Affairs
- effects of the full year FY 2007 continuing resolution on the Biologics Program
- description of the program resources changes, base resource activities, program accomplishments, program activity data, and performance plan analysis.

The Biologics Program funding table shows a three year span of program level resources, budget authority resources, and proposed user fees enacted in FY 2006, displayed in the FY 2007 President's Budget and FY 2007 Continuing Resolution, and proposed in the FY 2008 budget request.

	FY 2006 Actuals	FY 2007 Continuing Resolution	FY 2007 President's Budget	FY 2008 President's Budget	Increase or Decrease
Program Level	**$197,709,000**	**$191,745,000**	**$214,658,000**	**$215,835,000**	**$1,177,000**
Center	*$168,909,000*	*$163,418,000*	*$182,309,000*	*$183,170,000*	*$861,000*
FTE	*772*	*798*	*877*	*883*	*6*
Field	*$28,880,000*	*$28,327,000*	*$32,349,000*	*$32,665,000*	*$0*
FTE	*207*	*193*	*218*	*218*	*0*
Total FTE	**979**	**991**	**1,095**	**1,101**	**6**
Budget Authority	**$138,518,000**	**$138,565,000**	**$150,582,000**	**$155,073,000**	**$4,491,000**
Center	*$111,443,000*	*$111,404,000*	*$121,806,000*	*$125,763,000*	*$3,957,000*
Field	*$27,075,000*	*$27,161,000*	*$28,776,000*	*$29,310,000*	*$534,000*
Cost of Living – Pay	--	--	--	*$2,251,000*	*$2,251,000*
Modernizing Drug Safety	--	--	--	*$2,240,000*	*$2,240,000*
Total FTE	**730**	**776**	**833**	**838**	*5*
User Fees	**$59,191,000**	**$56,476,000**	**$64,076,000**	**$60,762,000**	**($3,314,000)**
PDUFA - Center	*$52,014,000*	*$52,014,000*	*$51,376,000*	*$47,492,000*	*($3,884,000)*
PDUFA - Field	*$1,478,000*	*$1,166,000*	*$3,151,000*	*$2,897,000*	*($254,000)*
MDUFMA - Center	*$5,452,000*	*$0*	*$9,127,000*	*$9,915,000*	*$788,000*
MDUFMA - Field	*$247,000*	*$0*	*$422,000*	*$458,000*	*$36,000*
Total FTE	**249**	**215**	**262**	**287**	**1**

The historical funding and FTE levels table shows a five year history of program level funding, budget authority funding, user fee funding, and program level FTE.

Historical Funding and FTE Levels

Fiscal Year	Program Level	Budget Authority	User Fee	Program Level FTE
2004 Actual	$148,391,000	$103,537,000	$44,854,000	1,064
2005 Actual	$170,684,000	$123,109,00	$47,575,000	1,041
2006 Actual	$197,709,000	$138,518,000	$59,191,000	979
2007 Continuing Resolution	$191,745,000	$138,565,000	$56,476,000	991
2007 President's Budget	$214,658,000	$150,582,000	$64,076,000	1,095
2008 President's Budget	$215,835,000	$155,073,000	$60,762,000	1,101

Statement of Budget Request

The Biologics Program is requesting $215,835,000 for its mission activities:

- ensuring the safety, efficacy, potency, and purity of biological products including vaccines, cells, tissues, gene therapies, and related drugs and devices intended for use in the prevention, diagnosis, and treatment of human diseases, conditions or injuries
- ensuring the safety of the nation’s supply of blood and blood products
- evaluating the safety and effectiveness of biological products before marketing, and monitor the pre-clinical and clinical testing of new biological products
- licensing biological products and manufacturing establishments, including plasmapheresis centers, blood banks, and vaccine and biologic product manufacturers
- conducting regulatory research to establish product standards and develop improved testing methods.

Program Description

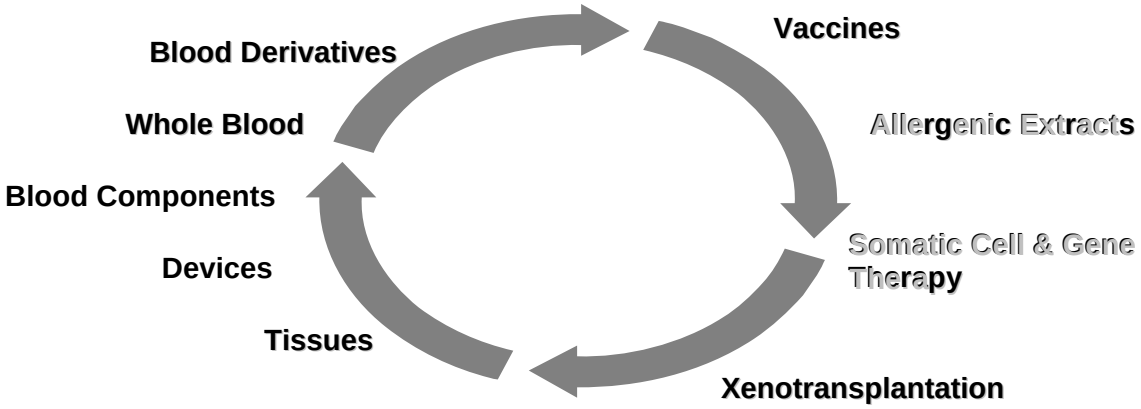
The Biologics Program ensures the safety and efficacy of a wide range of biologic products, including blood and blood products, human tissue, cell and gene therapies, vaccines, and allergenic products. The Center for Biologics Evaluation and Research (CBER) works with the National Institutes of Health (NIH), other government agencies and departments, academic institutions, and industry to facilitate product development and to counter potential threats to public health. CBER utilizes information technology to assist in problem detection and analysis and to facilitate prevention efforts. The products regulated by CBER touch the lives of people everyday. Some examples include: over 14 million units of blood and blood components transfused yearly in the United States, more than 235 million vaccinations administered, and over one million human tissues transplanted last year. In addition, there were more than 800 active human trials studying experimental cell and gene therapies, vaccines, and blood products for serious diseases such as HIV, cancer, diabetes, and heart disease. The graphic below illustrates the scope of the Biologic Program's work.

