



DEPARTMENT of HEALTH and HUMAN SERVICES

Fiscal Year

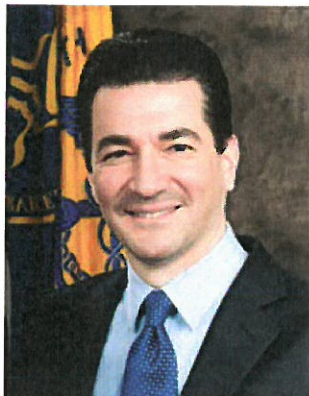
2018

Food and Drug Administration

Justification of Estimates for Appropriations Committees

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LETTER FROM THE COMMISSIONER



I am pleased to present the FY 2018 Food and Drug Administration (FDA) Budget. FDA has broad responsibilities to protect and promote public health by ensuring the safety, effectiveness, and security of human and animal drugs, biological products, and medical devices; ensuring the safety of our nation's food supply, cosmetics, radiation-emitting products; and regulating tobacco products.

These responsibilities continue to expand as we work to fulfill the mandates of groundbreaking legislation passed in recent years, including the 21st Century Cures Act of 2016 (Cures Act). The Cures Act is designed to help advance medical product development and to bring today's remarkable innovations and advances to patients who need them faster and more efficiently.

FDA accomplishments span areas of food safety, medical product innovation, safety and oversight, nutrition, and tobacco regulation. In 2016, FDA:

- approved 22 novel drugs, more than 800 generics, 91 medical devices, and 11 original applications for biological products
- mobilized more than 500 staff members to rapidly respond to the Zika virus outbreak
- awarded nearly \$22 million to states to improve produce safety
- modernized the Nutrition Facts label to help consumers make informed choices
- improved the alignment of field activities to FDA-regulated products
- conducted more than 165,000 tobacco retailer inspections.

Mindful of the current budget environment, the FY 2018 Budget will allow FDA to continue to obtain the most public health protection and promotion for the federal dollar. FDA is requesting a total of \$5.1 billion; an increase of almost 10 percent above the FY 2017 annualized Continuing Resolution. The FY 2018 request includes:

- a total of \$60 million to implement the Cures Act
- recalibration of FDA medical product user fees to more than \$2.5 billion, an increase of \$1.2 billion over FY 2017, consistent with the America First Budget Blueprint.

The FY 2018 request also includes reductions in budget authority targeted to certain areas where better tools and policies will allow us to do more with less, while preserving core mission activities. These reductions will be coupled with policy efforts to improve the efficiency of the programs that see reductions, to make sure that we are improving our effectiveness and taking a risk-based approach to our consumer protection mission.

FDA is fully committed to protecting and advancing the public health, based on the latest science, by helping to make the process for developing safe and effective medical products more efficient and less costly; strengthening food safety for domestic and imported products; reducing the harms of tobacco; and improving agency efficiency by taking a risk-based approach to our core mission to protect consumers, so that we can get the most public health protection for the resources that are entrusted to us.

A handwritten signature in blue ink, reading "Scott Gottlieb, M.D.", positioned above the printed name.

Scott Gottlieb, M.D., Commissioner of Food and Drugs

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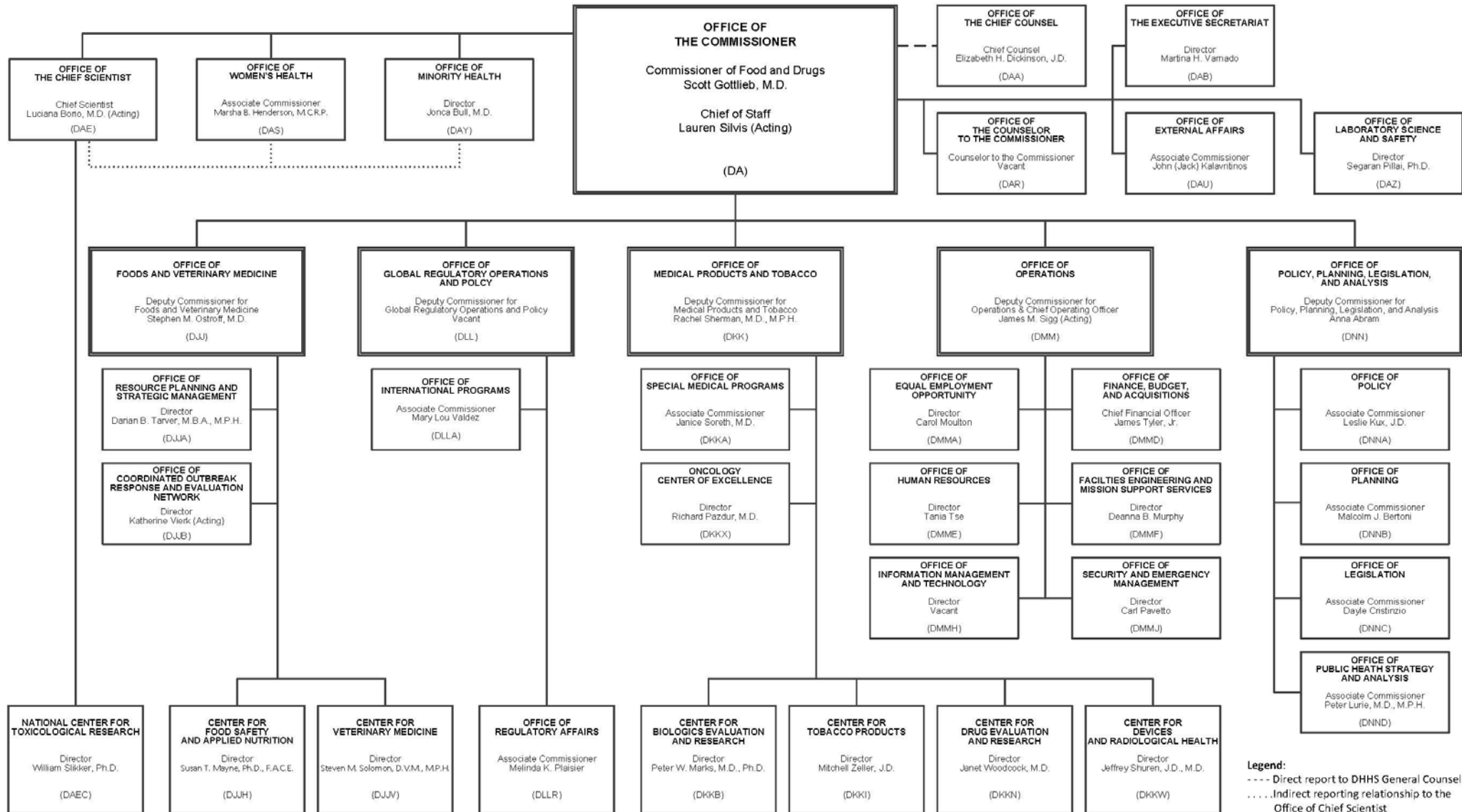
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FOOD AND DRUG ADMINISTRATION

18 May 2017



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EXECUTIVE SUMMARY

This Executive Summary describes the fiscal year (FY) 2018 Budget for the U.S. Food and Drug Administration (FDA). FDA is the agency within the U.S. Department of Health and Human Services (HHS) responsible for protecting and promoting public health by ensuring the safety, effectiveness, and security of human and animal drugs, biological products, and medical devices; ensuring the safety of food and feed, cosmetics, and radiation-emitting products; and regulating tobacco products.

RECENT ACCOMPLISHMENTS

FDA delivers significant, quantifiable results that help Americans every day and are a sound investment. A selection of recent accomplishments is presented below.

Medical Product Approvals

In calendar year 2016, FDA approved 22 novel drugs, 11 original applications for biological products, and 91 medical devices. These approvals included:

- the first treatment for spinal muscular atrophy and Duchenne muscular dystrophy
- new drugs for Parkinson's disease, primary biliary cirrhosis, and hepatitis C
- cancer drugs to treat ovarian cancer, bladder cancer, soft tissue sarcoma, and chronic lymphocytic leukemia
- two new diagnostic agents for detecting certain forms of cancer.

Eighty-six percent of the new drug approvals were approved first in the U.S., which remains faster than other regulators. Seventy-three percent of the new drugs used at least one expedited review pathway, including breakthrough designation.

In addition, 2016 marked the highest number of generic drug approvals and tentative approvals in the history of the FDA's generic drug program – more than 800. Many of these approvals were for first-time generic drugs, with the introduction of a generic counterpart for a brand-name product for which there was previously no generic.

Emergency Response and Medical Countermeasures

Since November 2015, FDA mobilized more than 500 staff members to respond to the Zika virus outbreak, including deployments to Zika-affected Puerto Rico. As part of the U.S. Government response efforts, FDA has worked to:

- protect the nation's blood and tissue supply

- facilitate the development and availability of diagnostics, including 15 diagnostics that are currently authorized for emergency use
- support development of vaccines and therapies
- review proposals for innovative products to suppress mosquito populations.

These efforts are part of the agency's Medical Countermeasures program, which is critical to ensuring that the United States is able to protect against chemical, biological, radiological, nuclear, and emerging infectious disease threats such as pandemic influenza, Ebola virus, and Zika virus.

Food Safety and Nutrition

Efforts to improve food safety through implementation of the Food Safety Modernization Act (FSMA) require partnerships to achieve our public health goals. In FY 2016, FDA awarded nearly \$22 million in funds to states to help implement the produce safety rule through training and compliance activities. Also in the past year, FDA signed two international systems recognition agreements – one with Canada and one with Australia – that recognize that their food safety protection systems levels are similar to FDA's. Work is occurring on more systems recognition agreements. These agreements will allow better risk-based deployment of FDA resources.

In May 2016, FDA finalized the first major update for the Nutrition Facts label in more than 20 years. This new label gives consumers better nutrition information based on the latest nutrition science. The new label lists added sugars in the foods and gives more realistic serving sizes to help consumers make informed choices about what, and how much, they eat.

In June 2016, FDA also issued a draft guidance that provides practical, short- and long-term voluntary sodium reduction targets for the food industry. The draft targets are intended to help consumers to gradually reduce sodium intake with limited effect on flavor and taste. FDA is still reviewing thousands of public comments to this draft guidance.

In May 2017, FDA extended the compliance date for menu labeling by a year. This regulation requires the disclosure of certain nutritional information for standard menu items in chain restaurants and similar retail food establishments. The additional time allows FDA to consider ways to reduce the cost and improve the flexibility of these requirements.

Program Alignment

In May 2017, as part of the broader agency Program Alignment initiative, FDA's Office of Regulatory Affairs (ORA) began implementation of a program-based management structure that aligns staff by FDA-regulated product. This organizational approach replaces a

management structure based on geographic regions. Program alignment benefits all FDA regulated industries and public health, as it allows for better vertical integration within field offices and labs by commodity category, such as food and feed, drugs, and devices. Program alignment also offers better horizontal integration between the field and headquarters programs. Program alignment improves agency efficiency, streamlines operations, and allows better cost accounting and personnel management.

Tobacco Regulation

FDA works to protect Americans from tobacco-related death and disease by regulating the manufacture, distribution, and marketing of tobacco products, and by educating the public about tobacco products and the dangers their use poses. FDA actions in FY 2016 included:

- issuing 17 new or revised guidances, four final rules and one proposed rule
- conducting more than 165,000 retailer inspections
- issuing more than 13,900 warning letters
- taking more than 3,600 civil money penalty actions
- issuing 31 No-Tobacco-Sale-Orders (NTSO) for violations of certain restrictions such as sales to minors
- making the first-ever marketing decision for a Modified Risk Tobacco Product (MRTP) application.

In 2016, FDA launched two new public education campaigns aimed at preventing and reducing tobacco use among youth and young adults.

On May 10, 2016, FDA finalized a rule – Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act – which extends FDA’s authority to all tobacco products, including electronic nicotine delivery systems (such as e-cigarettes and vape pens), cigars, hookah (waterpipe) tobacco, pipe tobacco and nicotine gels, among others. This final rule went into effect on August 8, 2016.

OVERVIEW OF THE BUDGET REQUEST

The FY 2018 Budget Request is \$5.1 billion, an overall increase of ten percent or \$456.1 million compared to the FY 2017 Annualized Continuing Resolution (CR) level. The budget includes \$1.9 billion for budget authority – a decrease of 31 percent or \$854.4 million compared to the FY 2017 Annualized CR level – and \$3.2 billion for user fees – an increase of 68 percent or \$1.3 billion compared to the FY 2017 Annualized CR level. The Budget supports a program level of \$3.2 billion for medical product safety and availability – an increase of 19 percent or \$504.8 million compared to the FY 2017 Annualized CR level – and \$1.3 billion for food safety – a decrease of six percent or \$82.8 million compared to the FY 2017 Annualized CR level.

Budget Structure and Strategic Plan Framework

The Executive Summary provides an overview of the FY 2018 Budget Request in terms of program and policy proposals. The Budget is also described in terms of budget authority and user fees and is broken down into the following major activities.

