BIOLOGICS

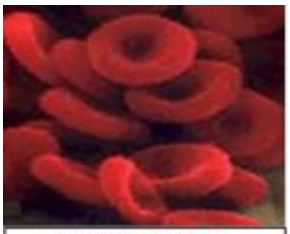
(Dollars in Thousands)	FY 2015 Final	FY 2015 Actuals	FY 2016 Enacted	FY 2017 President's Budget	FY 2017 +/- FY 2016
Biologics	**344,267**	**326,290**	**354,901**	**359,989**	**5,088**
Budget Authority	***211,382***	***211,362***	***215,443***	***215,443***	---
User Fees	***132,885***	***114,928***	***139,458***	***144,546***	***5,088***
Center	298,979	283,230	311,209	316,212	5,003
Budget Authority	171,096	171,079	174,052	174,052	---
User Fees	127,883	112,151	137,157	142,160	5,003
Prescription Drug (PDUFA)	*115,493*	*100,500*	*123,801*	*128,341*	4,540
Medical Device (MDUFA)	*10,549*	*11,402*	*11,475*	*11,897*	422
Generic Drug (GDUFA)	*1,052*	*240*	*1,072*	*1,092*	20
Biosimilars (BsUFA)	*789*	*9*	*809*	*830*	21
Field	45,288	43,060	43,692	43,777	85
Budget Authority	40,286	40,283	41,391	41,391	---
User Fees	5,002	2,777	2,301	2,386	85
Prescription Drug (PDUFA)	*4,810*	*2,584*	*2,084*	*2,161*	77
Medical Device (MDUFA)	*192*	*193*	*217*	*225*	8
FTE	**1,321**	**1,304**	**1,342**	**1,345**	**3**

Authorizing Legislation: Public Health Service Act; Federal Food, Drug, and Cosmetic Act; 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 of 1997; Medical Device User Fee and Modernization Act of 2002; Public Health Security and Bioterrorism Preparedness Response Act of 2002; Project Bioshield Act of 2004; Medical Device User Fee Stabilization Act of 2005; Food and Drug Administration Amendments Act of 2007 (FDAAA); Patient Protection and Affordable Care Act of 2010; Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA); Drug Quality and Security Act of 2013; Pandemic and All-Hazards Preparedness Reauthorization Act of 2013.

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The Biologics Control Act, passed in 1902, established the Biologics Program in the Department of Treasury's Hygienic Laboratory, which later became part of the National Institute of Health (NIH) in 1930. In 1972, the Biologics Program was transferred from NIH to FDA and became the Bureau of Biologics. In 1988, the Bureau became the Center for Biologics Evaluation and Research (CBER) which, with the Office of Regulatory Affairs' (ORA) field program, comprises the FDA Biologics Program.


Red Blood Cells

FDA's Biologics Program is responsible for protecting and enhancing public health by ensuring the safety, purity, potency and effectiveness of biological products − for the prevention, diagnosis, and treatment of human diseases, conditions, or injuries − including:

- vaccines (preventive and therapeutic)
- allergenics
- blood and blood products
- human tissues and cellular products

- gene therapies
- devices – specific subsets
- xenotransplantation[31] products.

FDA regulates complex biological products that involve novel and cutting-edge technologies and evolving science. FDA is responsible for the evaluation of the safety, purity potency and effectiveness of biological products and determines whether a product can be approved based on an evaluation of scientific data. Some cells and tissues for transplantation are regulated with a focus on prevention of the contamination of tissues and the spread of communicable disease.

FDA works with other Federal agencies, foreign governments and their national regulatory authorities, and international organizations such as the World Health Organization (WHO). FDA also protects the public against the threat of:

- emerging infectious diseases
- neglected tropical diseases
- potential bioterrorism agents.

To contribute to the improvement of public health in the years to come, CBER implemented a strategic plan which is a framework for guidance, decision-making, and future planning. This plan aligns with FDA's Strategic Priorities and the Department of Health and Human Services' (HHS) strategic plan by focusing on:

- protecting and improving public health
- facilitating the development of new technologies and the approval of products
- strengthening FDA as a preeminent regulatory organization for biological products

The work performed by the Biologics program supports FDA's priorities and the accomplishments represent significant efforts in support of the mission to protect and improve health both in the United States and globally. During the past year, the Biologics Program contributed to the improvement of public health with the following accomplishments:

- provided scientific and regulatory advice to sponsors and stakeholders on development of biological products to address the Ebola outbreak in West Africa
- evaluated investigational new drug (IND) applications related to Ebola
- utilized accelerated approval pathway to approve TRUMENBA and BEXSERO – vaccines designated as breakthrough therapies for the prevention of serogroup B meningococcal disease
- issued a Notice of Intent to Revoke (NOIR) license letter to a manufacturer for repeated violations of current Good Manufacturing Practice (cGMP).

The following selected accomplishments demonstrate the Biologics Program's delivery of its regulatory and public health responsibilities within the context of current priorities.[32]

[31] Xenotransplantation is any procedure that involves the transplantation, implantation or infusion into a human recipient of either (a) live cells, tissues, or organs from a nonhuman animal source, or (b) human body fluids, cells, tissues or organs that have had ex vivo contact with live nonhuman animal cells, tissues or organs

[32] Please visit FDA.gov for additional program information and detailed news items.