Field Biologics Activities

The Office of Regulatory Affairs (ORA) Field staff supports CBER 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 staff also respond to emergencies and investigate incidents of product tampering, terrorist events and natural disasters. To complement the regular field force, the Office of Criminal Investigations investigates instances of criminal activity in FDA regulated industries.

FDA regulates the following biological products



As this picture illustrates, the work of the Biologics Program is far-reaching and impacts the lives of millions of Americans.

Effects of Full Year FY 2007 Continuing Resolution

The analysis in this justification assumes funding levels for FY 2007 based on the enactment of the President's FY 2007 budget for the Biologics program. For comparison purposes, FDA budget tables also include a column in the FDA budget tables that reflects an FY 2007 Continuing Resolution (CR) level in the event that Congress enacts this level of appropriations for the remainder of FY 2007.

If FDA receives the CR rather than the FY 2007 President's budget request, this will have significant impact on FY 2007 performance for the Biologics Program:

- MDUFMA will terminate, which will increase the average review time for biologic device applications, slowing the availability of safe products to market, and postmarket surveillance of product safety will decline, leading to greater public health risks.

- The initiative addressing the safety of human tissue products used for transplantation will be postponed, and will likely result in an increase of preventable transmission of new and emerging infectious diseases. The FY 2007 CR level results in the loss of 8 FTE critically needed for the tissue program and will adversely impact FDA's ability to monitor adverse events and conduct inspections of tissue establishments and take needed actions.

- Absorption of the pay increase will reduce staff and increase the health risk of blood, tissue, and cell and gene therapies, along with diminished public confidence in these products. Outreach and interactions with innovators aimed at bringing new lifesaving products to patients faster and safely will be slowed. Ability to facilitate development of products needed to face new emerging disease threats would also be compromised.

- Essential public health activities for continued pandemic preparedness, as outlined in the DHHS Pandemic Plan, to select, test, produce and provide pandemic influenza seed strains and reagents needed to be prepared for rapid manufacturing in a pandemic will not be funded. Validating new, accelerated vaccine production methods will be slowed.

<u>Field Biologics Program</u>
If FDA receives the CR rather than the FY 2007 President's budget request, this will have significant impact on FY 2007 performance for the Field Biologics Program:

- ORA Blood Bank inspections will be reduced by 85 inspections, causing the inspection interval for blood banks to fall below the statutory inspection requirement of inspecting 50 percent of the inventory a year for the first time.

- ORA will only meet the performance goal of 325 Human Tissue establishment inspections allowing for firms in the human tissue industry to continue operating without in-depth ORA oversight.

- ORA will have to decrease the number of Bioresearch Monitoring inspections from 180 to 169, limiting FDA's ability to provide needed research oversight for integrity and the protection of human subjects.

- Funding under the continuing resolution causes a loss of 14 FTE for the Field Biologics Program.

If FDA receives the CR rather than the FY 2007 President's budget request, this will have significant impact on FY 2008 performance for the Biologics Program:

- Eliminating MDUFMA funding for the biologics program results in the loss of 31 FTE. The loss of this program will result in the inability to meet user fee goals for PMAs and 510(k)s, and cause delays and backlogs in the review process.

- The program and performance impacts described above as a result of a year long Continuing Resolution will carry over yet another year into FY 2008 in all areas mentioned above.

<u>Field Biologics Program</u>
If FDA receives the CR rather than the FY 2007 President's budget request, this will have significant impact on FY 2008 performance for the Field Biologics Program:

- Any new hires are unlikely to exceed 25 percent of typical productivity which means that FY 2008 inspection and laboratory analysis targets may not be met and ORA work will include a higher proportion of entry level tasks than in FY 2006.

- Despite ORA's desire to pursue risk based activities, newly hired employees will require intensive coaching and supervision and may need to assist an experienced ORA specialist for several months before assuming responsibility for complex risk based activities.

Program Resource Changes

Budget Authority

Pay Increase: +$2,251,000
The FDA request for pay inflationary costs is essential for FDA to accomplish its public health mission. Eighty percent of FDA's budget supports the agency workforce. Of this, payroll costs account for almost sixty percent of the total budget. The increase will allow FDA to maintain staff levels, including a national cadre of specially trained scientific staff. The total estimate for pay increases is $21,773,000. The Biologics Program's portion of this increase is $2,251,000. These resources are vitally important for FDA to fulfill its mission to protect the public health by helping safe and effective biologic products reach the market in a timely way, and by monitoring these products for continued safety after they are used.

Modernizing Drug Safety: +$2,240,000 and +5 FTE
The request would improve FDA's ability to resolve problems that challenge FDA's capacity to assure the safety for drugs and biologics. Specific challenge areas include better post-market surveillance, strengthened adverse event detection and analysis, and the need for enhanced communication of drug safety information to the medical community and other partners. The funds requested allow for high-priority drug safety activities:

- strengthened biologics adverse event databases and increased leveraging and information sharing with other partners

- increased adverse event detection, analysis, risk management, and communication capabilities of multidisciplinary integrated biologics safety teams

- enhanced involvement of epidemiologists and other safety experts throughout the product lifecycle, including in the prelicensure identification of safety data needs and in the design of and continuing review of post-marketing safety studies.