- **Food Safety** – ensures the food and feed supply is safe, sanitary, wholesome, and honestly labeled, and cosmetic products are safe and properly labeled.
- **Medical Product Safety and Availability** – ensures that safe and effective human and animal drugs, biological products, devices, and radiological products are available to improve the health of the people in the U.S. and that medical countermeasures – including drugs, vaccines, and diagnostic tests – to counter chemical, biological, radiological, nuclear, and emerging infectious disease threats – are safe, effective, and secure.
- **Tobacco Regulation** – protects Americans from tobacco-related death and disease by regulating the manufacture, distribution, and marketing of tobacco products, and by educating the public about tobacco products and the dangers their use poses.
- **Infrastructure: Facilities and Rent Investments** – ensures FDA staff have functioning offices and labs across the country to execute its food safety and medical product safety mission.

The Budget is structured around FDA’s strategic plan framework,¹ which provides strategic direction to help FDA continue to serve and protect the American people. FDA’s Strategic Goals include improving and safeguarding access to – and making better informed decisions about – the products FDA regulates, as well as providing effective oversight of these products. FDA links program-specific actions to support the following priorities within these goals:

- Regulatory Science
- Globalization
- Safety and Quality
- Smart Regulation
- Stewardship.

REGULATORY EFFICIENCIES AND USER FEE RECALIBRATION

FDA is committed to fostering an environment that enables industry to advance innovative, safe, and effective treatments and cures to the patients who need them as quickly as possible. To achieve this goal in FY 2018, FDA will implement programs and process improvements to

¹FDA Strategic Priorities 2014-2018, September 30, 2014, <http://www.fda.gov/aboutfda/reportsmanualsforms/reports/ucm227527.htm>.

achieve greater regulatory efficiency and speed the availability of innovative, safe, and effective medical products in the market. These improvements are described in the PDUFA VI, MDUFA IV, GDUFA II, and BSUFA II commitment letters submitted to Congress in January 2017.

Outcomes of these efforts will include:

- Streamlining clinical trials to reduce time and costs, consistent with the evidentiary standards in statute, by taking actions such as fostering the development and implementation of the science and technology of real-world evidence generation and utilization
- Increasing patient input and promoting patient-centered outcomes to integrate patient voice throughout the regulatory process, thereby better enabling patient perspectives to shape product development, review, and approval
- Increasing engagement with manufacturers, including providing standardized and predictable pathways for early interactions to help reduce uncertainty in medical product development
- Reducing review times by streamlining processes and gaining efficiencies to the greatest extent possible
- Reducing regulatory burden and leveraging FDA's statutory mandates, including recent enhancements through the 21st Century Cures Act
- Promoting greater preparedness for novel and emerging public health threats, including emerging infectious diseases.

In addition, the Budget includes a package of administrative actions that will promote regulatory efficiency and speed the development of safe and effective medical products including:

- Simplifying administrative requirements to reduce drug and device manufacturers' reporting burden
- Clarifying treatment of value-based purchasing arrangements
- Improving predictability for payers and enhance dissemination of evidence by fostering the exchange of scientifically sound information between manufacturers and payers pre-approval to reduce uncertainty and improve payer ability to more accurately set premiums.

In support of these efficiencies, the FY 2018 President's Budget recalibrates FDA medical product user fees to over \$2.5 billion in 2018, an increase of \$1.2 billion over the 2017 annualized CR level. The Budget supports through 100 percent user fee funding medical product review and approval activities associated with the prescription and generic drugs, biosimilar, medical device, and animal drugs programs, including operational and support costs

associated with White Oak campus operations, rent payments to the General Services Administration, other commercial rent and rent-related charges, as well as anticipated FY 2018 inflation for rent costs. Legislative revisions will be needed for all of these programs to ensure continuity of review and approval activities.

21ST CENTURY CURES ACT – FDA INNOVATION ACCOUNT

The 21st Century Cures Act (Cures Act) was enacted into law on December 13, 2016. The Cures Act established an “FDA Innovation Account” for FY 2017 – FY 2025 and authorizes funding, subject to the annual appropriation process, to carry out designated provisions of Title III, which focus on medical product development activities regulated by FDA.² For FY 2018, the Cures Act authorized \$60 million for the FDA Innovation Account. If these funds are appropriated and available, they would help FDA implement provisions to accelerate medical product innovation while reducing regulatory burden, to increase efforts for critical scientific and methodological research, and to increase the involvement of patients and their perspectives in research and the medical product development process, among others. The law also includes provisions aimed at reducing administrative burdens for researchers supported by the federal government, improving the provision of mental health services, and providing direct financial support for states addressing opioid abuse.

EXPORT CERTIFICATION

FDA is proposing an increase of \$4.3 million for the export certification program by increasing the statutory maximum for the certification fee from \$175 to \$600 per certification and including an inflation adjustment factor for the statutory maximum. 21 U.S.C. § 381(e)(4), originally enacted in 1996, currently limits the maximum export certification fee to \$175 per certification. Because of this cap and increases in the costs of maintaining the export certification program since the program’s inception, the certification program expenditures significantly exceed the current revenue of the program. Increasing the maximum fee to an inflation-adjusted \$600 per certification will allow the Agency to better recover its costs in implementing this program.

BUDGET AUTHORITY REDUCTIONS

The FY 2018 Budget Request includes reductions totaling \$127.2 million in budget authority, targeted to certain areas where better tools and policies will allow FDA to do more with less,

² In other Cures Act titles not focused on FDA, the Agency is required to provide consultation and serve on working groups, headed by other HHS agencies. These include, among others, consultation with the National Institutes of Health (NIH) on research on pregnant and lactating women, tick-borne diseases, animal care and research, and certain activities related to the NIH ClinicalTrials.gov data bank.

while preserving core mission activities. These reductions will be coupled with policy efforts to improve the efficiency of the programs that see reductions, to improve effectiveness and take a risk-based approach to FDA's consumer protection mission.

Food Safety

In FY 2018, FDA will preserve its most critical public health and safety activities, including outbreak response, implementation of FSMA regulations, and ensuring that foods are safe and properly labeled.

To reduce expenditures, FDA will reduce staff across the food safety program through attrition. Not backfilling critical vacancies may lead to a loss of some specialized expertise. FDA will also make targeted reductions to lower public health impact areas. This will include reduced funding for imported food safety through decreased international capacity building. FDA will reduce funding for cosmetics safety work, which will limit FDA's ability to monitor and take action against unsafe cosmetics. FDA will decrease funding for its research program, which supports work related to food safety technology, outbreak response, and FSMA implementation. FDA plans to reduce funding to programs that support state and local health organizations.

Medical Product Safety

In FY 2018, FDA will continue to uphold its public health mission to ensure the safety and efficacy of human and animal drugs, biological products, devices, and radiological products.

As a result of budget authority reductions, FDA will reduce staff across medical product safety programs through attrition. FDA will reduce support to scientific research activities, including contracts that promote drug safety and research studies, critical investments in innovation and research, and essential training and development opportunities for personnel.

At proposed budget levels FDA will support at lower funding levels regulated product field exams, import entry review, investigations, sample analysis, and inspections for surveillance, compliance, and follow up activities, both domestically and abroad. Risk assessments will be impacted along with sharing information with regulatory partners. FDA will reduce investment in lab equipment, maintenance, and operating expenses will limit capacity to analyze samples for surveillance and compliance purposes as well as detecting emerging threats or potential outbreaks from product contamination or adulteration.

WORKING CAPITAL FUND AUTHORITY

As part of the FY 2018 President's Budget, FDA is also requesting authority to establish a Working Capital Fund (WCF). A WCF will allow the FDA to operate in a more efficient business environment by relying on the collection of funds for administrative services directly from its customers. More specifically, the fund will help FDA achieve the following:

- create a customer-focused and service-oriented mechanism through improving customer investment and management accountability
- recapitalize resources to support IT infrastructure and other administrative service capital needs
- enhance transparency, accountability, and efficiency.

The Working Capital Fund will provide the environment for centralized offices to operate in a more efficient business environment by collecting funds from internal customers to finance operations and allow for infrastructure investments across fiscal years – particularly as it relates to capital investments in the IT area. Upon receiving authority to establish a Working Capital Fund, FDA will work toward implementation that aligns services and costs, based on consumption, to its program lines.

INFRASTRUCTURE: FACILITIES AND RENT INVESTMENTS

The FY 2018 Budget Request provides an increase of \$36.4 million over the FY 2017 Annualized CR level, which supports increased FTE levels associated with medical product user fees and facility costs related to real estate taxes, rental rates, maintenance, and utilities.

Proposed Appropriations Language Changes to Rent Cost Language

The FY 2018 President’s Budget proposes striking the “not to exceed” (NTE) language from FDA’s appropriation language for rent costs. A large majority of FDA’s owned buildings, including laboratories, were transferred to FDA from other federal agencies and these buildings as well as the associated site infrastructure were constructed between 30 to 60 years ago. Many of the buildings, including critical research and regulatory laboratories, are aged and the building systems, finishes, and layouts are past their useful life, creating unsafe and unhealthy work environments, which in turn compromises FDA’s ability to meet scientific needs. Historically funding for necessary major improvements for site infrastructure and building systems and equipment has been very limited and below the amount needed to even sustain the current poor condition. Accordingly, operations and maintenance costs are continuing to increase as more equipment and systems fail and more maintenance is needed to keep buildings operational. Major equipment failures could occur and the current “not to exceed” restriction severely limits FDA’s ability to address these needs as well as other increased maintenance costs to ensure FDA’s mission critical facilities remain operational. Without this flexibility, equipment and system failures will likely result in closing these critical buildings, which will have an immediate and significant impact on the FDA mission and the public health.

OVERVIEW OF PERFORMANCE

The *FDA Strategic Priorities 2014-2018* focus efforts to achieve FDA's public-health mission and to fulfill its role in supporting HHS' larger mission and strategic goals. The FY 2018 Budget is structured around these priorities and goals, as discussed in the Overview of the Budget Request.

Transparency and Accountability

In April 2011, FDA launched FDA-TRACK, which is the Agency-wide performance management system. FDA-TRACK monitors, analyzes, and reports monthly performance on all FDA program offices and on key cross-cutting initiatives. Each quarter, the FDA-TRACK team uses statistical models to analyze monthly performance data collected from each office and initiative. Face-to-face briefings are then conducted with the office directors responsible for each program who present their performance data and results to FDA executive leadership.

These briefings stimulate discussion and facilitate better communication, decision-making, plan of action and ultimately, performance. Briefing summaries and performance results are then posted to the FDA-TRACK website, allowing FDA's stakeholders to monitor progress on more than 600 performance measures and 100 key projects.

The objectives of FDA-TRACK can be explained through its name:

- **Transparency** – provides interested parties an unprecedented look into how FDA performs its work
- **Results** – highlights performance measures and results related to the agency’s public-health mission
- **Accountability** – requires senior managers to develop, track, and report performance measures to improve the agency’s accountability to the public and holds the program offices accountable for their priorities, plans and results
- **Credibility** – encourages sharing of FDA performance information which is essential for the agency’s credibility and provides the opportunity to submit suggestions for continuous improvement efforts
- **Knowledge-sharing** – enables the identification of common issues and interdependencies among program offices to improve FDA’s operational effectiveness, through better collaboration, and the sharing of ideas.

The performance measures in FDA-TRACK represent the foundational activities and outputs produced by FDA employees. Since the inception of FDA-TRACK, FDA has seen significant performance improvement in programs, including:

- the elimination of the backlog of generic new animal drug applications and
- increases in hospital participation in the MedSun Program.

On the operational side, FDA has dramatically improved its advisory committee vacancy rate and progressed to dramatically reduce its Freedom of Information Act backlog.

FDA-TRACK has enabled better performance by providing a medium to track progress, monitor results, discuss concerns, and communicate achievement. Over 53,000 visitors subscribe to the FDA-TRACK monthly updates.