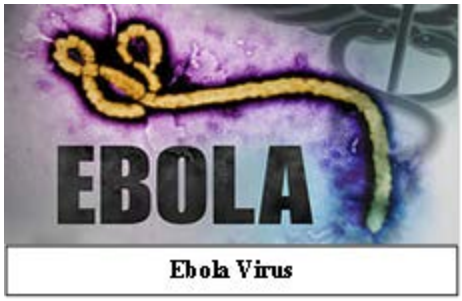
Improve and Safeguard Access

Within this Goal area, the Biologics Program addresses the following FDA Strategic Priorities: Safety and Quality, Regulatory Science, Globalization and Smart Regulation. FDA's Biologics Program is responsible for regulating a diverse range of products, from new and innovative vaccines and allergenics to novel cellular and gene therapies. To improve access to biological products, FDA uses all available tools, including regulatory science, to effectively evaluate products and improve predictability, consistency, transparency, and efficiency of the review process. These activities include:

- increasing preparedness to address public health threats
- supporting expedited regulatory pathways
- approving new biological products to treat and prevent diseases
- improving global public health through international collaboration
- issuing guidances to improve and safeguard access to biological products.

Increasing Preparedness to Address Public Health Threats as a Result of Bioterrorism, Pandemic and Emerging Infectious Diseases

Ebola



Ebola Virus

To help speed development and production programs for Ebola vaccines, FDA is providing scientific and regulatory advice to the regulated industry and U.S. government agencies that support medical product development, including the National Institute of Allergy and Infectious Diseases (NIAID), the Centers for Disease Control and Prevention (CDC), and the Biomedical Advanced Research and Development Authority (BARDA) within HHS and the U.S. Department of Defense (DOD). FDA's Biologics Program has expeditiously reviewed 18 IND applications for vaccines and other products intended to prevent or treat Ebola, allowing for the initiation of studies in humans. FDA has also responded to numerous requests for emergency use of investigational vaccines and Ebola convalescent plasma.

FDA is also collaborating with the World Health Organization (WHO) and international regulatory counterparts, including the European Medicines Agency and Health Canada, to exchange information about investigational products for Ebola. These efforts support regulatory collaboration to harmonize and accelerate the development of these and other biological products.

In September 2015, FDA participated in Health Canada's International Regulatory Forum (IRF). The IRF included a meeting of the African Vaccine Regulatory Forum (AVAREF) to discuss the experience of conducting joint reviews of Ebola vaccine clinical trial applications with African regulators to facilitate initiation of Ebola vaccine clinical trials in the affected countries. The discussion focused on "lessons learned" that could help guide future joint reviews within AVAREF.

On May 12, 2015, FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC) met in open session to discuss the development and licensure of Ebola vaccines.

Infectious Threats

In September 2015, FDA attended and participated in a WHO meeting in Geneva, Switzerland to discuss and plan for the international use of various smallpox vaccines in the event of an emergency.

In June 2015, FDA, together with NIH, co-sponsored a Respiratory Syncytial Virus (RSV) Vaccine Workshop. The purpose of the workshop was to explore the scientific, clinical, and regulatory challenges encountered in the development of RSV vaccines and to discuss approaches that may help overcome barriers. The workshop also reviewed the basic science and clinical data that inform the regulation of products currently under development.

On March 4, 2015, FDA's VRBPAC met in open session and made recommendations on the selection of strains to be included in the influenza virus vaccines for the 2015-2016 influenza season.

FDA is closely monitoring the Chikungunya virus (CHIKV) epidemic in the Caribbean, Puerto Rico, the US Virgin Islands, and sporadic outbreaks in Florida. FDA has taken the following steps to mitigate the risk of CHIKV infection in United States blood donors:

- collaborated with Puerto Rico's Department of Health to develop mitigation measures
- helped prevent Chikungunya virus transmission by allowing use of the investigational device – Intercept Blood System for platelets, prior to approval
- updated the Blood Products Advisory Committee on the Emergence of Chikungunya Virus Infections in the Western Hemisphere and the implications for blood transfusion safety
- promoted the development of tests for detection of CHIKV in blood donors.

Supporting Expedited Regulatory Pathways for Product Review

FDA understands advantages of expediting the availability of drugs that treat serious and life threatening diseases. Expedited regulatory pathways are especially important when a drug serves as the first available treatment for an illness or if the drug has significant benefits over existing treatments. Recently, FDA utilized fast track designation and priority review to approve the orphan drug product Coagadex, Coagulation Factor X (Human). It was approved for the on-demand treatment and control of bleeding episodes for individuals with hereditary Factor X deficiency. Until Coagadex, Coagulation Factor X's approval in October 2015, no specific coagulation factor replacement therapy was available for patients with hereditary Factor X deficiency.