User Fees

Current Law User Fees

PDUFA: -$3,884,000
In FY 2007, PDUFA collections included a one-time increase of $31,600,000 for the final year adjustment under PDUFA III. For FY 2008, adjustments include increases for inflation and other increases authorized by the PDUFA statute. The net decrease in FY 2008 for the Drugs program is due to this one-time, non-recurring FY 2007 Final Year adjustment. Because FDA has not completed the public comment period regarding FDA's proposed recommendations for PDUFA reauthorization, the FY 2008

PDUFA estimate is based on straight reauthorization of PDUFA III with no programmatic enhancements or adjustments.

In the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Congress renewed FDA's authority to the collect PDUFA user fees. This authority is effective for five years and directs FDA to strengthen and improve the process for the review of human drugs and to improve risk management for drugs approved under PDUFA. The authority to collect fees under PDUFA expires on September 30, 2007.

Proposals to reauthorize PDUFA are currently under discussion. The PDUFA user fee is expected to bring in $339,195,000 in collections, with the Biologics Program request totaling $50,389,000. These FY 2008 amounts assume that the current authorities in effect for PDUFA III continue in FY 2008. FDA may need to amend its budget request when Congress reauthorizes PDUFA IV and establishes new performance goals and fee levels.

PDUFA user fees help the Biologic's program perform four activities:

- speed review of applications for new biologic products to prevent, treat, and cure of diseases
- improve the quality and efficiency of drug development and review, and improve risk management for newly approved products
- conduct premarket inspections, including bio-research monitoring inspections
- speed the development of products by providing guidances and standards, and providing pre-submission support to sponsors through meetings and other interaction.

MDUFMA: +$824,000 and +1FTE

Enacted in 2002, MDUFMA improves the quality and timeliness of the medical device review. It authorizes FDA to collect user fees to supplement appropriations for the medical device review program. FDA collects fees from device manufacturers that submit premarket applications and premarket notifications. The authority to collect fees under MDUFMA expires on September 30, 2007.

Proposals to reauthorize MDUFMA are currently under discussion. The MDUFMA user fee is expected to bring in $47,500,000 in collections, with the Biologics program increase being $824,000, for a total of $10,373,000. These FY 2008 amounts assume that the current authorities in effect for MDUFMA continue in FY 2008. FDA may need to amend its budget request when Congress reauthorizes MDUFMA and establishes new performance goals and fee levels.

MDUFMA user fees help the Biologics Program perform four activities:

- speed the review and action on device premarket applications and biologics license applications without compromising safety

- speed the development of products by providing guidances and standards, and providing pre-submission support to sponsors through such things as meetings

- conduct premarket inspections, including bio-research monitoring inspections

- make safe and effective biological medical device products for the prevention, treatment and/or cure of diseases available to the U.S. health care system faster.

Proposed User Fees

Reinspection User Fee: + $434,000 and + 3 FTE (Non-Add)
The FY 2008 budget includes $23,276,000 in budget authority for reinspection related activities. The Budget also proposes a new mandatory user fee to support reinspection activities. Once legislation is enacted, which authorizes FDA to collect this user fee, the Administration will work with Congress to recategorize these fees as discretionary.

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. FDA currently funds this activity through discretionary appropriations. The total proposed collections for the Agency in FY 2008 are $23,276,000, with $434,000 of the collections being allocated to the Field component of the Biologics program.

Justification of Base

FDA ensures the safety and effectiveness of a wide range of biologic products. As shown in the diagram above, FDA regulated biologic products include blood and blood products, human tissue, cell and gene therapies, vaccines and allergenic products. To achieve its regulatory mission, FDA uses science in areas such as proteomics, genomics, gene therapies, xenotransplantation, new vaccine technologies and delivery methods, and novel cellular and tissue therapies. The table below illustrates how Biologics Program activities support FDA's strategic goals.

	FDA Strategic Goals		
	Enhance Patient and Consumer Protection and Empower Them With Better Information about Regulated Products	Increase Access to Innovative Products and Technologies to Improve Health	Improve Product Quality, Safety and Availability Through Better Manufacturing and Production Oversight
Program Area			
Counterterrorism and Medical Countermeasures	X	X	
Vaccines/Pandemic influenza		X	X
Gene Therapy		X	X
Human Cells, Tissues and Cellular and Tissue-Based Products		X	X
User Fees		X	
Critical Path		X	X
Product Safety	X		X

As the table illustrates, the work of the Biologics Program provides critical support to FDA's public health mission.

Counterterrorism and Medical Countermeasures

FDA plays a critical role in protecting the public health by ensuring the availability of safe and effective medical countermeasures for mitigating the public health consequences of a bioterrorism event. These products include biologic products such as vaccines, blood products, human tissues, and cells and gene therapies, as well as products to treat burn, blast and trauma injuries. FDA develops guidance, provides advice on the conduct of studies, and monitors adverse events from new products. FDA safeguards against contamination and tampering to ensure access to safe products. Efforts related to biologic products focus on seven areas:

- ensuring safe and effective biological products to support stockpiles
- ensuring medical products are available
- conducting research programs to increase access to new products
- evaluating data that may be used for product licensure if human efficacy studies are not feasible or ethical
- evaluating over 100 active investigational new drug applications (INDs) for new products

- facilitating the availability of anthrax vaccine and new vaccines for smallpox and anthrax, plague, tularemia, Venezuelan Equine Encephalitis, and other encephalitis-causing viruses

- monitoring production of biologics to ensure products meet safety, purity, potency, and efficacy requirements.