ALL PURPOSE TABLE

(Dollars in Thousands)	FY 2016 Final		FY 2016 Actuals		FY 2017 Annualized CR		FY 2018			
							President's Budget		President's Budget +/- FY 2017 CR	
	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000
Foods.....	3,841	1,009,849	3,841	998,230	3,888	992,972	3,686	922,014	-202	-70,958
Budget Authority.....	3,841	998,263	3,841	998,230	3,888	981,386	3,637	910,428	-251	-70,958
User Fees.....	---	11,586	---	---	---	11,586	49	11,586	49	---
Center.....	1,001	300,619	1,001	300,059	1,048	300,041	1,001	278,193	-47	-21,848
Budget Authority.....	1,001	300,069	1,001	300,059	1,048	299,491	999	277,643	-49	-21,848
User Fees.....	---	550	---	---	---	550	2	550	2	---
Food and Feed Recall.....	---	243	---	---	---	243	1	243	1	---
Voluntary Qualified Importer Program.....	---	243	---	---	---	243	1	243	1	---
Third Party Auditor Program.....	---	64	---	---	---	64	---	64	---	---
Field.....	2,840	709,230	2,840	698,171	2,840	692,931	2,685	643,821	-155	-49,110
Budget Authority.....	2,840	698,194	2,840	698,171	2,840	681,895	2,638	632,785	-202	-49,110
User Fees.....	---	11,036	---	---	---	11,036	47	11,036	47	---
Food and Feed Recall.....	---	1,000	---	---	---	1,000	4	1,000	4	---
Food Reinspection.....	---	4,575	---	---	---	4,575	19	4,575	19	---
Voluntary Qualified Importer Program.....	---	4,320	---	---	---	4,320	18	4,320	18	---
Third Party Auditor Program.....	---	1,141	---	---	---	1,141	6	1,141	6	---
Human Drugs.....	5,681	1,390,656	5,681	1,451,570	5,935	1,324,422	6,472	1,611,504	537	287,082
Budget Authority.....	2,065	487,332	2,065	487,299	2,121	486,398	914	179,139	-1,207	-307,259
User Fees.....	3,616	903,324	3,616	964,271	3,814	838,024	5,558	1,432,365	1,744	594,341
Center.....	4,648	1,185,398	4,648	1,267,547	4,823	1,119,903	5,397	1,414,764	574	294,861
Budget Authority.....	1,257	351,163	1,257	351,135	1,304	350,488	328	94,353	-976	-256,135
User Fees.....	3,391	834,235	3,391	916,412	3,519	769,415	5,069	1,320,411	1,550	550,996
Prescription Drug (PDUFA).....	2,436	601,643	2,436	617,004	2,522	533,134	3,113	795,071	591	261,937
Generic Drug (GDUFA).....	877	215,867	877	286,312	906	219,018	1,645	451,771	739	232,753
Biosimilars (BsUFA).....	71	16,298	71	12,007	89	16,706	309	72,976	220	56,270
Outsourcing Facility.....	7	427	7	1,089	2	557	2	593	---	36
Field.....	1,033	205,258	1,033	184,023	1,112	204,519	1,075	196,740	-37	-7,779
Budget Authority.....	808	136,169	808	136,164	817	135,910	586	84,786	-231	-51,124
User Fees.....	225	69,089	225	47,859	295	68,609	489	111,954	194	43,345
Prescription Drug (PDUFA).....	38	12,276	38	8,662	51	10,878	162	37,391	111	26,513
Generic Drug (GDUFA).....	187	55,167	187	38,403	236	55,973	314	71,717	78	15,744
Biosimilars (BsUFA).....	---	1,382	---	400	7	1,416	12	2,485	5	1,069
Outsourcing Facility.....	---	264	---	394	1	342	1	361	---	19
Biologics.....	1,341	354,775	1,341	329,156	1,379	339,082	1,409	366,230	30	27,148
Budget Authority.....	806	215,317	806	215,308	821	214,907	406	95,893	-415	-119,014
User Fees.....	534	139,458	534	113,848	558	124,175	1,003	270,337	445	146,162
Center.....	1,102	311,094	1,102	286,622	1,133	295,735	1,174	325,101	41	29,366
Budget Authority.....	572	173,937	572	173,929	582	173,606	197	61,398	-385	-112,208
User Fees.....	530	137,157	530	112,693	551	122,129	977	263,703	426	141,574
Prescription Drug (PDUFA).....	487	123,801	487	102,934	487	109,704	837	226,459	350	116,755
Medical Device (MDUFA).....	43	11,475	43	9,731	55	10,508	128	34,010	73	23,502
Generic Drug (GDUFA).....	---	1,072	---	26	5	1,088	7	1,502	2	414
Biosimilars (BsUFA).....	---	809	---	2	4	829	5	1,732	1	903
Field.....	238	43,681	238	42,534	246	43,347	235	41,129	-11	-2,218
Budget Authority.....	235	41,380	235	41,379	239	41,301	209	34,495	-30	-6,806
User Fees.....	4	2,301	4	1,155	7	2,046	26	6,634	19	4,588
Prescription Drug (PDUFA).....	4	2,084	4	1,152	6	1,847	20	5,311	14	3,464
Medical Device (MDUFA).....	---	217	---	3	1	199	6	1,323	5	1,124

(Dollars in Thousands)	FY 2016 Final		FY 2016 Actuals		FY 2017 Annualized CR		FY 2018			
							President's Budget		President's Budget +/- FY 2017 CR	
	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000
Animal Drugs and Feed.....	925	188,615	925	188,042	948	190,540	920	183,280	-28	-7,260
Budget Authority.....	807	158,635	807	158,629	817	158,333	612	107,606	-205	-50,727
User Fees.....	118	29,980	118	29,413	131	32,207	308	75,674	177	43,467
Center.....	595	122,508	595	122,848	608	124,497	596	121,749	-12	-2,748
Budget Authority.....	476	94,005	476	94,001	480	93,826	301	49,117	-179	-44,709
User Fees.....	118	28,503	118	28,847	128	30,671	295	72,632	167	41,961
Animal Drug (ADUFA).....	81	20,125	81	20,459	87	20,879	236	57,775	149	36,896
Animal Generic Drug (AGDUFA).....	37	8,378	37	8,388	41	9,792	59	14,857	18	5,065
Field.....	331	66,107	331	65,194	340	66,043	324	61,531	-16	-4,512
Budget Authority.....	331	64,630	331	64,628	337	64,507	311	58,489	-26	-6,018
User Fees.....	---	1,477	---	566	3	1,536	13	3,042	10	1,506
Animal Drug (ADUFA).....	---	411	---	378	2	427	8	1,665	6	1,238
Animal Generic Drug (AGDUFA).....	---	259	---	188	1	302	2	570	1	268
Food Reinspection.....	---	807	---	---	---	807	3	807	3	---
Devices and Radiological Health.....	2,243	450,221	2,243	447,605	2,289	440,988	2,352	489,696	63	48,708
Budget Authority.....	1,647	323,170	1,647	323,157	1,674	322,555	917	140,069	-757	-182,486
User Fees.....	596	127,051	596	124,448	615	118,433	1,435	349,627	820	231,194
Center.....	1,718	351,990	1,718	354,457	1,743	342,819	1,827	396,261	84	53,442
Budget Authority.....	1,129	240,750	1,129	240,740	1,148	240,292	462	73,842	-686	-166,450
User Fees.....	588	111,240	588	113,717	595	102,527	1,365	322,419	770	219,892
Prescription Drug (PDUFA).....	---	---	---	---	---	---	5	1,292	5	1,292
Medical Device (MDUFA).....	556	104,991	556	108,007	563	96,150	1,328	314,750	765	218,600
Mammography Quality Standards Act (MQSA).....	32	6,249	32	5,710	32	6,377	32	6,377	---	---
Field.....	525	98,231	525	93,148	546	98,169	525	93,435	-21	-4,734
Budget Authority.....	517	82,420	517	82,417	526	82,263	455	66,227	-71	-16,036
User Fees.....	8	15,811	8	10,731	20	15,906	70	27,208	50	11,302
Medical Device (MDUFA).....	---	2,199	---	409	12	2,014	62	13,316	50	11,302
Mammography Quality Standards Act (MQSA).....	8	13,612	8	10,322	8	13,892	8	13,892	---	---
National Center for Toxicological Research (BA Only).....	299	63,331	299	63,329	304	63,211	304	60,211	---	-3,000
Family Smoking Prevention and Tobacco Control Act.....	780	564,117	780	476,525	910	563,045	930	625,646	20	62,601
Center (UF Only).....	745	547,454	745	466,776	860	546,413	880	611,096	20	64,683
Field (UF Only).....	35	16,663	35	9,749	50	16,631	50	14,550	---	-2,081
FDA Headquarters.....	1,209	299,524	1,209	301,574	1,273	293,259	1,332	322,486	59	29,227
Budget Authority.....	814	191,549	814	191,374	828	191,201	558	125,432	-270	-65,769
User Fees.....	395	107,975	395	110,200	445	102,058	774	197,054	329	94,996
Prescription Drug (PDUFA).....	208	52,139	208	54,405	213	46,202	358	82,622	145	36,420
Medical Device (MDUFA).....	31	6,259	31	8,293	37	5,732	134	29,260	97	23,528
Generic Drug (GDUFA).....	86	24,690	86	26,680	110	25,050	159	47,270	49	22,220
Biosimilars (BsUFA).....	---	1,354	---	190	7	1,388	20	4,602	13	3,214
Animal Drug (ADUFA).....	2	913	2	813	4	947	22	5,475	18	4,528
Animal Generic Drug (AGDUFA).....	1	388	1	209	1	453	5	1,452	4	999
Family Smoking Prevention and Tobacco Control Act.....	64	20,789	64	19,119	70	20,749	70	24,815	---	4,066
Mammography Quality Standards Act (MQSA).....	2	248	2	491	2	253	2	253	---	---
Food and Feed Recall.....	---	75	---	---	---	75	---	75	---	---
Food Reinspection.....	---	480	---	---	---	480	2	480	2	---
Voluntary Qualified Importer Program.....	---	277	---	---	---	277	1	277	1	---
Third Party Auditor Program.....	---	73	---	---	---	73	---	73	---	---
Outsourcing Facility.....	---	290	---	---	1	379	1	400	---	21
FDA White Oak Consolidation	---	52,346	---	48,944	---	51,765	---	56,882	---	5,117
Budget Authority.....	---	48,044	---	48,044	---	47,953	---	12,561	---	-35,392
User Fees.....	---	4,302	---	900	---	3,812	---	44,321	---	40,509
Prescription Drug (PDUFA).....	---	4,302	---	900	---	3,812	---	25,548	---	21,736
Medical Device (MDUFA).....	---	---	---	---	---	---	---	8,072	---	8,072
Generic Drug (GDUFA).....	---	---	---	---	---	---	---	5,571	---	5,571
Biosimilars (BsUFA).....	---	---	---	---	---	---	---	662	---	662
Animal Drug (ADUFA).....	---	---	---	---	---	---	---	80	---	80
Animal Generic Drug (AGDUFA).....	---	---	---	---	---	---	---	17	---	17
Family Smoking Prevention and Tobacco Control Act.....	---	---	---	---	---	---	---	4,371	---	4,371