FDA granted breakthrough therapy designation to both Trumenba and Bexsero, vaccines to prevent serogroup B Meningococcal disease. A breakthrough therapy drug is a drug intended alone or in combination with one or more other drugs to treat a serious or life threatening disease or condition. In addition, the preliminary clinical evidence must indicate that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. FDA may grant the designation of breakthrough therapy, as set forth in Section 902 of FDASIA. In addition, FDA approved Trumenba and Bexsero under the accelerated approval regulatory pathway. In the case of these vaccines that means that effectiveness was based on an immune response reasonably likely to predict clinical benefit. By making use of surrogate endpoints, accelerated approval can help reduce the time it takes for needed medical products to become available to the public.

In April 2015, FDA published a final guidance for Industry and FDA staff "Approval and De Novo Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions." The guidance introduces a new, voluntary program for certain medical devices that demonstrate the potential to address unmet medical needs for life threatening or irreversibly debilitating diseases or conditions and are subject to premarket approval applications (PMAs) or de novo requests, which are premarket pathway options for reclassifying a product.

The "Expedited Access Pathway" or "EAP" program will help patients have more timely access to these medical devices by expediting their development, assessment, and review. The EAP program will also preserve the statutory standard of reasonable assurance of safety and effectiveness for premarket approval and the statutory standards for granting a de novo request consistent with the Agency's statutory mission to protect and promote public health.

Approving New Biological Products to Treat and Prevent Diseases

In addition to the aforementioned work on Ebola and approvals for the meningococcal B vaccines, the Biologics Program reviewed and approved an array of biological products to treat and prevent diseases.

Selected Product Approvals in 2015

Below are some of CBER's product approvals that occurred in the last calendar year. This list does not represent any degree of importance or priority ranking of products.[33]

Date	Product Name	Purpose or Benefit
Nov 2015	BioThrax	New indication to prevent disease following suspected exposure to the bacterium that causes anthrax. First vaccine to receive approval based on Animal Rule.
Oct 2015	ImlygicMelanoma	The first FDA-approved oncolytic virus therapy, for the treatment of melanoma lesions in the skin and lymph nodes.
Jun 2015	ADVIA Centaur HIV Ag/Ab Combo (CHIV) Assay	The CHIV assay is intended to be used as an aid in the diagnosis of HIV infection in pediatric and adult populations, including pregnant women.
Apr 2015	Raplixa (Fibrin Sealant [human])	First licensed biological product manufactured using spray drying technology and intended to help control bleeding during surgery, when standard surgical techniques are ineffective or impractical
Jan 2015	Bexsero	A vaccine to prevent invasive meningococcal disease caused by meningitis B in individuals ages 10 through 25.

Improving Global Public Health through International Collaboration, Including Research and Information Sharing

FDA has participated in various meetings with WHO to facilitate regulatory capacity building of national regulatory authorities in developing countries.

In October 2015, FDA attended the 2015 WHO Expert Committee on Biological Standardization (ECBS) meeting in Geneva, Switzerland. The purpose of the meeting was to review and discuss

[33] Complete information on Biological approvals can be found at: http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicalApprovalsbyYear/default.htm

the establishment, discontinuation, and replacement of WHO biological reference materials, as well as the adoption of WHO guidelines and recommendations.

On October 23, 2015, FDA served on the roundtable panel at the International Alliance for Biological Standardization (IABS) meeting in Geneva, Switzerland. The purpose of the meeting was to exchange information on surveillance research on the development of narcolepsy following vaccination with adjuvanted influenza A (H1N1) vaccines.

In July 2015, FDA attended a WHO conference of collaborating centers on in vitro Diagnostic Devices in Potters Bar, England. During the meeting, updates on infectious disease markers and WHO guidelines were discussed. FDA also provided updates on Babesia microti testing and various infectious markers including Ebola, CHIKV, Dengue, and West Nile Virus.

On May 16, 2015, FDA sponsored a meeting of the International Pharmaceutical Regulators Forum (IPRF) Gene Therapy Working Group. Members of ten international regulatory authorities participated. The group discussed regulatory requirements and approaches for evaluating the dissemination profile of gene therapy products in animals to support the safe clinical development of this product class.

On February 26, 2015, FDA held the jointly sponsored 18th US-Japan Cellular and Gene Therapy Conference to exchange ideas on cutting edge areas of biomedical research and to enhance opportunities for collaborations among scientists from Japan and the US.

Selected Guidances Published in 2015

Below are guidances issued by FDA in the last calendar year. These guidances help address various issues.[34]

Date	#	Title	Description
Dec 2015	FDA-2014-D-2175-0001FDA-2014-D-2175-0001	Recommendations for Assessment of Blood Donor Suitability, Donor Deferral and Blood Product Management in Response to Ebola Virus	Provides recommendations to blood establishments on donor and product management to ensure blood supply safety in response to potential future Ebola outbreaks.
Sep 2015	FDA-2013-D-1213	Use of Donor Screening Tests To Test Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products for Infection With Treponema pallidum (Syphilis); Guidance for Industry; Availability	Provides establishments that make donor eligibility determinations for donors of HCT/P products with updated recommendations concerning donor testing for evidence of Treponema pallidum (Syphilis).
Aug 2015	FDA-2015-D-2818	Rare Diseases: Common Issues in Drug Development	Advances and facilitates the development of drugs and biologics to treat rare diseases. Also, assists sponsors in conducting more efficient and successful development programs.