Vaccines

Vaccines are among the most cost-effective means for preventing disease and thus reducing the spread of infections and reducing health care costs. FDA regulates the safety and effectiveness of vaccine products. Many of these are pediatric vaccines that have contributed to the dramatic reduction or elimination of life-threatening childhood diseases in the United States, such as diphtheria, measles, and polio. Newer vaccines are improving the lives of adolescents and adults by preventing diseases such as meningococcal disease, shingles, and cervical cancer, the second most common cancer in women worldwide. In addition, there are vaccines under development that may be able to prevent emerging infectious diseases, such as pandemic influenza viruses, severe acute respiratory syndrome (SARS), HIV-1, and malaria. As with all medical products, vaccines undergo review of laboratory and clinical data by highly trained scientists and clinicians to ensure their safety, efficacy, purity, and potency. FDA also reviews additional studies that may be conducted after 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.

<u>Vaccines – Field Activities</u>
The Office of Regulatory Affairs (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 vaccine and anti-viral drug products. ORA's efforts focus on four areas:

- conducting annual inspections of approved flu vaccine manufacturers

- conducting bioresearch monitoring inspections in support of CBER's review of new applications submitted by flu manufacturers

- identifying and intercepts counterfeit products either claiming to prevent or treat flu symptoms

- providing technical support to CBER, HHS agencies, and flu vaccine manufacturers during high priority product development.

Gene Therapy

One of the most exciting areas in biomedical research today is human gene therapy – the replacement of a person's faulty genetic material with normal genetic material to treat or cure a disease or an abnormal medical condition. Over time and with proper oversight, this may become a useful weapon to fight diseases such as cancer, diabetes, high blood pressure, heart disease, and other genetic disorders.

FDA issues guidance in areas of novel product development. FDA encourages dialogue on new product development to help define the best scientific approaches and reduce product development time and risk. FDA focuses on how best to evaluate essential issues of safety and efficacy. FDA facilitates product development and avoids unnecessary regulatory burdens while protecting human study subjects. Public input helps FDA and product developers address issues involving risks and benefits of research to develop novel gene therapy and cellular therapy products.

Since FY 2000, FDA has received over 489 requests to study gene therapy and to develop gene therapy products. Presently, FDA is overseeing about 249 active investigational new drug gene therapy studies.

Human Cells, Tissues and Cellular and Tissue Based Products (HCT/Ps)

FDA's new regulatory framework helps increase the safety of human tissues used in transplantation. Human tissue transplants continue to increase from about 350,000 in 1990, to over 1 million annually. Over the past decade advances have expanded the uses of tissue products. HCT/Ps covers many medical products such as skin replacement following severe burns, tendons and ligaments to repair injuries, bone replacement, and corneas to restore eyesight.

Using the new framework for human tissue products, FDA intends to encourage the development of new products. FDA has three primary goals with respect to human tissue regulation:

- prevent the spread of communicable diseases
- ensure safety and efficacy are demonstrated for cellular and tissue-based products that are also drug, biological, and medical device products
- enhance public confidence in these products to fulfill their great potential for improving and saving lives.

FDA also monitors safety and protects recipients of human tissues from infectious disease threats.

Human Cells, Tissues and Cellular and Tissue Based Products (HCT/Ps) – Field Activities

FDA is in the process of implementing its new risk-based approach to assure the safety of human cells, tissues, and cellular and tissue-based products (HCT/Ps). FDA is using a comprehensive approach for regulating existing and new cell and tissue products to respond to a rapidly growing industry.

This program is being implemented to prevent infectious disease transmission and contamination and to increase the quality and consistency of products. ORA helps ensure that tissues are recovered, processed, stored and distributed in a manner that reduces the risks of serious infectious diseases and contamination with infectious agents. ORA performs inspections to monitor the recovery and processing of HCT/Ps and the testing and screening of donors and assures that HCT/Ps do not contain communicable disease agents, that they are not contaminated, and that they do not become contaminated during manufacturing.

Blood Safety

FDA's goal is to ensure the U.S. blood system continues to be the world's safest by minimizing infectious disease transmission and other hazards. FDA is strengthening efforts to protect the blood supply and minimize risk to patients of acquiring HIV, hepatitis, Creutzfeldt-Jakob Disease (CJD), variant CJD (the human form of Mad Cow Disease), West Nile Virus (WNV), Chagas disease, emerging blood-borne diseases, and diseases from potential bioterrorism agents. FDA is engaged in significant efforts to increase blood safety:

- issuing and enforcing standards for blood collection and manufacturing of blood products
- facilitating development of products to improve blood safety and availability; preserve blood cells, blood products, and substitutes; testing and safety technologies; HIV blood tests; and public health screening
- updating existing guidance for consistency with new scientific information and eliminate outdated guidance documents
- addressing emerging infectious diseases by ensuring compliance of plasma fractionation establishments, blood donor and recipient notification and look back, and FDA emergency and Class I recalls affecting blood safety response procedures
- responding to emerging potential threats in a timely and coordinated approach.

Blood Safety – Field Activities

Blood and Blood Products are vitally important products in medical treatment. ORA monitors the collection of whole blood and the processing, manufacturing, and preparation of products derived from human blood to assure consumer protection from defective products which many endanger public health. ORA's efforts are focused in two areas:

- performing inspections of blood establishments engaged in the collection, manufacturing, preparation or processing of human blood or blood products

- inspecting laboratories that perform testing on blood products and donors to confirm donor screening for communicable disease agents.