(Dollars in Thousands)	FY 2016 Final		FY 2016 Actuals		FY 2017 Annualized CR		FY 2018			
							President's Budget		President's Budget +/- FY 2017 CR	
	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000
Other Rent and Rent Related	---	119,560	---	119,059	---	115,794	---	132,894	---	17,100
<i>Budget Authority.....</i>	---	<i>73,484</i>	---	<i>73,484</i>	---	<i>73,344</i>	---	<i>59,889</i>	---	<i>-13,455</i>
<i>User Fees.....</i>	---	<i>46,076</i>	---	<i>45,575</i>	---	<i>42,449</i>	---	<i>73,005</i>	---	<i>30,556</i>
<i>Prescription Drug (PDUFA).....</i>	---	<i>29,724</i>	---	<i>26,302</i>	---	<i>26,340</i>	---	<i>34,848</i>	---	<i>8,508</i>
<i>Medical Device (MDUFA).....</i>	---	<i>4,558</i>	---	<i>5,158</i>	---	<i>4,174</i>	---	<i>12,679</i>	---	<i>8,505</i>
<i>Generic Drug (GDUFA).....</i>	---	<i>6,862</i>	---	<i>6,862</i>	---	<i>6,962</i>	---	<i>17,702</i>	---	<i>10,740</i>
<i>Biosimilars (BsUFA).....</i>	---	<i>617</i>	---	<i>617</i>	---	<i>633</i>	---	<i>1,203</i>	---	<i>570</i>
<i>Animal Drug (ADUFA).....</i>	---	<i>228</i>	---	<i>228</i>	---	<i>236</i>	---	<i>2,101</i>	---	<i>1,865</i>
<i>Animal Generic Drug (AGDUFA).....</i>	---	<i>97</i>	---	<i>97</i>	---	<i>113</i>	---	<i>252</i>	---	<i>139</i>
<i>Family Smoking Prevention and Tobacco Control Act</i>	---	<i>3,502</i>	---	<i>6,311</i>	---	<i>3,495</i>	---	<i>3,724</i>	---	<i>229</i>
<i>Food and Feed Recall.....</i>	---	<i>43</i>	---	---	---	<i>43</i>	---	<i>43</i>	---	---
<i>Food Reinspection.....</i>	---	<i>204</i>	---	---	---	<i>204</i>	---	<i>204</i>	---	---
<i>Voluntary Qualified Importer Program.....</i>	---	<i>170</i>	---	---	---	<i>170</i>	---	<i>170</i>	---	---
<i>Third Party Auditor Program.....</i>	---	<i>45</i>	---	---	---	<i>45</i>	---	<i>45</i>	---	---
<i>Outsourcing Facility.....</i>	---	<i>26</i>	---	---	---	<i>34</i>	---	<i>34</i>	---	---
GSA Rental Payments	---	224,105	---	220,122	---	235,570	---	249,783	---	14,213
<i>Budget Authority.....</i>	---	<i>161,683</i>	---	<i>161,683</i>	---	<i>176,347</i>	---	<i>128,490</i>	---	<i>-47,857</i>
<i>User Fees.....</i>	---	<i>62,422</i>	---	<i>58,439</i>	---	<i>59,223</i>	---	<i>121,293</i>	---	<i>62,070</i>
<i>Prescription Drug (PDUFA).....</i>	---	<i>25,512</i>	---	<i>25,512</i>	---	<i>22,607</i>	---	<i>53,640</i>	---	<i>31,033</i>
<i>Medical Device (MDUFA).....</i>	---	<i>7,978</i>	---	<i>7,978</i>	---	<i>7,306</i>	---	<i>25,591</i>	---	<i>18,285</i>
<i>Generic Drug (GDUFA).....</i>	---	<i>14,705</i>	---	<i>14,705</i>	---	<i>14,920</i>	---	<i>20,213</i>	---	<i>5,293</i>
<i>Biosimilars (BsUFA).....</i>	---	<i>1,080</i>	---	---	---	<i>1,107</i>	---	<i>3,076</i>	---	<i>1,969</i>
<i>Animal Drug (ADUFA).....</i>	---	<i>1,141</i>	---	<i>1,141</i>	---	<i>1,184</i>	---	<i>3,156</i>	---	<i>1,972</i>
<i>Animal Generic Drug (AGDUFA).....</i>	---	<i>583</i>	---	<i>583</i>	---	<i>681</i>	---	<i>1,327</i>	---	<i>646</i>
<i>Family Smoking Prevention and Tobacco Control Act</i>	---	<i>10,592</i>	---	<i>8,520</i>	---	<i>10,572</i>	---	<i>13,444</i>	---	<i>2,872</i>
<i>Food and Feed Recall.....</i>	---	<i>73</i>	---	---	---	<i>73</i>	---	<i>73</i>	---	---
<i>Food Reinspection.....</i>	---	<i>348</i>	---	---	---	<i>348</i>	---	<i>348</i>	---	---
<i>Voluntary Qualified Importer Program.....</i>	---	<i>290</i>	---	---	---	<i>290</i>	---	<i>290</i>	---	---
<i>Third Party Auditor Program.....</i>	---	<i>77</i>	---	---	---	<i>77</i>	---	<i>77</i>	---	---
<i>Outsourcing Facility.....</i>	---	<i>43</i>	---	---	---	<i>58</i>	---	<i>58</i>	---	---
Color Certification.....	36	8,518	36	8,915	36	9,682	37	10,062	1	380
Export Certification.....	26	4,696	26	5,053	26	4,696	26	4,696	---	---
Export Certification (Proposed).....	---	---	---	---	---	---	---	4,280	---	4,280
Priority Review Vouchers (PRV) Tropical Disease.....	---	---	---	---	---	---	---	---	---	---
Priority Review Vouchers (PRV) Pediatric Disease	---	7,686	---	---	---	7,686	---	7,686	---	---
Food and Drug Safety -- No Year (P.L. 113-6).....	---	---	---	2,073	---	---	---	---	---	---
Food Safety.....	---	---	---	---	---	---	---	---	---	---
Drug Safety.....	---	---	---	2,073	---	---	---	---	---	---
21st Century Cures (BA Only).....	---	---	---	---	---	20,000	---	60,000	---	40,000
MCMi.....	---	---	---	---	---	---	---	---	---	---
Subtotal, Salaries and Expenses.....	16,381	4,737,999	16,381	4,660,197	16,988	4,652,712	17,468	5,107,350	480	454,638

(Dollars in Thousands)	FY 2016 Final		FY 2016 Actuals		FY 2017 Annualized CR		FY 2018			
							President's Budget		President's Budget +/- FY 2017 CR	
	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000
Buildings and Facilities (Budget Authority).....	---	8,788	---	7,539	---	8,771	---	8,771	---	-
Total Program Level	16,381	4,746,787	16,381	4,667,736	16,988	4,661,484	17,468	5,116,121	480	454,637
Non-Field Activities.....	11,378	3,202,818	11,378	3,177,180	11,854	3,127,943	12,574	3,616,585	720	488,642
Field Activities.....	5,003	1,139,170	5,003	1,092,819	5,134	1,121,641	4,894	1,051,206	-240	-70,435
White Oak, Rent Activities, and B&F.....	---	404,799	---	395,664	---	411,900	---	448,330	---	36,430
User Fees:										
Current Law										
Prescription Drug (PDUFA).....	3,172	851,481	3,172	836,871	3,279	754,524	4,495	1,262,182	1,216	507,658
Medical Device (MDUFA).....	631	137,677	631	139,579	668	126,083	1,658	439,001	990	312,918
Generic Drug (GDUFA).....	1,151	318,363	1,151	372,988	1,257	323,011	2,125	615,746	868	292,735
Biosimilars (BsUFA).....	71	21,540	71	13,216	107	22,079	346	86,736	239	64,657
Animal Drug (ADUFA).....	83	22,818	83	23,019	93	23,673	266	70,252	173	46,579
Animal Generic Drug (AGDUFA).....	38	9,705	38	9,465	43	11,341	66	18,475	23	7,134
Family Smoking Prevention and Tobacco Control Act.....	844	599,000	844	510,475	980	597,861	1,000	672,000	20	74,139
Subtotal, Current Law.....	5,990	1,960,584	5,990	1,905,613	6,427	1,858,572	9,956	3,164,392	3,529	1,305,820
Indefinite										
Mammography Quality Standards Act (MQSA).....	43	20,109	43	16,523	42	20,522	42	20,522	---	---
Color Certification.....	36	8,518	36	8,915	36	9,682	37	10,062	1	380
Export Certification.....	26	4,696	26	5,053	26	4,696	26	4,696	---	---
Export Certification (Proposed).....	---	---	---	---	---	---	---	4,280	---	4,280
Priority Review Vouchers (PRV) Tropical Disease.....	---	---	---	---	---	---	---	---	---	---
Priority Review Vouchers (PRV) Pediatric Disease.....	---	7,686	---	---	---	7,686	---	7,686	---	---
Food and Feed Recall.....	---	1,434	---	---	---	1,434	5	1,434	5	---
Food Reinspection.....	---	6,414	---	---	---	6,414	24	6,414	24	---
Voluntary Qualified Importer Program.....	---	5,300	---	---	---	5,300	20	5,300	20	---
Third Party Auditor Program.....	---	1,400	---	---	---	1,400	6	1,400	6	---
Outsourcing Facility.....	7	1,050	7	1,483	4	1,370	4	1,446	---	76
Subtotal, Indefinite.....	112	56,607	112	31,974	108	58,504	164	63,240	56	4,736
Total User Fees.....	6,102	2,017,191	6,102	1,937,587	6,535	1,917,077	10,120	3,227,632	3,585	1,310,555
Total Budget Authority, Pre-Transfer.....	10,279	2,729,596	10,279	2,730,149	10,453	2,744,407	7,348	1,888,489	-3,105	-855,918
BA, S&E.....	10,279	2,720,808	10,279	2,722,610	10,453	2,735,636	7,348	1,879,718	-3,105	-855,918
BA, B&F.....	---	8,788	---	7,539	---	8,771	---	8,771	---	-
Total Program Level, Pre-Transfer.....	16,381	4,746,787	16,381	4,667,736	16,988	4,661,484	17,468	5,116,121	480	454,637
HHS OIG transfer (BA Only).....	---	-1,500	---	-1,500	---	-1,497	---	---	---	1,497
Total Budget Authority, Post-Transfer.....	10,279	2,728,096	10,279	2,728,649	10,453	2,742,910	7,348	1,888,489	-3,105	-854,421
Total User Fees.....	6,102	2,017,191	6,102	1,937,587	6,535	1,917,077	10,120	3,227,632	3,585	1,310,555
Total Program Level, Post-Transfer.....	16,381	4,745,287	16,381	4,666,236	16,988	4,659,986	17,468	5,116,121	480	456,135

*For FY 2016 and FY 2017, the Pre-Transfer levels do not reflect the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2018, FDA proposes to discontinue the transfer.

** FTE figures do not include an estimated 81 reimbursable, 2 CRADA, 2 FOIA, 44 PEPFAR, and 17 EBOLA.

***The Drug Quality and Security Act (P.L. 113-54) authorized FDA to collect fees for the licensure and inspection of certain third-party logistics providers and wholesale drug distributors. 21 U.S.C. §§ 360eee-3(c); 353(e)(3). The program is still under development and a fee estimate is not available at this time.

****The FY 2017 estimates for PDUFA and MDUFA reflect the August 2016 Federal Register Notices, including fifth-year adjustments to PDUFA and MDUFA collections.

*****Color Certification does not reflect the availability of mandatory funds sequestered in the prior fiscal year.

*****FY 2016 Final and Actuals reflected transfer of \$15 million from the GSA Rent activity to the Foods program. These funds will be used by the Office of Regulatory Affairs to support the relocation of its leased San Francisco District Office and Laboratory located in Alameda, CA

*****FY 2016 FTE actuals may include fluctuations between pay and non-pay activities for budget authority and user fees associated with medical product review and approval processes when compared to prior fiscal years.

*****The FY 2016, FY 2017, and FY 2018 columns have been updated to reflect reallocated funding across the programs addressing previous reorganizations that consolidated economists in Headquarters and established the Oncology Center of Excellence, as well as to better align the funding structure to services related to intergovernmental affairs.

*****Does not reflect priority review voucher user fee for Medical Countermeasures as FDA continues to develop an estimated fee level.

*****The prescription and generic drug, biosimilar, and medical device user fee programs expire on October 1, 2017. The Budget includes legislative proposals to reauthorize these four user fee programs. The Budget also includes legislative proposals to increase fees for the animal drug and animal generic drug user fee programs in their fifth and final year of authorization.

MAJOR ACTIVITIES TABLE

(Dollars in Thousands)	FY 2016 Final						FY 2017 Annualized CR						FY 2018 President's Budget						FY 2018 President's Budget +/- FY 2017 CR					
	Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total	
	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000
Programs																								
Budget Authority:																								
Foods	3,841	998,263	---	---	3,841	998,263	3,888	981,386	---	---	3,888	981,386	3,637	910,428	---	---	3,637	910,428	-251	-70,958	---	---	-251	-70,958
Center	1,001	300,069	---	---	1,001	300,069	1,048	299,491	---	---	1,048	299,491	999	277,643	---	---	999	277,643	-49	-21,848	---	---	-49	-21,848
Field	2,840	698,194	---	---	2,840	698,194	2,840	681,895	---	---	2,840	681,895	2,638	632,785	---	---	2,638	632,785	-202	-49,110	---	---	-202	-49,110
Human Drugs	---	---	2,065	487,332	2,065	487,332	---	---	2,121	486,398	2,121	486,398	---	---	914	179,139	914	179,139	---	---	-1,207	-307,259	-1,207	-307,259
Center	---	---	1,257	351,163	1,257	351,163	---	---	1,304	350,488	1,304	350,488	---	---	328	94,353	328	94,353	---	---	-976	-256,135	-976	-256,135
Field	---	---	808	136,169	808	136,169	---	---	817	135,910	817	135,910	---	---	586	84,786	586	84,786	---	---	-231	-51,124	-231	-51,124
Biologics	---	---	805	215,317	805	215,317	---	---	821	214,907	821	214,907	---	---	406	95,893	406	95,893	---	---	-415	-119,014	-415	-119,014
Center	---	---	571	173,937	571	173,937	---	---	582	173,606	582	173,606	---	---	197	61,398	197	61,398	---	---	-385	-112,208	-385	-112,208
Field	---	---	235	41,380	235	41,380	---	---	239	41,301	239	41,301	---	---	209	34,495	209	34,495	---	---	-30	-6,806	-30	-6,806
Animal Drugs and Feeds	646	125,305	161	33,330	807.2	158,635	655	125,067	162	33,267	817	158,333	524	92,679	88	14,927	612	107,606	-131	-32,388	-74	-18,340	-205	-50,727
Center	331	63,549	145	30,456	476.2	94,005	334	63,428	146	30,398	480	93,826	222	35,581	79	13,536	301	49,117	-112	-27,847	-67	-16,862	-179	-44,709
Field	315	61,756	16	2,874	331.0	64,630	321	61,639	16	2,869	337	64,507	302	57,098	9	1,391	311	58,489	-19	-4,541	-7	-1,478	-26	-6,018
Devices and Radiological Health	---	---	1,647	323,170	1,647	323,170	---	---	1,674	322,555	1,674	322,555	---	---	917	140,069	917	140,069	---	---	-757	-182,486	-757	-182,486
Center	---	---	1,129	240,750	1,129	240,750	---	---	1,148	240,292	1,148	240,292	---	---	462	73,842	462	73,842	---	---	-686	-166,450	-686	-166,450
Field	---	---	517	82,420	517	82,420	---	---	526	82,263	526	82,263	---	---	455	66,227	455	66,227	---	---	-71	-16,036	-71	-16,036
National Center for Toxicological Research	49	10,233	250	53,098	299	63,331	50	10,214	254	52,997	304	63,211	50	7,214	254	52,997	304	60,211	---	-3,000	---	---	---	-3,000
FDA Headquarters	361	81,277	453	93,772	814	191,549	368	81,952	460	92,780	828	191,201	352	79,751	206	35,710	558	125,432	-16	-2,201	-254	-57,070	-270	-65,769
FDA White Oak Consolidation	---	---	---	---	---	48,044	---	---	---	---	---	47,953	---	---	---	---	12,561	---	---	---	---	---	---	-35,392
Other Rent and Rent Related	---	37,078	---	36,406	---	73,484	---	37,008	---	36,337	---	73,344	---	37,008	---	22,881	---	59,889	---	---	---	-13,456	---	-13,455
GSA Rental Payments	---	67,500	---	94,183	---	161,683	---	82,343	---	94,004	---	176,347	---	82,343	---	46,147	---	128,490	---	---	---	-47,857	---	-47,857
SUBTOTAL, BA Salaries and Expenses	4,897	1,319,656	5,382	1,336,608	10,279	2,720,808	4,961	1,317,969	5,492	1,333,245	10,453	2,715,635	4,563	1,209,423	2,785	587,763	7,348	1,819,718	-398	-108,546	-2,707	-745,482	-3,105	-895,918
21st Century Cures	---	---	---	---	---	---	---	---	---	20,000	---	20,000	---	---	---	60,000	---	60,000	---	---	---	---	---	40,000
MCMi	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Building and Facilities	---	---	---	---	---	8,788	---	---	---	---	---	8,771	---	---	---	---	8,771	---	---	---	---	---	---	---
Total BA, Pre-Transfer	4,897	1,319,656	5,382	1,336,608	10,279	2,729,596	4,961	1,317,969	5,492	1,353,245	10,453	2,744,407	4,563	1,209,423	2,785	647,763	7,348	1,888,489	-398	-108,546	-2,707	-705,482	-3,105	-855,918