[34] Complete information on CBER guidances can be found at:
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances
Complete information on CBER rules can be found at:
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ActsRulesRegulations/default.htm

Date	#	Title	Description
Jun 2015	FDA-2013-D-0576	Considerations for the Design of Early-Phase Clinical Trials of Cellular and Gene Therapy Products; Guidance for Industry	Provides recommendations regarding clinical trials in which the primary objectives are the initial assessments of safety, tolerability, or feasibility of administration of investigation products
Apr 2015	FDA-2014-D-0363-0003	Approval and De Novo Medical Devices Intended for Unmet Medical Need for Life Threatening or Irreversibly Debilitating Diseases or Conditions	A voluntary program for medical devices that address unmet medical needs for life threatening or debilitating diseases or conditions, subject to premarket approval (PMA) applications or de novo classifications.

Enhance Oversight

Within this Goal area, the Biologics Program addresses the following FDA Strategic Priorities: Safety and Quality, Regulatory Science, Globalization and Smart Regulation. FDA's oversight of production, manufacturing, and the global supply chain, and surveillance of postmarket product use plays a critical role in assuring the safety of FDA-regulated products.

In addition, regulatory oversight has enabled FDA to:

- develop standards
- reduce risks in the manufacturing, production, and distribution of FDA-regulated products
- strengthen the detection and surveillance of potential problems
- improve the response to identified and emerging problems with FDA-regulated products.

Activities related to enhanced oversight include:

- providing outreach to the blood industry
- enhancing the surveillance of biological products
- issuing guidances to enhance oversight of biological products.

In addition, FDA's field work also plays an integral role in assuring the safety of FDA-regulated products. The field staff provides surveillance through inspections at domestic and foreign manufacturing facilities and clinical study sites, including blood and tissue establishments, vaccine and allergenic facilities, device manufacturers, gene and cell therapy facilities, and plasma fractionators. FDA performs inspections to oversee clinical investigators and institutional review boards to ensure that the rights of human subjects participating in clinical trials are protected.

Postmarket inspections are conducted after products are approved. These inspections are performed to assure that products are manufactured in compliance with cGMP and other applicable FDA regulations. These efforts help to ensure that the biologics industry continuously reviews the quality standards of its manufacturing operations to maintain the safety and effectiveness of biological products on the U.S. market.

For example, in FY 2015, FDA issued a Notice of Intent to Revoke (NOIR) license letter to a sterile drug and allergenic extract manufacturer. Prior to issuance of the notice, FDA

investigators repeatedly documented significant violations of cGMP. The firm was cited for failing to establish and follow written procedures designed to prevent microbiological contamination. In addition, the firm was cited for failing to investigate unexplained discrepancies of a batch to meet its specifications and for failing to adequately maintain a system for monitoring environmental conditions. The firm's corrective actions will be assessed upon re-inspection and further action will be taken if continued significant violations are documented.

Providing Outreach to the Blood Industry

The blood collection industry is experiencing significant reductions in collections of Whole Blood and Red Blood Cells due to decreased demand for red blood cells for transfusion. FDA has participated in meetings of the HHS Advisory Committee on Blood and Tissue Safety and Availability (ACBTSA) to discuss the sustainability of the blood collection industry. In addition, FDA has met with trade organizations to discuss their concerns. As part of its ongoing blood safety efforts, FDA is implementing a transfusion-transmitted infections monitoring system (TTIMS) through contracts with blood organizations. TTIMS will evaluate the safety of more than 50 percent of the US blood supply by monitoring infectious disease agents including HIV, Hepatitis B, and Hepatitis C viruses in blood donations.

On September 17-18, 2015, FDA held a public workshop "New Methods to Predict the Immunogenicity of Therapeutic Coagulation Proteins" in partnership with the National Heart, Lung and Blood Institute, National Institutes of Health (NIH), the National Hemophilia Foundation, and the Plasma Protein Therapeutics Association. The purpose of the workshop was to discuss recent scientific progress in identifying the genetic determinants for an unwanted immune response to therapeutic coagulation proteins (immunogenicity), and to identify and discuss potential new methods to predict such immunogenicity.

On July 10, 2015, FDA issued a letter suspending the license of United States Blood Bank, Inc. (USBB). During a recent inspection of USBB, FDA identified deviations from applicable sections of the Code of Federal Regulations and the standards in USBB's license. Based on the observations cited in the suspension letter, FDA has reasonable justification to believe that grounds for revocation of the license exist under 21 CFR 601.5(b)(1)(iv), and that the establishment's operations present a danger to the public health.

On June 1, 2015, the Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC) met in open session to hear presentations from FDA on a risk assessment for global geographic-based variant Creutzfeldt-Jakob disease (vCJD) risk for US donors, and current measures to reduce the risk of vCJD from transfusion in the United States.