User Fees

The Prescription Drug User Fee Act (PDUFA) authorized the collection of fees to enhance the review process, and established fees for applications, establishments, and approved products. PDUFA enables FDA to strengthen the review and monitoring of drug safety, increase interaction with sponsors, and develop principles for improving first-cycle reviews. The Biologics Program met or exceeded most of the PDUFA performance goals from FY 1994 through FY 2005. PDUFA is authorized for a five-year period. The current PDUFA legislation sunsets at the end of FY 2007.

The Medical Device User Fee and Modernization Act of 2002 (MDUFMA) provides resources for FDA to provide earlier access to safe and effective medical devices. MDUFMA has three major provisions. These provisions allow for the collection of fees for pre-market applications, allow third parties to conduct establishment inspections, and place new regulatory requirements on reprocessed single use devices. The Biologics Program has met or exceeded its MDUFMA performance goals. The current MDUFMA legislation sunsets at the end of FY 2007.

Product Safety

FDA ensures the continued quality and safety of approved biologic products. Biological products are derived from living organisms and therefore do not have the same consistency as products derived from chemical combinations. FDA engages in post-approval activities to develop and validate test methods and establish standards for biological products. FDA ensures that quality standards are met by manufacturers and establishments. Efforts to ensure product safety of biologic products include work in six areas:

- conducting product safety biomedical research in new cells used to produce drugs and biologics

- developing new assays and assessing the reliability of current assays to monitor product safety

- enhancing surveillance through the use of healthcare databases and establish programs using cutting edge technology

- addressing adverse events that did not appear during the development process

- evaluating errors that occur during manufacturing processes or storage of biological products

- establishing data links for safety monitoring that include information about patients and product exposure.

Selected FY 2006 Accomplishments

Vaccines

FDA supports efforts to produce pandemic influenza vaccine in the shortest possible time and protecting the greatest number of people, using a vaccine that is safe, effective, and easy to deliver. Congress appropriated $20 million for FDA in the FY 2006 Emergency Supplemental Appropriations Act for pandemic influenza activities. The Center for Biologics Evaluation and Research (CBER) received $16.727 million and 75 FTE. CBER is using these funds to address one of the five HHS pandemic influenza priorities - developing vaccines and vaccine production capacity. These funds enhance programs to facilitate development of pandemic vaccines and increase manufacturing capacity using both new and existing technologies. The resources allow FDA to demonstrate results in six areas:

- develop a preparedness strategy and emergency response plan
- develop new technologies and systems enabling high volume production of vaccines
- facilitate vaccines made with new technologies
- monitor vaccines administered to patients using modern analytic tools to identify vaccine safety signals
- provide outreach and training in manufacturing quality
- conduct inspections of facilities to assure product quality and prevent problems that threaten product safety or availability.

FDA released two draft guidance documents for pandemic and seasonal influenza vaccines. These documents provide recommendations on data needed to show safety and effectiveness for new vaccines. The documents also outline the approach of accelerated approval for both seasonal and influenza vaccine.

Influenza vaccination saves lives and medical costs

The economic burden of influenza related illness is anywhere from $71.3 to $166 billion each year. Influenza in children is a serious disease that results in frequent hospitalizations and outpatient visits. Children are the major transmitters of influenza in the community and home.

A recent study claims that investing $2.8 million to vaccinate children less than 5 years of age saves $3.5 million in health care costs. Influenza vaccine is also cost effective in elderly adults. CBER regulates yearly activities including the development and testing of reference standards, vaccine reference strains, and potency testing. CBER works with national and international public health agencies on influenza surveillance.

In fiscal year 2006, FDA approved a number of new vaccines. On June 8, 2006, FDA approved Gardasil, the first vaccine to prevent cervical cancer, precancerous genital lesions, and genital warts due to human papillomavirus (HPV) types 6, 11, 16, and 18. HPV is the most common sexually-transmitted infection in the United States. The Centers for Disease Control and Prevention (CDC) estimates that about 6.2 million Americans become infected with genital HPV each year and that over half of all sexually active men and women become infected at some time in their lives. On average, there are 9,710 new cases of cervical cancer and 3,700 deaths in the United States each year. Worldwide, cervical cancer is the second most common cancer in women. It is estimated that there are over 470,000 new cases and 233,000 deaths from cervical cancer each year.

On May 25, 2006, FDA approved the first vaccine for the prevention of shingles in people 60 years of age and older. Shingles is caused by the varicella-zoster virus, the same virus that causes chickenpox. After an attack of chickenpox, the varicella-zoster virus lies dormant in certain nerve tissue. Shingles can occur in people of all ages, but most commonly in those over 60 years of age, and this risk increases as people get older. Shingles is estimated to affect 2 in every 10 people in their lifetime. Shingles presents as clusters of blisters, which develop on one side of the body and can cause severe pain that may last for weeks, months, or years after the virus reappears.

On February 3, 2006, FDA approved RotaTeq, the only vaccine approved in the United States that helps protect infants against rotavirus, a viral infection that may cause diarrhea, vomiting, fever, and dehydration. RotaTeq, a live oral vaccine, is administered to infants between the ages of 6 and 32 weeks. CDC estimated rotavirus infection results in about 55,000 hospitalizations annually of infants and young children in this country. Death from rotavirus is rare in the United States. However, in developing countries rotavirus has been estimated to cause up to several hundred thousand deaths annually in infants and young children.