(Dollars in Thousands)	FY 2016 Final						FY 2017 Annualized CR						FY 2018 President's Budget						FY 2018 President's Budget +/- FY 2017 CR					
	Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total		Food Safety		Medical Product Safety and Availability		Total	
	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000
Programs																								
Total User Fees	---	16,551	5,221	1,393,122	6,102	2,017,191	---	16,551	5,519	1,292,982	6,535	1,917,077	160	42,297	8,923	2,503,273	10,120	3,227,632	160	25,746	3,404	1,210,291	3,584	1,310,555
Current Law																								
Prescription Drug (PDUFA)	---	---	3,172	851,481	3,172	851,481	---	---	3,279	754,524	3,279	754,524	---	---	4,495	1,262,182	4,495	1,262,182	---	---	1,216	507,658	1,216	507,658
Medical Device (MDUFA)	---	---	631	137,677	631	137,677	---	---	668	126,083	668	126,083	---	---	1,658	439,001	1,658	439,001	---	---	990	312,918	990	312,918
Generic Drug (GDUFA)	---	---	1,151	318,363	1,151	318,363	---	---	1,257	323,011	1,257	323,011	---	---	2,125	615,746	2,125	615,746	---	---	868	292,735	868	292,735
Biosimilars (BsUFA)	---	---	71	21,540	71	21,540	---	---	107	22,079	107	22,079	---	---	346	86,736	346	86,736	---	---	239	64,657	239	64,657
Animal Drug (ADUFA)	---	---	83	22,818	83	22,818	---	---	93	23,673	93	23,673	93	22,914	173	47,338	266	70,252	93	22,914	80	23,665	173	46,579
Animal Generic Drug (AGDUFA)	---	---	38	9,705	38	9,705	---	---	43	11,341	43	11,341	12	2,832	54	15,643	66	18,475	12	2,832	11	4,302	23	7,134
Family Smoking Prevention and Tobacco Control Act	---	---	---	---	844	599,000	---	---	---	---	980	597,861	---	---	---	---	1,000	672,000	---	---	---	---	20	74,139
Mammography Quality Standards Act (MQSA)	---	---	43	20,109	43	20,109	---	---	42	20,522	42	20,522	---	---	42	20,522	42	20,522	---	---	---	---	---	---
Color Certification	---	---	---	---	36	8,518	---	---	---	---	36	9,682	---	---	---	---	37	10,062	---	---	---	---	---	380
Export Certification	---	2,003	26	2,693	26	4,696	---	2,003	26	2,693	26	4,696	---	2,003	26	2,693	26	4,696	---	---	---	---	---	---
Export Certification (Proposed)	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	4,280	---	---	---	---	4,280	---	4,280
Priority Review Vouchers (PRV) Tropical Disease	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Priority Review Vouchers (PRV) Pediatric Disease	---	---	---	7,686	---	7,686	---	---	---	---	---	7,686	---	---	---	7,686	---	7,686	---	---	---	---	---	---
Food and Feed Recall	---	1,434	---	---	---	1,434	---	1,434	---	---	---	1,434	5	1,434	---	5	1,434	5	---	---	---	---	5	---
Food Reinspection	---	6,414	---	---	---	6,414	---	6,414	---	---	---	6,414	24	6,414	---	24	6,414	24	---	---	---	---	24	---
Voluntary Qualified Importer Program	---	5,300	---	---	---	5,300	---	5,300	---	---	---	5,300	20	5,300	---	20	5,300	20	---	---	---	---	20	---
Third Party Auditor Program	---	1,400	---	---	---	1,400	---	1,400	---	---	---	1,400	6	1,400	---	6	1,400	6	---	---	---	---	6	---
Outsourcing Facility	---	---	7	1,050	7	1,050	---	---	4	1,370	4	1,370	---	---	4	1,446	4	1,446	---	---	---	76	---	76
Total Program Level, Pre-Transfer	4,897	1,336,207	10,603	2,729,730	16,381	4,746,787	4,961	1,334,520	11,011	2,646,227	16,988	4,661,483	4,723	1,251,720	11,708	3,151,036	17,468	5,116,121	-238	-82,800	697	504,809	479	454,637
HHS OIG transfer					---	-1,500					---	-1,497					---	---						1,497
Total BA, Post-Transfer	4,897	1,319,656	5,382	1,336,608	10,279	2,728,096	4,961	1,317,969	5,492	1,353,245	10,453	2,742,910	4,563	1,209,423	2,785	647,763	7,348	1,888,489	-398	-108,546	-2,707	-705,482	-3,105	-854,421
Total Program Level, Post-Transfer	4,897	1,336,207	10,603	2,729,730	16,381	4,745,287	4,961	1,334,520	11,011	2,646,227	16,988	4,659,986	4,723	1,251,720	11,708	3,151,036	17,468	5,116,121	-238	-82,800	697	504,809	479	456,135

* Total Budget Authority includes \$10 million for the China Initiative for FY 2016, FY 2017, and FY 2018, and \$5 million for foreign High Risk Inspections for FY 2016 and FY 2017. FDA White Oak Consolidation, Building and Facilities Account, Family Smoking Prevention and Tobacco Control Act, and Color Certification User Fees are not included in Food Safety and Nutrition and Medical Product Safety and Availability activities. Medical Countermeasures are included in Medical Product Safety and Availability activities.

** For FY 2016 and FY 2017, the Pre-Transfer levels do not reflect the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2018, FDA proposes to discontinue the transfer.

***The FY 2016, FY 2017, and FY 2018 columns have been updated to reflect reallocated funding across the programs addressing previous reorganizations that consolidated economists in Headquarters and established the Oncology Center of Excellence, as well as to better align the funding structure to services related to intergovernmental affairs.

BUDGET AUTHORITY CROSSWALK

(Dollars in Thousands)	FY 2016 Final		FY 2017 Annualized CR		Changes						FY 2018			
					Reductions		BA Recalibration		Total		President's Budget		+/- FY 2017	
	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000
Salaries and Expenses Account:														
Foods.....	3,841	983,263	3,888	981,386	-251	-70,958	---	---	-251	-70,958	3,637	910,428	-251	-70,958
Center.....	1,001	300,069	1,048	299,491	-49	-21,848	---	---	-49	-21,848	999	277,643	-49	-21,848
Field.....	2,840	683,194	2,840	681,895	-202	-49,110	---	---	-202	-49,110	2,638	632,785	-202	-49,110
Human Drugs.....	2,065	487,332	2,121	486,398	-27.0	-17,823	-1,180	-289,436	-1,207	-307,259	914	179,139	-1,207	-307,259
Center.....	1,257	351,163	1,304	350,488	---	-11,235	-976	-244,900	-976	-256,135	328	94,353	-976	-256,135
Field.....	808	136,169	817	135,910	-27	-6,588	-204	-44,536	-231	-51,124	586	84,786	-231	-51,124
Biologics.....	806	215,317	821	214,907	-16.0	-7,467	-399	-111,547	-415	-119,014	406	95,893	-415	-119,014
Center.....	572	173,937	582	173,606	-5	-4,789	-380	-107,419	-385	-112,208	197	61,398	-385	-112,208
Field.....	235	41,380	239	41,301	-11	-2,678	-19	-4,128	-30	-6,806	209	34,495	-30	-6,806
Animal Drugs and Feeds.....	807	158,635	817	158,333	-31.0	-8,357	-174	-42,370	-205	-50,727	612	107,606	-205	-50,727
Center.....	476	94,005	480	93,826	-12	-3,817	-167	-40,892	-179	-44,709	301	49,117	-179	-44,709
Field.....	331	64,630	337	64,507	-19	-4,540	-7	-1,478	-26	-6,018	311	58,489	-26	-6,018
Devices and Radiological Health.....	1,647	323,170	1,674	322,555	-55.0	-10,900	-702	-171,586	-757	-182,486	917	140,069	-757	-182,486
Center.....	1,129	240,750	1,148	240,292	-34	-5,758	-652	-160,692	-686	-166,450	462	73,842	-686	-166,450
Field.....	517	82,420	526	82,263	-21	-5,142	-50	-10,894	-71	-16,036	455	66,227	-71	-16,036
National Center for Toxicological Research.....	299	63,331	304	63,211	---	-3,000	---	---	---	-3,000	304	60,211	---	-3,000
FDA Headquarters.....	814	191,549	828	191,201	-11	-8,699	-259	-57,070	-270	-65,769	558	125,432	-270	-65,769
FDA White Oak Consolidation.....	---	48,044	---	47,953	---	---	---	-35,392	---	-35,392	---	12,561	---	-35,392
Other Rent and Rent Related.....	---	73,484	---	73,344	---	---	---	-13,455	---	-13,455	---	59,889	---	-13,455
GSA Rental Payments.....	---	176,683	---	176,347	---	---	---	-47,857	---	-47,857	---	128,490	---	-47,857
Subtotal, Salaries and Expenses Account.....	10,279	2,720,808	10,453	2,715,636	-391.0	-127,204	-2,714	-768,713	-3,105	-895,917	7,348	1,819,718	-3,105	-895,918
21st Century Cures.....	---	---	---	20,000	---	40,000	---	---	---	40,000	---	60,000	---	40,000
Buildings and Facilities Account.....	---	8,788	---	8,771	---	---	---	---	---	---	---	8,771	---	-
Total Budget Authority, Pre-Transfer.....	10,279	2,729,596	10,453	2,744,407	-391	-87,204	-2,714	-768,713	-3,105	-855,918	7,348	1,888,489	-3,105	-855,918
Non-Field Activities.....	5,548	1,414,804	5,694	1,432,115	-111	-19,146	-2,434	-610,973	-2,545	-630,119	3,149	801,996	-2,545	-630,119
Field Activities.....	4,731	1,007,793	4,759	1,005,877	-280	-68,058	-280	-61,036	-560	-129,094	4,199	876,782	-560	-129,095
Rent Activities, B&F, and White Oak.....	---	306,999	---	306,415	---	---	---	-96,704	---	-96,704	---	209,711	---	-96,704
HHS OIG transfer.....	---	-1,500	---	-1,497	---	1,497	---	---	---	1,497	---	-	---	1,497
Total Budget Authority, Post-Transfer.....	10,279	2,728,096	10,453	2,742,910	-391	-85,707	-2,714	-768,713	-3,105	-854,421	7,348	1,888,489	-3,105	-854,421

* For FY 2016 and FY 2017, the Pre-Transfer levels do not reflect the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2018, FDA proposes to discontinue the transfer.

**The FY 2016, FY 2017, and FY 2018 columns have been updated to reflect reallocated funding across the programs addressing previous reorganizations that consolidated economists in Headquarters and established the Oncology Center of Excellence, as well as to better align the funding structure to services related to intergovernmental affairs.

TECHNICAL NOTES

Details in this document may not add to the totals due to rounding. Budget data in this book are presented “comparably” to the FY 2018 Budget, since the location of programs may have changed in prior years or be proposed for change in FY 2018. This approach allows increases and decreases in this book to reflect true funding changes.