TSEAC discussed FDA's geographical-based donor deferral policies and other strategies, including leukocyte reduction of blood components, to reduce the risk of transfusion-transmitted vCJD. FDA was seeking the advice of the Committee in developing future recommendations to reduce this risk. The committee also heard update presentations on the following topics:

- the vCJD situation worldwide
- an update on the United Kingdom's Transfusion Medicine Epidemiological Review
- vCJD in the United States
- the bovine spongiform encephalopathy (BSE) situation worldwide
- U.S. Department of Agriculture's regulatory approaches to reduce risk of foodborne BSE exposure.

On May 22, 2015, FDA issued a Federal Register notice of final rulemaking entitled, "Requirements for Blood and Blood Components Intended for Transfusion or for Further Manufacturing Use." This final rule, which becomes effective on May 23, 2016, revises and updates existing regulations that require blood establishments to assess a donor's medical history to determine that the donor is in good health and to screen the donor for factors that can adversely affect the safety, purity, or potency of blood and blood components. The final rule contains a flexible approach that will allow FDA to add or remove test requirements based on changes in science including epidemiology or technological advancements. The rule was initiated as part of the Department of Health and Human Services' Blood Action Plan. The Blood Action Plan was developed in 1998 in response to recommendations from Congress, the Government Accountability Office, and the Institute of Medicine. The rulemaking is one of the final remaining action items under the Blood Action Plan. FDA participated in industry webinars explaining the new rule in September and October. In addition, FDA also presented the requirements of the new rule and responded to industry inquiries at the annual AABB meeting in October 2015.

In May 2015, FDA's Blood Products Advisory Committee met in open session to discuss strategies for implementation of serological and nucleic acid testing for Babesia microti in blood donors. The committee also heard update presentations on the following topics:

- FDA considerations for Hemoglobin S Testing in blood donors
- FDA considerations for revised blood donor deferral policy for men who have sex with men

In December 2014, FDA announced it will take the necessary steps to recommend a change to the blood donor deferral period for men who have sex with men from indefinite deferral to one year since the last sexual contact. This decision was made following a review by FDA and Health and Human Services (HHS), and taking into account the recommendations of advisory committees to HHS and FDA, In May 2015, FDA issued a draft guidance entitled "Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products," which recommended this proposed change in policy. The finalized guidance was recently issued in December 2015.

Enhancing the Surveillance of Biological Products

FDA continues to enhance how it monitors the marketplace to help protect patients and ensure that products are safe and effective. The surveillance of biological products is an evolving effort that continues to require enhanced methods, technology, and collaboration.

In September 2015, FDA posted a protocol for a study entitled "Kawasaki Disease and PCV13 Vaccine" to the Sentinel website. The study used PRISM to evaluate Kawasaki Disease and Prevnar 13, a pneumococcal conjugate vaccine.

In September 2015, FDA posted a protocol for a study entitled "Influenza Vaccines and Febrile Seizures in the 2013-2014 and 2014-2015 Influenza Seasons." This study will assess the risk of febrile seizures following inactivated influenza vaccination (IIV) with or without concomitant Prevnar 13 (PCV13) by influenza vaccination during the 2013-14 and 2014-15 influenza seasons among children ages 6 months through 23 months of age.

In April 2015, FDA posted the results of a Post Licensure Rapid Immunization Safety Monitoring System (PRISM) study which evaluated more than 650,000 females, ages 9 -23 years

of age and more than 1.4 million doses of the human papillomavirus vaccine, Gardasil and found no association between venous thromboembolism and Gardasil.

In April 2015, FDA posted the results of a report entitled "Accessing the Freshest Feasible Data for Conducting Active Influenza Vaccine Safety Surveillance (PRISM)." The objective of this activity was 1) to establish and assess an active surveillance system for seasonal influenza vaccines; 2) to conduct near real-time surveillance for two health outcomes of interest, anaphylaxis and seizure, following influenza vaccination.

FDA initiated a pilot study of TreeSCAN utilizing PRISM data for the Gardasil 4 vaccine and a revised protocol for a pilot study of TreeSCAN utilizing PRISM data for the HPV4 Vaccine was posted to the Mini-Sentinel website on March 30, 2015.

FDA also engaged a new partnership with Hospital Corporation of America to enable safety assessments of intravenously administered medical products in the hospital setting, where the majority of blood and blood-derived products are administered.

FDA is planning the first protocol-based study designed to mine healthcare data in Sentinel and to detect if there are any serious, unexpected adverse events after vaccination for Gardasil 9.

FDA responded to eight potential, three ongoing, and one new product shortage in FY 2015.

In an effort to streamline the recall process, in FY 2015 FDA began delegating class I recall authority to the Centers. Class I recalls are the highest risk recalls and are conducted in a situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse health consequences or death. The delegation of Class I recall authority streamlines the review and approval process for Class I recalls resulting in earlier issuance of a notice of recall classification determination to a firm. A notice communicates FDA's decision and the firm's responsibilities under 21 CFR part 7, Subpart C – Recalls, Including Product Corrections – Guidance on Policy, Procedures, and Industry Responsibilities. Further, earlier notification results in the publication of the recall and its classification in FDA's Enforcement Report in a timelier manner.