Vaccines – Field Activities

Pandemic Flu Initiative: ORA is a working member of FDA's Pandemic Flu Task Force, and serves as the lead of the Enforcement WorkGroup which oversees FDA's surveillance of internet sites that promote the sale of fraudulent products purporting to treat or cure seasonal or avian flu. ORA has also assumed a key, collaborative role in coordinating inspections of the Strategic National Stockpile with HHS and CDC.

Actions to Address Fraudulent Avian Flu Therapies: FDA issued 32 Warning Letters and 3 Cyber Letters to firms or individuals selling fraudulent seasonal or avian flu products via at least 69 Internet sites. In addition, 1 Temporary Restraining Order (TRO)/Injunction was granted against a firm that was selling fraudulent cures for influenza via 20 different websites. These actions have resulted in the correction or removal of fraudulent claims/websites from the Internet in a number of instances.

Blood and Blood Products

On January 9, 2006, FDA approved the first immune globulin product for the prevention of serious infections in patients with Primary Immune Deficiency (PID). Vivaglobin provides new delivery options for PID patients. PID patients require regular treatment with immune globulin to fight off or prevent infections.

On August 16, 2006, FDA licensed a new facility and manufacturer to produce Cytogam (Cytomegalovirus Immune Globulin Intravenous). This product prevents severe infections with cytomegalovirus (for example, human disease in people with transplants who are on immunosuppressive treatment).

FDA reduced the risk of transmission of viruses such as HIV and hepatitis B and C through blood transfusion by improvements in blood safety. The risk for HIV and hepatitis C has been reduced from 1 in 100 units in the 1980's to less than 1 in a million units at present.

FDA approved the first blood test to screen donors of blood, organs, cells, and tissues for West Nile Virus (WNV) in December 2005. The Procleix WNV Assay, developed by Gen-Probe Inc. and marketed by Chiron Corporation, detects viral genetic material. This new test will reduce the risk of WNV infection in patients who receive blood and other biologic products. This approval is the result of an extensive effort among FDA, other public health agencies, State health departments, test kit manufacturers, and the blood industry. FDA is developing guidance for industry on the use of these tests and triggers for single donation testing in areas of high prevalence.

Blood and Blood Products – Field Activities

$4.2 Million Fine for American Red Cross: On September 7, 2006, FDA issued an Adverse Determination Letter to the American Red Cross (ARC) fining the company $4.2 M for its failure to comply with Federal laws and regulations related to the collection of blood products. This fine demonstrates FDA's constant surveillance of ARC facilities pursuant to a Consent Decree of Permanent Injunction as well as FDA's commitment to keep the blood supply safe.

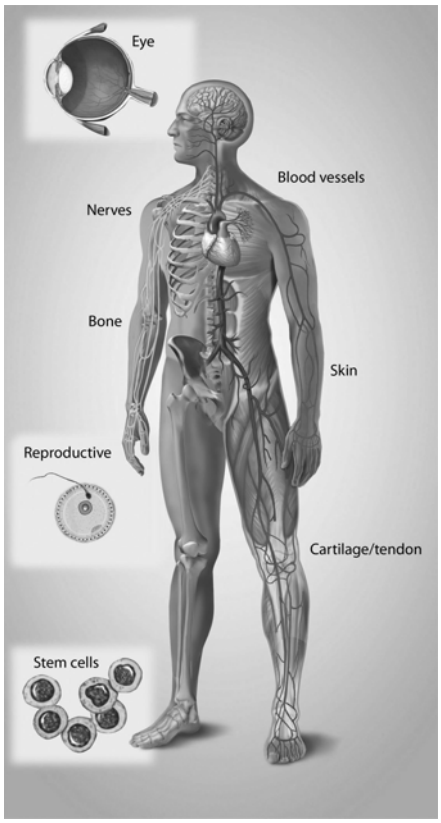
West Nile Virus Test Protects the Blood Supply

With support from FDA, CDC, and NIH manufacturers developed investigational WNV nucleic acid tests (NAT) tests that were rapidly put in place to protect the blood supply. West Nile Virus (WNV) is typically transmitted to humans by mosquito bites. It was first detected in the United States in 1999, and has reoccurred each year for seven consecutive years, causing close to 20,000 human cases of disease and at least 762 deaths since 2002. It is estimated that between 1 and 2 million people have been infected with WNV. In 2002, it was discovered that WNV could be transmitted in blood and an urgent effort to develop a blood test began. Blood banks across the United States participated in using the NAT tests, resulting in the detection and removal of approximately 1,600 infected donations.

In 2005, screening for WNV detected 399 cases of WNV in blood donors and prevented their donations from entering the blood supply. No cases of transfusion-transmitted WNV were reported in 2005. To further enhance blood safety, voluntary individual investigational donor testing was implemented in 2005 during periods of high disease activity in areas with a large number of cases of WNV. As of September 30, 2006, 260 donors with presumptive WNV were detected through screening but no transfusion-transmitted cases have been reported.

Human Tissues

The transplantation of human tissues presents unique safety issues, such as the risks of transmitting infectious diseases from donor to recipient and of contamination of tissues during processing. These risks can be significantly reduced, but not completely eliminated. Since 1993, FDA has required tissue establishments to screen and test donors. Since 1997, FDA has required tissue establishments to prepare, validate, and follow written procedures to prevent contamination and cross-contamination during processing. In response to the increase in tissue transplants and the threats to tissue safety, FDA now has a new framework for the regulation of human cells, tissues, and cellular and tissue-based products. It promotes the use of current tools and methods to reduce risks of infectious disease transmission and contamination and includes a broader range of tissues. In addition, the new regulations encourage a comprehensive yet flexible approach to quality in manufacturing throughout the entire process, from donor assessment to the final product, including adverse event reporting. FDA conducted extensive outreach and sought input throughout the process. FDA recognizes the new regulations, along with the evolution of the science, will pose many challenges. FDA will continue to conduct outreach to enhance the quality and performance of both the industry and FDA. These efforts should result in enhanced safety and public confidence.