FY 2018 REALLOCATIONS

(Dollars in Thousands)	Oncology Center of Excellence		Economists		Inter- governmental Affairs		Total	
	FTE	\$000	FTE	\$000	FTE	\$000	FTE	\$000
Salaries and Expenses Account:								
Foods.....	---	---	-18	-3,925	---	-140	-18	-4,065
Center.....			-18	-3,925			-18	-3,925
Field.....					---	-140	---	-140
Human Drugs.....	-13	-3,575	---	---	-3	-596	-16	-4,171
Center.....	-13	-3,575			-3	-558	-16	-4,133
Field.....					---	-38	---	-38
Biologics.....	---	---	---	---	---	-126	---	-126
Center.....					---	-115	---	-115
Field.....					---	-11	---	-11
Animal Drugs and Feeds.....	---	---	---	---	---	-17	---	-17
Center.....							---	---
Field.....					---	-17	---	-17
Devices and Radiological Health.....	---	---	---	---	---	-83	---	-83
Center.....					---	-58	---	-58
Field.....					---	-25	---	-25
National Center for Toxicological Research.....							---	---
FDA Headquarters.....	13	3,575	18	3,925	3	962	34	8,462
FDA White Oak Consolidation.....							---	---
Other Rent and Rent Related.....							---	---
GSA Rental Payments.....							---	---
Subtotal, Salaries and Expenses Account.....	---	---	---	---	---	---	---	---
21st Century Cures.....								
Buildings and Facilities Account.....								
Total Budget Authority.....	---	---	---	---	---	---	---	---
Non-Field Activities.....	---	---	---	---	---	231	---	231
Field Activities.....	---	---	---	---	---	-231	---	-231
Rent Activities, B&F, and White Oak.....	---	---	---	---	---	---	---	---

*Reflects reallocated funding across the programs addressing previous reorganizations that established the Oncology Center of Excellence and consolidated economists in Headquarters, as well as to better align the funding structure to services related to intergovernmental affairs.

APPROPRIATIONS LANGUAGE

Salaries and Expenses

For necessary expenses of the Food and Drug Administration, including hire and purchase of passenger motor vehicles; for payment of space rental and related costs pursuant to Public Law 92–313 for programs and activities of the Food and Drug Administration which are included in this Act; for rental of special purpose space in the District of Columbia or elsewhere; for miscellaneous and emergency expenses of enforcement activities, authorized and approved by the Secretary and to be accounted for solely on the Secretary's certificate, not to exceed \$25,000; and notwithstanding section 521 of Public Law 107–188; [\$4,681,392,000]^[1] \$2,527,960,000: *Provided*, That of the amount provided under this heading, [\$851,481,000 shall be derived from prescription drug user fees authorized by 21 U.S.C. 379h, and shall be credited to this account and remain available until expended; \$137,677,000 shall be derived from medical device user fees authorized by 21 U.S.C. 379j, and shall be credited to this account and remain available until expended; \$318,363,000 shall be derived from human generic drug user fees authorized by 21 U.S.C. 379j-42, and shall be credited to this account and remain available until expended; \$21,540,000 shall be derived from biosimilar biological product user fees authorized by 21 U.S.C. 379j-52, and shall be credited to this account and remain available until expended; \$22,818,000]\$24,142,000 shall be derived from animal drug user fees authorized by 21 U.S.C. 379j-12, and shall be credited to this account and remain available until expended; [\$9,705,000]\$12,100,000 shall be derived from animal generic drug user fees authorized by 21 U.S.C. 379j-21, and shall be credited to this account and remain available until expended; [\$599,000,000]\$672,000,000 shall be derived from tobacco product user fees authorized by 21 U.S.C. 387s, and shall be credited to this account and remain available until expended: *Provided further*, That in addition to and notwithstanding any other provision under this heading, amounts collected for [prescription drug user fees, medical device user fees, human generic drug user fees, biosimilar biological product user fees,] animal drug user fees[,], and animal generic drug user fees that exceed the respective fiscal year [2016]2018 limitations are appropriated and shall be credited to this account and remain available until expended: *Provided further*, That fees derived from [prescription drug, medical device, human generic drug, biosimilar biological product,] animal drug[,], and animal generic drug assessments for fiscal year [2016]2018, including any such fees collected prior to fiscal year [2016]2018 but credited for fiscal year [2016]2018, shall be subject to the fiscal year [2016]2018 limitations: *Provided further*, That the Secretary may accept payment during fiscal year [2016] 2018 of user fees specified under this heading and authorized for fiscal year [2017]2019, prior to the due

^[1] Please note that brackets indicate deleted text and italics indicate new text.

date for such fees, and that amounts of such fees assessed for fiscal year [2017]2019 for which the Secretary accepts payment in fiscal year [2016]2018 shall not be included in amounts under this heading: *Provided further*, That none of these funds shall be used to develop, establish, or operate any program of user fees authorized by 31 U.S.C. 9701: [*Provided further*, That of the total amount appropriated: (1) \$987,328,000 shall be for the Center for Food Safety and Applied Nutrition and related field activities in the Office of Regulatory Affairs; (2) \$1,394,136,000 shall be for the Center for Drug Evaluation and Research and related field activities in the Office of Regulatory Affairs; (3) \$354,901,000 shall be for the Center for Biologics Evaluation and Research and for related field activities in the Office of Regulatory Affairs; (4) \$187,825,000 shall be for the Center for Veterinary Medicine and for related field activities in the Office of Regulatory Affairs; (5) \$430,443,000 shall be for the Center for Devices and Radiological Health and for related field activities in the Office of Regulatory Affairs; (6) \$63,331,000 shall be for the National Center for Toxicological Research; (7) \$564,117,000 shall be for the Center for Tobacco Products and for related field activities in the Office of Regulatory Affairs; (8) not to exceed \$171,418,000 shall be for Rent and Related activities, of which \$52,346,000 is for White Oak Consolidation, other than the amounts paid to the General Services Administration for rent; (9) not to exceed \$238,274,000 shall be for payments to the General Services Administration for rent; and (10) \$289,619,000 shall be for other activities, including the Office of the Commissioner of Food and Drugs, the Office of Foods and Veterinary Medicine, the Office of Medical and Tobacco Products, the Office of Global and Regulatory Policy, the Office of Operations, the Office of the Chief Scientist, and central services for these offices:] *Provided further*, That not to exceed \$25,000 of this amount shall be for official reception and representation expenses, not otherwise provided for, as determined by the Commissioner: [*Provided further*, That any transfer of funds pursuant to section 770(n) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 379dd(n)) shall only be from amounts made available under this heading for other activities: *Provided further*, That of the amounts that are made available under this heading for "other activities", and that are not derived from user fees, \$1,500,000 shall be transferred to and merged with the appropriation for "Department of Health and Human Services—Office of Inspector General" for oversight of the programs and operations of the Food and Drug Administration and shall be in addition to funds otherwise made available for oversight of the Food and Drug Administration:] *Provided further*, That funds may be transferred from one specified activity to another with the prior [approval] *notification* of the Committees on Appropriations of both Houses of Congress.

In addition, mammography user fees authorized by 42 U.S.C. 263b, export certification user fees authorized by 21 U.S.C. 381, priority review user fees authorized by 21 U.S.C. 360n and 360ff, food and feed recall fees, food reinspection fees, and voluntary qualified importer program fees authorized by 21 U.S.C. 379j-31, outsourcing facility fees authorized by 21 U.S.C. 379j-62, prescription drug wholesale distributor licensing and inspection fees authorized by 21

U.S.C. 353(e)(3), [and] third-party logistics provider licensing and inspection fees authorized by 21 U.S.C. 360eee-3(c)(1), [and] third-party auditor fees authorized by 21 U.S.C. 384d(c)(8), *and Medical Countermeasure Priority Review Voucher User Fees authorized by 21 U.S.C. 360bbb-4a*, shall be credited to this account, to remain available until expended.

Buildings and Facilities

For plans, construction, repair, improvement, extension, alteration, demolition, and purchase of fixed equipment or facilities of or used by the Food and Drug Administration, where not otherwise provided, [\$11,788,000] \$8,771,000, to remain available until expended.

Salaries and Expenses (Legislative Proposal)

In addition, contingent upon the enactment of authorizing legislation, the Secretary shall charge a fee for prescription drug review activities, medical device review activities, biosimilar biological products review activities, and human generic drugs review activities: *Provided*, That fees of \$1,262,182,000, for prescription drug reviews, shall be credited to this account and remain available until expended; \$439,001,000 for medical device reviews, shall be credited to this account and remain available until expended; \$615,746,000 for human generic drug reviews, shall be credited to this account and remain available until expended; and \$86,736,000 for biosimilar biological product reviews, shall be credited to this account and remain available until expended: *Provided further*, That, in addition and notwithstanding any other provision under this heading, amounts collected for prescription drug user fees, medical device user fees, biosimilar biological product user fees, and human generic drug user fees that exceed the respective fiscal year 2018 limitations are appropriated and shall be credited to this account and remain available until expended: *Provided further*, That fees derived from prescription drug reviews, medical device reviews, biosimilar biological products reviews, and human generic drugs reviews for fiscal year 2018 received during fiscal year 2018, including any such fees assessed prior to fiscal year 2018 but credited for fiscal year 2018, shall be subject to the fiscal year 2018 limitations: *Provided further*, That the Secretary may accept payment during fiscal year 2018 of user fees specified in this paragraph and authorized for fiscal year 2019, prior to the due date for such fees, and that amounts of such fees assessed for fiscal year 2019 for which the Secretary accepts payment in fiscal year 2018 shall not be included in amounts in this paragraph.

In addition, contingent upon the enactment of authorizing legislation, the Secretary shall increase the fees for animal drug review activities and animal generic drug review activities: *Provided*, That additional fees of \$46,110,000, for animal drug reviews, shall be

credited to this account and remain available until expended; and \$6,375,000, for animal generic drug reviews, shall be credited to this account and remain available until expended.

FY 2018 PROPOSED GENERAL PROVISIONS

SEC. __. INCREASE IN EXPORT CERTIFICATION FEES.—

Section 801(c)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 381(c)(4)) is amended—

(1) in subparagraph (B) by striking “but shall not exceed \$175 for each certification” and inserting “in an amount specified in subparagraph (c)”; and

(2) by adding at the end the following new subparagraphs:

“(c) The fee for each written export certification issued by the Secretary under this paragraph shall not exceed—

“(i) \$600 for fiscal year 2018; and

“(ii) for each subsequent fiscal year, the prior fiscal year maximum amount multiplied by the inflation adjustment under section 738(c)(2)(c), applied without regard to the limitation in clause (ii)(II) of such section.

“(F) The Secretary shall, for each fiscal year, publish in the Federal Register a notice of the export certification fee under this paragraph for such year, not later than 60 days before such fee takes effect.”

"SEC. __. FDA WORKING CAPITAL FUND.

(a) There is hereby established in the Treasury of the United States a Working Capital Fund (the Fund) to be administered by the Food and Drug Administration (FDA), without fiscal year limitation, for the payment of salaries, travel, and other expenses necessary to the maintenance and operation of (1) a supply service for the purchase, storage, handling, issuance, packing, or shipping of stationery, supplies, materials, equipment, and blank forms, for which stocks may be maintained to meet, in whole or in part, the needs of the FDA and requisitions of other Government Offices, and (2) such other services as the Commissioner of the FDA, subject to review by the Secretary of Health and Human Services, determines may be performed more advantageously as central services. The Fund shall be reimbursed from applicable discretionary resources, notwithstanding any otherwise applicable purpose limitations, available when services are performed or stock furnished, or in advance, on a basis of rates which shall include estimated or actual charges for personal services, materials, equipment, information technology, and other expenses. Charges for equipment and information technology shall include costs associated with maintenance, repair, and depreciation (including improvement and replacement).

(b) Of any discretionary resources appropriated in this Act for fiscal year 2018 for “Department of Health and Human Services, Food and Drug Administration, Salaries and Expenses”, not to exceed \$5,000,000 of amounts available as of September 30 may be transferred to and merged with the Fund established under subsection (a), notwithstanding any otherwise applicable purpose limitations.

(c) No amounts may be transferred pursuant to this section that are designated by the Congress as an emergency requirement pursuant to a concurrent resolution on the budget or the Balanced Budget and Emergency Deficit Control Act of 1985.

SEC. __. 21ST CENTURY CURES.—

Sec. XXX. For necessary expenses to carry out the purposes described under section 1002(b)(4) of the 21st Century Cures Act, in addition to amounts available for such purposes under the heading "Salaries and Expenses", \$60,000,000, to remain available until expended: Provided, That amounts appropriated in this paragraph are appropriated pursuant to section 1002(b)(3) of the 21st Century Cures Act, are to be derived from amounts transferred under section 1002(b)(2)(A) of such Act, and may be transferred by the Secretary of Health and Human Services to other accounts of the Department solely for the purposes provided in such Act: Provided further, That such transfer authority is in addition to any other transfer authority provided by law.