In FY 2015, FDA classified two Class I (highest risk), 466 Class II (lower risk), and 183 Class III (lowest risk) recalls of biologic products. Additionally in FY 2015, FDA issued four warning letters related to biologic products.

Selected Guidances Published in 2015

Below are guidances issued by FDA in the last calendar year. These guidances help address various issues.[35]

[35] Complete information on CBER guidances can be found at: http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances

Date	#	Title	Description
Dec 2015	FDA-2015-D-1211-0098	Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products; Guidance for Industry	Provides blood establishments that collect blood or blood components with revised donor deferral recommendations for individuals at increased risk for transmitting HIV infection
Feb 2015	FDA-2015-D-0349	Investigating and Reporting Adverse Reactions Related to Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) Regulated Solely under Section 361 of the Public Health Service Act and 21 CFR Part 1271; Draft Guidance	Provides recommendations for complying with the requirements for investigating and reporting adverse reactions involving communicable disease in recipients of HCT/Ps
Feb 2015	FDA-2004-D-0500	Brief Summary and Adequate Directions for Use: Disclosing Risk Information in Consumer-Directed Print Advertisements and Promotional Labeling for Human Prescription Drugs	Assists manufacturers, packers, and distributors with meeting requirements for drug advertising and the requirement that directions for use be included with promotional labeling when print materials are for consumers
Feb 2015	FDA-2014-D-1525	Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application	Describes when FDA will act against a state-licensed pharmacy, Federal facility, or outsourcing facility that mixes, dilutes, or repackages biological products without a biologics license application

Selected Rules Published in 2015

Below are rules published by CBER in the last calendar year. These rules help address various issues. [36]

Date	#	Title	Description
May 2015	FDA-2006-N-0040-0009	Requirements for Blood and Blood Components Intended for Transfusion or for further Manufacturing Use	Revises existing regulations requiring blood establishments to assess medical history and screen for factors that can affect the safety, purity, or potency of blood and blood components.

[36] For more information on FDA rules please visit http://www.fda.gov/RegulatoryInformation/RulesRegulations/default.htm.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2013 Actual	$296,866,000	$194,638,000	$102,228,000
FY 2014 Actual	$321,064,000	$210,912,000	$110,152,000
FY 2015 Actual	$326,290,000	$211,362,000	$114,928,000
FY 2016 Enacted	$354,901,000	$215,443,000	$139,458,000
FY 2017 President's Budget	$359,989,000	$215,443,000	$144,546,000

BUDGET REQUEST

The FY 2017 Budget Request is $359,989,000, of which $215,443,000 is budget authority and $144,546,000 is user fees. The budget authority remains the same compared to the FY 2016 Enacted level and user fees increase by $5,088,000. The FY 2017 Budget allows the Biologics Program to advance public health through innovative regulation that promotes the safety, purity, potency, effectiveness, and timely delivery of biological products to patients.

FDA will to continue to facilitate the development of science and new technologies to bring products to market by:

- developing and issuing guidance and regulations to communicate scientific and regulatory requirements
- providing recommendations and frameworks for product development
- developing policy
- taking appropriate regulatory actions on premarket product submissions.

In addition, FDA will advance regulatory research to facilitate product review and will use tools, including regulatory science, to effectively evaluate products and improve predictability, consistency, transparency, and efficiency of the review process.

FDA will strive to ensure the safety of biological products by conducting a robust postmarket program after products are approved and evaluating the results of clinical studies, including collecting, analyzing, and acting on product, patient, and consumer information and healthcare data to move to active surveillance. In addition, FDA will use statistical data analysis and mathematical models for improved epidemiological and risk assessment of regulated products.

FDA is also strategizing to harmonize existing regulatory standards and is cooperating with international scientific efforts to establish and maintain reference materials and standards for biologics. FDA will also improve global public health through international collaboration by facilitating global access to vaccines and biological products that address critical health needs, including promoting research and sharing information to address global diseases and emerging threats impacting human populations. In addition, FDA will continue to address threats as a result of bioterrorism, pandemic, and emerging infectious diseases, including facilitating development, evaluation, and availability of high-priority medical products and countermeasures.

In 2016, FDA will continue building the infrastructure to process electronic New Drug Applications, Abbreviated New Drug Applications, Biologic License Applications, and Investigational New Drug submissions for biological products. FDA will support electronic

registration and integration of the Unique Facility Identifier into IT systems that support ORA's medical product related regulatory work, including ORA's Official Establishment Inventory (OEI).

FDA will also continue to support the President's National Strategy for Combating Antibiotic Resistant Bacteria, by facilitating the development of better diagnostics, therapeutics, and vaccines for the management of antimicrobial resistant organisms. FDA will use animal model development to support vaccine and antimicrobial drug development for high priority bacterial pathogens such as *Staphylococcus aureus*, *Mycobacterium tuberculosis* (TB), *Klebsiella pneumonia*, and *Clostridium difficile*.