The diagram to the left identifies FDA regulated human tissues and cells used in transplantation.

Human Tissues – Field Activities

FDA Orders Two Tissue Firms to Cease Manufacturing: In FY 2006, FDA ordered two tissue recovery firms, Biomedical Tissue Services, Ltd., and Donor Referral Services, to cease their manufacturing operations and to retain existing inventories of human cells, tissues and cellular and tissue-based products (HCT/Ps.) These actions demonstrate that the framework FDA has put into place to regulate HCT/Ps addresses and prevents the spread of communicable diseases by these products.

Human Tissue Recovery: ORA assisted the Agency in its efforts to develop a comprehensive approach that provides appropriate regulatory oversight of the human tissue industry. Through these efforts, ORA contributes towards identifying leveraging opportunities for coverage of the industry, reviewing guidance documents and regulations, and enhancing the inspection process. In FY2006, ORA also issued an import alert focusing on the importation of human cells, tissues, cellular, and tissue-based products

User Fees

CBER Continues to Meet or Exceed the User Fee Performance Goals

CBER continues to meet or exceed the user fee performance goals in the Prescription Drug User Fee Act (PDUFA) III and the Medical Device User Fee and Modernization Act (MDUFMA). This success in accomplishing thorough but timely scientific review of biological product applications and related device applications has meant that more safe and effective products are reaching those in need more efficiently and rapidly. We reviewed and acted on 96 % of New Drug Applications (NDA) and Biologics License Applications (BLA) within the review goal dates exceeding the target of 90% review and goal-date action. We also exceeded the target of having 75% of pre-market notifications (510K) for new medical devices reviewed and acted on within 90 days of receipt by completing 92% of the 510Ks within the prescribed timeframe.

PDUFA

PDUFA has provided FDA with needed resources for the review of human drug and biologic applications. Fees have been used to help reduce the time required for evaluating human drug applications and to support review quality. FDA has submitted annual performance and financial reports to Congress on progress in streamlining the drug review process and use of PDUFA fees.

On November 14, 2005, FDA held a public meeting entitled, "Prescription Drug User Fee Act: Public Meeting," on the NIH campus. The meeting included presentations by FDA and a series of panels representing different interest groups, such as patient advocates, consumers, industry, health professionals, and academic researchers. The purpose of the public meeting was to hear views as FDA prepares to work on amended authorizing legislation for PDUFA. The authority for PDUFA expires in September 2007.

FDA also issued a white paper entitled “Adding Resources and Improving Performance in FDA Review of New Drug Applications,” on November 10, 2005. The document shows the evolution of the PDUFA program since its enactment in 1992. The paper also outlines how fees are collected and how the fees are utilized. Information on the Agency’s PDUFA performance and financial reports, including the white paper, can be accessed at www.fda.gov/oc/pdufa.

MDUFMA

FDA facilitated the recent approval of rapid tests for HIV and of tests to monitor HIV drug resistance. These are examples of successful regulation under the framework established by MDUFMA. FDA aims to apply regulation in a risk-based manner. Certain areas in FDA’s oversight, including blood screening tests, raise unique concerns. FDA seeks to address these in a helpful manner and welcomes public and industry input.

On April 28, 2006, FDA issued guidance to industry that provided information about the real-time review process for premarket approval application (PMA) supplements and outlined the procedures for requesting and submitting these types of documents.

FDA issued guidance which provides updated information as to which firms qualify for small business fees and discounts for FY 2007. On September 30, 2007, the user fee provisions of MDUFMA will expire. To help evaluate the program and prepare for reauthorization, FDA sought input about aspects of MDUFMA that worked well and areas for which change should be considered. The third annual MDUFMA Stakeholders Meeting was held on November 17, 2005 in Gaithersburg, Maryland. The meeting provided a forum for feedback on how the user fee process is working, and recommendations for improvement of the device review program.

FDA is conducting negotiations with industry on MDUFMA II. CBER has met or exceeded the MDUFMA review performance goals for FY 2005. FDA MDUFMA performance and financial reports can be accessed at www.fda.gov/oc/mdufma.

Product Safety

CBER has emphasized the development and implementation of product safety teams to address areas such as adverse events and product manufacturing and quality issues and to respond to emerging threats. Safety issues, including continuous safety surveillance of licensed biological products to detect new information about adverse events, have significantly increased public health protections. Increasing the amount of information available to guide consumer decisions on product use and eliminating false and misleading product information contribute to a public better informed about biologic products.

The fundamental aim in CBER's continuous safety surveillance of licensed biological products is to detect new information about side effects or other factors. This information can help physicians more accurately weigh a product's risks against its anticipated benefits and can help patients to use these products as safely as possible. Recent presentations to CBER advisory committees and publications in the medical literature illustrate this surveillance-based growth in knowledge about the safety of biological therapeutic and prophylactic products.