APPROPRIATION LANGUAGE ANALYSIS

Language Provision	Explanation
Prescription Drug User Fee	The Administration will propose legislation to allow FDA to collect fees for prescription drugs. The additional resources are estimated at \$1,262,182,000. This will strengthen and improve the process for the review of human drugs and improve risk management for drugs approved under PDUFA.
Medical Device User Fee	The Administration will propose legislation to allow FDA to collect fees for medical devices. The additional resources are estimated at \$439,001,000. This will strengthen the review processes and meet performance goals for the medical device program.
Generic Drug User Fee	The Administration will propose legislation to allow FDA to collect fees for generic drugs. The additional resources are estimated at \$615,746,000. This will help bring timely review for human generic drug applications and reduce backlog of human generic drug applications.
Biosimilar User Fee	The Administration will propose legislation to allow FDA to collect fees for biosimilars. The additional resources are estimated at \$86,736,000. This provides a mechanism and structure for the collection of development-phase user fees to support FDA's biosimilar review program activities.
Animal Drug User Fee	The Administration will propose legislation to allow FDA to collect fees for animal drugs. The additional resources are estimated at \$46,110,000. This will help ensure a cost-efficient, high quality animal drug review process that is predictable and performance driven.
Animal Generic Drug User Fee	The Administration will propose legislation to allow FDA to collect fees for animal generic drug. The additional resources are estimated at \$6,375,000. This will help protect human and animal health and accelerate innovation in the industry.
Export Certification Fee	The Administration will propose legislation to allow FDA to increase the funding cap for the export certification fee from \$175 per certification to \$600 per certification for an estimated total of \$8,976,000. This proposal, and the increased certification fee ceiling it promotes, is necessary to ensure that FDA can efficiently implement the export certification program, while ensuring that other public health programs do not suffer.
Working Capital Fund	A Working Capital Fund (WCF) supports agency-wide business services. The WCF would serve as a revolving fund with extended availability and serves as the funding mechanism for centralized business services support across FDA. Services rendered under the WCF would be performed at pre-established rates to cover the cost of business operations.

AMOUNTS AVAILABLE FOR OBLIGATION

(dollars in thousands)	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
<u>General Fund Discretionary Appropriation:</u>			
Appropriation.....	2,728,649	2,742,910	1,888,489
Total Discretionary Appropriation.....	2,728,649	2,742,910	1,888,489
<u>Mandatory Appropriation:</u>			
CRADA.....	2,000	2,000	2,000
Total Mandatory Appropriation.....	2,000	2,000	2,000
<u>Offsetting Collections:</u>			
Non-Federal Sources.....	1,937,587	1,917,077	3,227,632
Total Offsetting Collections.....	1,937,587	1,917,077	3,227,632
Total Obligations.....	4,668,236	4,661,986	5,118,121

*For FY 2016 and FY 2017, the levels reflect the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2018, FDA proposes to discontinue the transfer.

**FY 2016 Actuals reflected transfer of \$15 million from the GSA Rent activity to the Foods program. These funds will be used by the Office of Regulatory Affairs to support the relocation of its leased San Francisco District Office and Laboratory located in Alameda, CA

***The FY 2016, FY 2017, and FY 2018 columns have been updated to reflect reallocated funding across the programs addressing previous reorganizations that consolidated economists in Headquarters and established the Oncology Center of Excellence, as well as to better align the funding structure to services related to intergovernmental affairs.

SUMMARY OF CHANGES

(dollars in thousands)	Budget Authority	User Fees	Program Level	FTE
FY 2017 Annualized CR.....	2,744,407	1,917,077	4,661,484	16,988
FY 2018 Program Changes				
Budget Authority Changes				
Reductions.....	-127,205	---	-127,205	-391
BA Recalibration.....	-768,713	---	-768,713	-2,714
21st Century Cures.....	40,000		40,000	---
Total Budget Authority Changes.....	-855,918	---	-855,918	-3,105
User Fee Changes				
Current Law				
Prescription Drug (PDUFA).....	---	507,658	507,658	1,216
Medical Device (MDUFA).....	---	312,918	312,918	990
Generic Drug (GDUFA).....	---	292,735	292,735	868
Biosimilars (BsUFA).....	---	64,657	64,657	239
Animal Drug (ADUFA).....	---	46,579	46,579	173
Animal Generic Drug (AGDUFA).....	---	7,134	7,134	23
Family Smoking Prevention and Tobacco Control Act.....	---	74,139	74,139	20
Indefinite				
Mammography Quality Standards Act (MQSA).....	---	---	---	---
Color Certification.....	---	380	380	1
Export Certification.....	---	4,280	4,280	---
Priority Review Vouchers (PRV) Tropical Disease.....	---	---	---	---
Priority Review Vouchers (PRV) Pediatric Disease	---	---	---	---
Food and Feed Recall.....	---	---	---	5
Food Reinspection.....	---	---	---	24
Voluntary Qualified Importer Program.....	---	---	---	20
Third Party Auditor Program.....	---	---	---	6
Outsourcing Facility.....	---	76	76	---
Subtotal, Current Law.....	---	1,310,555	1,310,555	3,585
Net Program Changes.....	-855,918	1,310,555	454,637	480
Total FDA Request for FY 2018.....	1,888,489	3,227,632	5,116,121	17,468

* The FY 2017 level does not reflect the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2018, FDA proposes to discontinue the transfer.

** FTE figures do not include an estimated 81 reimbursable, 2 CRADA, 2 FOIA, 44 PEPFAR, and 17 EBOLA.

***The FY 2017 and FY 2018 columns have been updated to reflect reallocated funding across the programs addressing previous reorganizations that consolidated economists in Headquarters and established the Oncology Center of Excellence, as well as to better align the funding structure to services related to intergovernmental affairs.

BUDGET AUTHORITY BY ACTIVITY

(dollars in thousands)	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
Salaries and Expenses Account:			
Foods.....	998,230	981,386	910,428
Center.....	300,059	299,491	277,643
Field.....	698,171	681,895	632,785
Human Drugs.....	487,299	486,398	179,139
Center.....	351,135	350,488	94,353
Field.....	136,164	135,910	84,786
Biologics.....	215,308	214,907	95,893
Center.....	173,929	173,606	61,398
Field.....	41,379	41,301	34,495
Animal Drugs and Feeds.....	158,629	158,333	107,606
Center.....	94,001	93,826	49,117
Field.....	64,628	64,507	58,489
Devices and Radiological Health.....	323,157	322,555	140,069
Center.....	240,740	240,292	73,842
Field.....	82,417	82,263	66,227
National Center for Toxicological Research.....	63,329	63,211	60,211
FDA Headquarters.....	189,874	191,201	125,432
FDA White Oak Consolidation.....	48,044	47,953	12,561
Other Rent and Rent Related.....	73,484	73,344	59,889
GSA Rental Payments.....	161,683	176,347	128,490
Subtotal, Salaries and Expenses Account.....	2,719,037	2,715,636	1,819,718
Food and Drug Safety -- No Year (P.L. 113-6).....	2,073	---	---
Food Safety.....	---	---	---
Drug Safety.....	2,073	---	---
21st Century Cures.....	---	20,000	60,000
Buildings and Facilities Account.....	7,539	8,771	8,771
Total Budget Authority.....	2,728,649	2,744,407	1,888,489
FTE.....	10,279	10,453	7,348

*For FY 2016 and FY 2017, the Pre-Transfer levels do not reflect the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2018, FDA proposes to discontinue the transfer.

** FTE figures do not include an estimated 81 reimbursable, 2 CRADA, 2 FOIA, 44 PEPFAR, and 17 EBOLA.

***FY 2016 Actuals reflected transfer of \$15 million from the GSA Rent activity to the Foods program. These funds will be used by the Office of Regulatory Affairs to support the relocation of its leased San Francisco District Office and Laboratory located in Alameda, CA.

****The FY 2016, FY 2017, and FY 2018 columns have been updated to reflect reallocated funding across the programs addressing previous reorganizations that consolidated economists in Headquarters and established the Oncology Center of Excellence, as well as to better aligning the funding structure to services related to intergovernmental affairs.

APPROPRIATIONS HISTORY

Salaries and Expenses

(dollars)	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
General Fund Appropriation*:				
FY 2009 1/.....	2,638,197,000		3,168,794,000	2,622,267,000
FY 2010.....	3,371,218,000	3,230,218,000	3,230,218,000	3,237,218,000
FY 2011.....	3,989,507,000		3,720,044,000	3,650,783,000
FY 2012.....	4,256,673,000	3,599,871,000	3,599,871,000	3,788,336,000
FY 2013				
Base.....	4,449,283,000	4,153,933,000	4,197,658,000	4,203,577,000
Sequestration.....	---	---	---	-207,550,000
Subtotal.....	4,449,283,000	4,153,933,000	4,197,658,000	3,996,027,000
FY 2014.....	4,613,104,000	4,280,164,000	4,346,670,000	4,346,670,000
FY 2015 2/.....	4,689,706,000	4,428,900,000	4,443,356,000	4,443,356,000
FY 2016.....	4,889,642,000	4,579,118,000	4,589,562,000	4,681,392,000
FY 2017.....	4,953,946,000	4,649,566,000	4,655,689,000	4,685,089,000
FY 2018.....	5,044,110,000			

* Excludes Indefinite user fees.

1/ FY 2009 Appropriation does not include Supplemental Appropriation

2/ The FY 2015 Enacted level requires the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. In addition to the funding displayed in the table above, the FY 2015 Enacted level includes \$25 million in emergency funding for FDA's role in the U.S. Government response to contain, treat, and prevent the spread of Ebola.

FOODS

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
Foods.....	1,009,849	998,230	992,972	922,014	-70,958
<i>Budget Authority.....</i>	<i>998,263</i>	<i>998,230</i>	<i>981,386</i>	<i>910,428</i>	<i>-70,958</i>
<i>User Fees.....</i>	<i>11,586</i>	<i>---</i>	<i>11,586</i>	<i>11,586</i>	<i>---</i>
Center.....	300,619	300,059	300,041	278,193	-21,848
Budget Authority.....	300,069	300,059	299,491	277,643	-21,848
User Fees.....	550	---	550	550	---
Food and Feed Recall.....	243	---	243	243	---
Voluntary Qualified Importer Program.....	243	---	243	243	---
Third Party Auditor Program.....	64	---	64	64	---
Field.....	709,230	698,171	692,931	643,821	-49,110
Budget Authority.....	698,194	698,171	681,895	632,785	-49,110
User Fees.....	11,036	---	11,036	11,036	---
Food and Feed Recall.....	1,000	---	1,000	1,000	---
Food Reinspection.....	4,575	---	4,575	4,575	---
Voluntary Qualified Importer Program.....	4,320	---	4,320	4,320	---
Third Party Auditor Program.....	1,141	---	1,141	1,141	---
FTE.....	3,841	3,841	3,888	3,686	-202

Authorizing Legislation: Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321-399); Federal Import Milk Act (21 U.S.C. 142-149); Public Health Service Act (42 U.S.C. 201, et seq.); Food Additives Amendment of 1958; Color Additives Amendments of 1960; The Fair Packaging and Labeling Act (15 U.S.C. 1451-1461); Safe Drinking Water Act (21 U.S.C. 349); Saccharin Study and Labeling Act; Infant Formula Act of 1980; Drug Enforcement, Education, and Control Act of 1986; Nutrition Labeling and Education Act of 1990; Dietary Supplement Health and Education Act of 1994; Food Quality Protection Act of 1996; Federal Tea Tasters Repeal Act (42 U.S.C. 41); Safe Drinking Water Act Amendments of 1996 (21 U.S.C. 349); Food and Drug Administration Modernization Act of 1997; Antimicrobial Regulation Technical Corrections Act of 1998; Public Health Security and Bioterrorism Preparedness and Response Act of 2002; Food Allergen Labeling and Consumer Protection Act of 2004; Sanitary Food Transportation Act of 2005; Food and Drug Administration Amendments Act of 2007; Food and Drug Administration Food Safety Modernization Act of 2011 (Public Law 111-353); Dietary Supplement and Nonprescription Drug Consumer Protection Act (21 U.S.C. 379aa-1).

Allocation Methods: Direct Federal/intramural; Contract; Competitive grant

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The purpose of the Foods Program is to protect and promote human health by ensuring the safety of the American food supply, dietary supplements, and cosmetics, as well as the proper labeling of food and cosmetics. The Foods Program began with the passage of the 1906 Pure Food and Drugs Act.

FDA's Foods Program is part of the Foods and Veterinary Medicine (FVM) Program. The FVM Program includes the Foods and the Animal Drugs and Feeds Programs and field activities in the Office of Regulatory Affairs (ORA). In collaboration with ORA, the Center for Food Safety and Applied Nutrition (CFSAN) administers the Foods Programs and the Center for Veterinary Medicine (CVM) administers the Animal Drugs and Feeds Programs.³

CFSAN ensures the safety of the human food supply, dietary supplements, and cosmetics as well as the proper labeling of foods and cosmetics. The Foods Program ensures that the nation's food supply is wholesome and honestly labeled, and that nutrition labeling is informative and accurate. The Foods Program also promotes a nutritionally healthy food supply.

The Center for Veterinary Medicine protects human and animal health by approving safe and effective drugs for animals, and ensuring the safety of feed and devices for animals.

The Office of Foods and Veterinary Medicine (OFVM) provides leadership and strategic direction to Foods and Veterinary Medicine programs and oversees all CFSAN and CVM activities. OFVM also manages the crosscutting outbreak response and evaluation team, leads all external communications and stakeholder engagement, and coordinates FVM wide resource planning.