USER FEES

Current Law User Fees: +$5.1 million

Center: +$5.0 million / Field: +$0.1 million

The Biologics Program request includes an increase of $5.1 million for current law user fees, which will allow FDA to fulfill its mission of protecting the public health, treating and curing diseases, and accelerating innovation in the industry.

PERFORMANCE

The Biologics Program's performance measures focus on biological product review, manufacturing diversity and capacity for influenza vaccine production, strengthening detection and surveillance of FDA-regulated products and postmarket inspections in order to ensure the safety, purity, potency, and effectiveness of biological products, as detailed in the following table.

The following selected items highlight notable results and trends detailed in the performance table.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2016 Target	FY 2017 Target	FY 2017 +/- FY 2016
233207: Review and act on standard New Molecular Entity (NME) New Drug Application (NDA) and original BLA submissions within 10 months of the 60 day filing date. *(Output)*	FY 2014: 100% Target 90% (Target Exceeded)	90%	90%	Maintain
233208: Review and act on priority NME NDA and original BLA submissions within 6 months of the 60 day filing date. *(Output)*	FY 2014: 100% Target 90% (Target Exceeded)	90%	90%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2016 Target	FY 2017 Target	FY 2017 +/- FY 2016
233209: Review and act on standard non-NME original NDA submissions within 10 months of receipt. *(Output)*	FY 2014: NA (No submissions received)	90%	90%	Maintain
233210: Review and act on priority non-NME original NDA submissions within 6 months of receipt. *(Output)*	FY 2014: NA (No submissions received)	90%	90%	Maintain
233205: Complete review and action on complete blood bank and source plasma BLA submissions within 12 months after submission date. *(Output)*	FY 2014: 100% Target: 90% (Target Exceeded)	90%	90%	Maintain
233206: Complete review and action on complete blood bank and source plasma BLA supplements within 12 months after submission date. *(Output)*	FY 2014: 100% Target: 90% (Target Exceeded)	90%	90%	Maintain
233211: Review and act on new non-user fee, non-blood product applications within 12 months of receipt. *(Output)*	FY 2014: 100% Target: 60% (Target Exceeded)	60%	60%	Maintain
234101: Increase manufacturing diversity and capacity for influenza vaccine production. *(Output)*	FY 2015: Continued evaluation of new methods to produce high-yield influenza vaccine reference strains. (Target Met)	Continue evaluation of new methods to produce high-yield influenza vaccine reference strains	Continue evaluation of new methods to produce high-yield influenza vaccine reference strains	N/A

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2016 Target	FY 2017 Target	FY 2017 +/- FY 2016
231301: Percentage of Lot Distribution Reports that were entered into the Regulatory Management System – Biologics License Applications (RMS-BLA) within 7 Days.	FY 2015: 95% (Historical Actual)	85%	85%	Maintain
234202: Number of registered domestic blood bank and biologics manufacturing inspections. *(Output)*	FY 2015: 957 Target: 900 (Target Exceeded)	900	900	Maintain
234203: Number of human foreign and domestic tissue establishment inspections. *(Output)*	FY 2015: 656 Target: 570 (Target Exceeded)	570	570	Maintain

Review Performance Measures

FDA continues to exceed PDUFA and non-user fee, non-blood product, and blood bank and source plasma review measures. Performance results for FY 2015 will not be available until the review of the applications for the FY 2015 cohort is complete, typically sometime within the next fiscal year. The non-New Molecular Entities (NME) performance goals are important because the PDUFA V agreement requires FDA to report on the review performance for non-NME and NME product applications separately. Cohort years where no non-NME applications were submitted by industry are indicated by saying NA for the actual data. For additional information on the PDUFA approvals, see the "Approving New Biological Products" section listed above in the program narrative.

Influenza Performance Measure

This performance measure supports the Department's national preparedness efforts in combating seasonal influenza, by increasing manufacturing diversity and capacity for influenza vaccine production. Further information on this measure can be found in the Department's Online Performance Appendix.

In FY 2015, FDA met the target to continue evaluation of new methods to produce high-yield influenza vaccine reference strains. Activities to meet this target included the following.

FDA continued efforts to develop new methods for determining influenza vaccine potency, an important component in the evaluation of high-yield influenza vaccine viruses. An international collaborative study, involving multiple manufacturers and regulatory agencies, was initiated to compare several alternative methods. The study will continue in FY 2016. In addition, improvements were made to the alternative potency assays under development at FDA that included the ability to accurately measure the potency of influenza B vaccines in addition to influenza A vaccines. Assay development and evaluation will continue in FY 2016.

FDA continued evaluation of methods to assess the relative yields of candidate vaccine viruses. FDA participated in an international collaborative study that compared the influenza virus yields and virus hemagglutinin (HA) production from several candidate vaccine strains. This study is ongoing and will continue in FY 2016. Studies at FDA, designed to increase the yields of candidate vaccines by targeted manipulation of the virus genome, demonstrated the feasibility of improving virus yields for H1N1 vaccine viruses. These studies will continue in FY 2016.