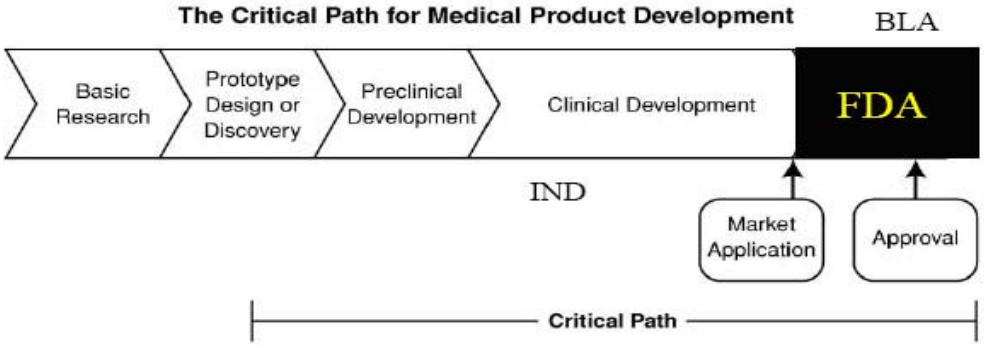
CBER also monitors the safety of newly licensed vaccines after they are introduced to the public. This critical surveillance ensures that new vaccines are safe when used in larger and more diverse populations than that which can be studied in prelicensure clinical trials. Surveillance also helps to maintain the public's confidence in vaccination, so that dreaded infectious diseases can be effectively prevented.

Research, Development and Evaluation

FDA research, development, and evaluation activities can improve predictability and efficiency along the critical path from laboratory concept to commercial product. FDA's Critical Path initiative is aimed at resolving challenges in the development of complex biological products, thereby helping make new products available. This initiative improves product safety through the use of new scientific tools. FDA's critical path program has five main areas:

- improve access to blood products for trauma victims by developing and evaluating animal and cell-based tests for the safety of blood substitutes
- evaluate biomarkers that predict medical product safety in order to streamline clinical trials and support personalized medicine
- develop and evaluate animal and cell-based models of disease used to predict safe gene therapy vectors
- ensure safety and availability of the blood supply by evaluating improved blood donor test kits for detection of malaria and other parasites
- develop and evaluate animal and cell-based models of disease used to test the efficacy of vaccines against the agents that cause anthrax, plague, smallpox, and Ebola.

The following diagram shows an idealized critical path that encompasses the drug, biological product and medical device development process. At the far left ideas coming out of basic scientific research enter into an evaluation process. Products are then subject to a series of more rigorous evaluation steps as they move from left to right along the path.



The Critical Path initiative encompasses the full spectrum FDA activities and enables the Biologics Program to address the challenges of regulating complex biological products in a rigorous and efficient manner.

Biologics
Program Activity Data (PAD)

PROGRAM WORKLOAD AND OUTPUTS	FY 2006 Actuals	FY 2007 CR [4]	FY 2007 PB	FY 2008 PB
Total Original License Application (BLA) Reviews[1]	33	30	35	35
BLA Approvals	10	8	20	20
Median BLA Approval Time (months)	13.7	14.5	14.0	14.0
License Supplement (BLA) Reviews[1]	1,675	1,500	2,000	2,000
NDA & NDA Supplement Approvals	49	20	35	35
ANDA & ANDA Supplement Approvals	9	8	10	10
PMA & PMA Supplement Reviews[1]	28	15	30	30
510(k) Reviews[1]	82	40	95	95
Commercial IND/IDE Receipts	115	125	150	150
IND/IDE Amendments Receipts[2]	9,124	9,300	9,300	9,300
Active INDs/IDEs[2]	2,855	2,900	2,900	2,900
Adverse Event Report Receipts [3]	21,956	22,500	22,500	22,500
Biological Product Deviation Report Receipts	38,621	38,650	38,650	40,000

[1]Total of approval, and complete decisions. Does not include refuse-to-file decisions or withdrawals.
[2] Includes IND, IDE, Master File and license master file receipts.
[3] Includes MedWatch, Foreign reports and VAERs reports. Does not include Fatality Reports or Medical Device Reports for CBER-regulated medical devices.
[4] Assumes the MDUFMA appropriation trigger is not met and the program expires.

BIOLOGICS FIELD

PROGRAM OUTPUTS- DOMESTIC INSPECTIONS	FY 2006 Actuals	FY2007 Continuing Resolution	FY2007 President's Budget	FY2008 President's Budget
Bioresearch Monitoring Program Inspections	88	169	180	180
Blood Bank Inspections	1,139	1,045	1,130	1,130
Source Plasma Inspections	145	174	174	190
Pre-License, Pre-Approval (Pre-Market) Inspections	22	6	6	6
GMP Inspections	26	30	30	30
GMP (Device) Inspections	6	16	16	32
Human Tissue Inspections	354	385	484	484
Total Above Domestic Inspections	**1,780**	**1,825**	**2,020**	**2,052**
PROGRAM OUTPUTS- IMPORT/FOREIGN INSPECTIONS				
Blood Bank Inspections	0	12	12	24
Pre-License Inspections	1	4	4	4
GMP Inspections	15	15	15	15
Total Above Foreign FDA Inspections	**16**	**31**	**31**	**43**
Import Field Exams/Tests	66	100	100	100
Import Line Decisions	44,418	49,350	49,350	54,829
Percent of Import Lines Physically Examined	0.15%	0.20%	0.20%	0.18%

Performance Analysis

During the latest completed performance period, (FY 2005), the Biologics Program successfully achieved all seven performance targets. So far, the Biologics program successfully achieved the FY 2006 targets that have completed performance data available. The Biologics program expects to meet the other targets when data becomes available later in FY 2007. For more information about these performance goals and results, please see the Performance Detail section.