Lot Distribution Report Performance Measure

This is a new performance goal that measures how efficiently FDA gathers and enters information from lot distribution reports that are created by the manufacturer into the Regulatory Management System - Biologics License Applications (RMS-BLA). Quick and reliable access to this information will help FDA conduct epidemiological analyses of adverse event reports in an effort to discover unsafe manufacturing conditions and remove unsafe products from the supply chain before they can do harm to the public.

PROGRAM ACTIVITY DATA

Biologics Program Activity Data (PAD)

CBER Workload and Outputs	FY 2015 Actual	FY 2016 Estimate	FY 2017 Estimate
Original Biologics License Applications (BLA)			
Workload [1]	20	20	20
Total Decisions [2]	36	36	36
Approved	15	15	15
BLA Efficacy Supplements			
Workload [1]	17	17	17
Total Decisions [2]	36	36	36
Approved	16	16	16
BLA Manufacturing Supplements			
Workload [1]	1,084	1,084	1,084
Total Decisions [2]	1,218	1,218	1,218
Approved	1,096	1,096	1,096
BLA Labeling Supplements			
Workload [1]	181	181	181
Total Decisions [2]	189	189	189
Approved	165	165	165
Original New Drug Application (NDA)			
Workload [1]	0	0	0
Total Decisions [2]	1	1	1
Approved	0	0	0
NDA Efficacy Supplements			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0
NDA Manufacturing Supplements			
Workload [1]	12	12	12
Total Decisions [2]	29	29	29
Approved	22	22	22
NDA Labeling Supplements			
Workload [1]	7	7	7
Total Decisions [2]	7	7	7
Approved	7	7	7
Original Abbreviated New Drug Application			
Workload [1]	0	0	0
Total Decisions [2]	1	1	1
Approved	1	1	1
ANDA Efficacy Supplements			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0

CBER Workload and Outputs	FY 2015 Actual	FY 2016 Estimate	FY 2017 Estimate
ANDA Manufacturing Supplements			
Workload [1]	2	2	2
Total Decisions [2]	0	0	0
Approved	0	0	0
ANDA Labeling Supplements			
Workload [1]	0	0	0
Total Decisions [2]	3	3	3
Approved	3	3	3
Device 510Ks			
Workload [1]	56	56	56
Total Decisions [2]	87	87	87
Final Decision - SE	39	39	39
Device Premarket Applications (PMA)			
Workload [1]	2	2	2
Total Decisions [2]	9	9	9
Approved	5	5	5
Device Premarket Applications (PMA) Supplements			
Workload [1]	45	45	45
Total Decisions [2]	47	47	47
Approved	22	22	22
Investigational New Drugs (IND)			
Receipts: IND (new)	401	401	401
Receipts: IND Amendments	9,092	9,092	9,092
Total Active IND [3]	2,336	2,336	2,336
Investigational Device Exemptions (IDE)			
Receipts: IDE (new)	18	18	18
Receipts: IDE Amendments	296	296	296
Total Active IDE [3]	144	144	144
Patient Safety			
Adverse Event Reports Received [4]	60,708	62,000	63,000
Biological Deviation Reports Received	46,590	47,000	47,000
Sponsor Assistance Outreach			
Meetings	406	406	406
Final Guidance Documents [5]	34	30	30
Admin/Management Support			
Advisory Committee Meetings Held	8	13	13
FOI Requests Processed	264	320	320

[1] Workload includes applications received and filed.

[2] Total Decisions include approved, denied, withdrawn, approvable, approvable pending inspection, not approvable, exempt, major deficiency, substantially equivalent (SE), not substantially equivalent (NSE), de novo and complete response (CR).

[3] Total Active includes investigational applications received and existing applications for which CBER has received at least one amendment (IND) or supplement (IDE) during the FY being reported.

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

[5] Includes all FDA final guidances issued by CBER and other FDA centers that pertain to biological products.

Field Biologics Program Activity Data (PAD)

Field Biologics Program Workload and Outputs	FY 2015 Actuals	FY 2016 Estimate	FY 2017 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,835***	***2,047***	***2,047***
Bioresearch Monitoring Program Inspections	97	100	100
Blood Bank Inspections	893	1,060	1,060
Source Plasma Inspections	175	194	194
Pre-License, Pre-Market Inspections	54	7	7
GMP Inspections	27	28	28
GMP (Device) Inspections	6	7	7
Human Tissue Inspections	600	661	661
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS	***67***	***47***	***47***
Bioresearch Monitoring Program Inspections	19	11	11
Foreign Human Tissue Inspections	1	0	0
Blood Bank Inspections	7	8	8
Pre-License, Pre-market Inspections	8	2	2
GMP Inspections (Biologics & Device)	32	20	20
TOTAL UNIQUE COUNT OF FDA BIOLOGIC ESTABLISHMENT INSPECTIONS	***1,902***	***2,094***	***2,094***
IMPORTS			
Import Field Exams/Tests	85	45	45
Import Line Decisions	150,673	176,313	206,317
Percent of Import Lines Physically Examined	0.06%	0.03%	0.02%
GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,902***	***2,094***	***2,094***

Page intentionally left blank