The following accomplishments demonstrate the Foods Program's delivery of its regulatory and public health responsibilities and progress towards reaching the FDA and FVM Strategic Plan goals. Most of the Foods Program activities fall under FDA's Strategic Plan goal of Enhanced Oversight. These activities include scientific analysis and support, policy, regulatory research, and guidance development.

Enhance Oversight of Food Safety and Nutrition

Outbreaks of foodborne illness and contamination events have a substantial impact on public health:

- An estimated 48 million foodborne illnesses occur every year.
- An estimated 128,000 hospitalizations and 3,000 deaths result⁴.
- Foodborne illnesses cost an average of \$3,630 per case.

³ The Center for Veterinary Medicine does not implement the Foods Program, and the Center for Food Safety and Applied Nutrition does not implement the Animal Drugs and Feeds Program.

⁴ CDC. 2011. Estimates of Foodborne Illness in the United States. A comparable analysis cannot be made between CDC's 2011 estimates of foodborne illnesses and findings from earlier years due to a new methodology being used in 2011.

- More than \$36 billion per year in medical costs, lost productivity, and other burdens to society.⁵

The FVM Strategic Plan⁶ provides a framework for implementing the Food Safety Modernization Act (FSMA) and other legislative authorities. The Plan prioritizes the prevention of foodborne and feed-borne illness of both known and unknown origins. The Foods Program addresses food safety risks at multiple points of the food supply chain. The program accomplishes this through regulations, guidance, technical assistance, training, outreach, consumer information, and model codes for food service establishments.

The FVM Strategic Plan also emphasizes nutrition-related priorities of the Foods Program. Poor diet is a key risk factor for chronic diseases – the leading cause of death and disability in the United States. Chronic diseases and conditions – such as heart disease, stroke, cancer, diabetes, obesity, and arthritis – are among the most common, costly, and preventable of all health problems. In 2010, 86 percent of all health care spending was for people with one or more chronic medical conditions.⁷

The Foods Program ensures that nutrition labeling is informative and accurate. The Program promotes a nutritionally healthy food supply to reduce the hundreds of thousands of deaths each year attributable to poor diet.

In addition to the high-priority initiatives identified in the FVM Strategic Plan, the Foods Program conducts other important activities related to food safety, nutrition, and cosmetics. These include:

- review of infant formula notifications from manufacturers before marketing a new formula
- premarket regulation of ingredients and packaging, such as review of food additive and color additive petitions
- postmarket monitoring for chemical contaminants
- authorization of nutrient content and health claims
- regulation of dietary supplements
- cosmetics safety and labeling.

The FDA Food Safety Modernization Act

⁵ Minor, T., Lasher, A., Klontz, K., Brown, B., Nardinelli, C. and Zorn, D. (2015), The Per Case and Total Annual Costs of Foodborne Illness in the United States. *Risk Analysis*, 35: 1125–1139. doi:10.1111/risa.12316

⁶ <https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofFoods/UCM507379.pdf>

⁷ Centers for Disease Control and Prevention. "Chronic Disease Prevention and Health Promotion: Chronic Disease Overview." <http://www.cdc.gov/chronicdisease/overview/>, Accessed October 23, 2015.

On January 4, 2011, the FDA Food Safety Modernization Act (FSMA) was signed into law, significantly reforming food safety laws. FSMA is transforming the nation's food safety system from reactive to proactive by allowing FDA to focus on preventing food safety problems before they occur rather than reacting to problems after the fact. FSMA guides the food safety system in implementing effective measures to prevent contamination. FSMA engages all domestic and foreign participants in the food system to do their part to minimize the likelihood of harmful contamination. For example, FSMA requires food importers to ensure that their suppliers meet U.S. safety standards.

FDA faces unique food safety challenges in the 21st century. The FDA Food Safety Modernization Act (FSMA) enables FDA to better protect the public health by:

- shifting the food safety paradigm from reactive to preventive
- strengthening FDA's technical expertise and capacity to support industry in implementing the new prevention standards
- furthering federal, state, local and territorial partnerships and investing in training and capacity to ensure efficient, high quality, and consistent oversight nationwide
- broadening interaction with foreign partners and increasing oversight of importers by placing more responsibility for the safety of imported foods on them.

FSMA gives FDA new enforcement authorities to achieve high rates of industry compliance with prevention- and risk-based food and feed safety standards and to better respond to and contain food safety problems when they occur.

FDA finalized seven foundational FSMA rules in 2015 and 2016, and is conducting extensive outreach to industry to ensure that stakeholders understand the new requirements. These seven foundational FSMA rules provide a framework for the food industry to implement effective measures to prevent contamination.⁸

Selected Rules Published in 2016

Below are FSMA-related rules published by the Foods Program in the last calendar year. These rules help address various issues. This list does not represent any degree of importance or priority ranking among the published rules.

Date	#	Title	Description
Jul 2016	FDA-2002-N-	FSMA Final Rule: Amendments to	Updates FDA's food facility registration requirements to better protect public health

⁸ <http://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm253380.htm>

	0323	Registration of Food Facilities	by requiring additional registration information to improve accuracy of the food facility registration database.
May 2016	FDA 2013-N-1425	FSMA Final Rule: Mitigation Strategies to Protect Food Against Intentional Adulteration	Prevents intentional adulteration from acts intended to cause wide-scale harm to public health, including acts of terrorism targeting the food supply.
Apr 2016	FDA-2013-N-0013	FSMA Final Rule: Sanitary Transportation of Human and Animal Food	Prevents practices during transportation that create food safety risks, such as failure to properly refrigerate food and inadequate cleaning of vehicles between loads.

In 2016, FDA issued the final two foundational rules: Sanitary Transportation of Human and Animal Food and Mitigation Strategies to Protect Food Against Intentional Adulteration.

Sanitary Transportation of Human and Animal Food (published in April 2016) advances FDA's efforts to protect foods from farm to table by keeping foods safe from contamination during transportation. This rule creates a modern risk-based framework for food safety by preventing practices during transportation that create food safety risks – such as failure to properly refrigerate and protect food, and inadequate cleaning of vehicles between loads.

The rule builds on safeguards envisioned in the 2005 Sanitary Food Transportation Act (SFTA). Because of illness outbreaks resulting from human and animal food contaminated during transportation, and incidents and reports of unsanitary transportation practices, there have long been concerns about the need for regulations to ensure that foods are transported safely. The rule establishes requirements for vehicles and transportation equipment, transportation operations, records, training and waivers.

Mitigation Strategies to Protect Food Against Intentional Adulteration (published in May 2016) directs domestic and foreign food facilities (required to register under the Federal Food, Drug, and Cosmetic Act) to address hazards that may be intentionally introduced by terrorist acts. These food facilities must develop strategies to minimize or prevent vulnerabilities identified at actionable process steps in a food operation.

Voluntary Qualified Importer Program (VQIP) Guidance

FSMA gives FDA new authorities to ensure that foods imported into the United States meet the same safety standards as those set for domestically produced foods. As part of FSMA implementation, FDA published final guidance in November 2016 to establish a voluntary, fee-based program to expedite review and import of foods into the United States from importers with a proven food safety track record. This program, the Voluntary Qualified Importer Program (VQIP), will benefit both importers and consumers. VQIP allows FDA to focus its resources on the potentially dangerous food imports that are most likely to harm the public.

In addition to establishing mandatory standards for importers of food, FDA is establishing the VQIP for importers who achieve and maintain a high level of control over the safety and security of their supply chains.

Amendments to Registration of Food Facilities

Also published under FSMA authority in 2016, the Amendments to Registration of Food Facilities final rule updates FDA's food facility registration requirements to better protect public health. The final rule requires additional registration information to improve the accuracy of the food facility registration database for facilities both in the United States and abroad.

Food facilities that manufacture/process, pack or hold food for consumption in the United States are required to register with the FDA. This final rule adds new provisions to the current regulations that require the following:

- an email address for registration
- renewal of registration every two years
- assurance that inspection will be permitted in accordance with the Federal Food, Drug, and Cosmetic Act.

This final rule will support FDA's efforts to act quickly in response to food-related emergencies and will help the FDA to use its inspectional resources more efficiently.

Improved Outbreak Response

The Foods Program and the Coordinated Outbreak Response and Evaluation (CORE) team rapidly detect and respond to major foodborne illness outbreaks. This team coordinates activities across FDA field and compliance offices, state investigative and laboratory resources, and local city and county resources. The CORE team works cooperatively with other federal agencies such as CDC and USDA to ensure timely and effective resolution of foodborne illness outbreaks. Examples include:

- the E. coli outbreak associated with flour

- the Hepatitis A outbreaks associated with frozen strawberries from Egypt
- the *Listeria monocytogenes* outbreak associated with frozen vegetables.

To prepare for outbreak responses, FDA field offices support and provide technical assistance to laboratories awarded International Organization for Standardization (ISO) Cooperative Agreement Program (CAP) grants and to laboratories seeking or maintaining their accreditation.

This program continues to add national food/feed testing laboratories. By 2016, a total of 23 laboratories have joined the program and several are working towards ISO accreditation.

Improved Pathogen Detection and Traceability



In 2013, FDA established the first national pilot network of whole genome sequencers (WGS) – GenomeTrakr. Whole genome sequencing reveals the complete DNA make-up of an organism. This technology allows researchers

to perform basic foodborne pathogen identification during foodborne illness outbreaks.

The Network is now in its fifth year and has collected more than 100,000 whole bacterial genome sequences from the FDA Network and collaborating sites. These genome sequences are stored in a publicly accessible database at The National Institutes of Health. FDA developed outbreak traceback methodology based on whole bacterial genomes that can determine the source of certain outbreaks down to the farm level.

Applying WGS helps the Foods Program to:

- investigate outbreaks faster and more efficiently
- add innovative technology protocols for testing and surveillance, enhancing confidence in regulatory actions
- identify emerging antimicrobial resistance threats in the food supply.

Implementing WGS reduces the time needed to conduct outbreak investigations and improves FDA's ability to pinpoint the source of contamination events. Sample collection and sequence cataloging from food production sites can help monitor compliance with FDA's rules on safe food-handling practices, enhancing preventive controls for food safety.

In 2016, FDA collected sequences as a regular part of foodborne outbreak investigations and compliance actions. So far, FDA has used WGS to support more than 300 outbreak investigations and compliance actions.

For example, from 2013 to 2016 FDA used GenomeTrakr to link *Listeria monocytogenes* to a common frozen vegetable source. During this three-year period *Listeria monocytogenes* sickened nine individuals, three of whom died. The low level and sporadic nature of the *Listeria* contamination associated with this product – which led to the recall of more than 11 different frozen vegetable ingredients in more than 350 different products – would have been difficult to identify without WGS.

The combination of real-time clinical and food/environmental surveillance using WGS has reduced the average number of illnesses in *Listeria* outbreaks from 9 to 3 over the past two years and has increased the number of illnesses that could be linked to specific food sources.

The FDA Foods Program applies WGS regularly to trace foodborne outbreaks for *Salmonella* and *Listeria monocytogenes*.⁹ By generating about two whole genomes per hour, GenomeTrakr is rapidly increasing the number of *Salmonella* and *Listeria monocytogenes* genomes in the database. The network includes more than 40 state, international, FDA, and federal partner (CDC and USDA-FSIS) laboratories.

FDA's enhanced ability to pinpoint outbreaks is particularly important because of the global nature of the food supply. Guidelines and recommendations for global deployment of WGS to World Health Organization member countries are needed. FDA is participating in meetings with the World Health Organization and the Food and Agriculture Organization that could lead to such guidelines and recommendations.

Because of its extraordinary success in 2015, The American Society for Microbiology (ASM) asked FDA scientists to host a second "Conference on Rapid Next-Generation Sequencing and Bioinformatic Pipelines for Enhanced Molecular Epidemiological Investigation of Pathogens in 2016." FDA scientists will also participate in the ASM Microbe 2017 meeting. Information from such meetings holds promise for advancing FDA's ability to respond quickly and effectively to foodborne illness outbreaks and allows FDA to present information about the applications and public health impact of whole genome sequencing to members of the scientific community.

Developed Novel Technologies to Improve Food Safety

Addressing emerging safety concerns as food science technology advances remains a priority for the Foods Program. In FY 2016, FDA scientists used the results of a 3-year study of foodborne illness outbreaks associated with *Salmonella* Newport¹⁰ contaminated vegetables grown on the Delaware/Maryland/Virginia (Delmarva) peninsula to develop guidance to growers. FDA produce microbiologists helped to lead the research direction and focus of the Delmarva Food Safety Taskforce, the committee of scientists and extension specialists from the Delmarva states and FDA.

In another study aimed at understanding foodborne illness, Foods program scientists applied a new genomic tool known as RNASEQ technology for the first time. This technology actually detects the factors involved in providing survival differences among pathogens living in identical environments. Pilot studies with the technology have begun to reveal the adaptive traits that let *Salmonella* Newport to persist within tomatoes and other produce. These

⁹ *Listeria monocytogenes* are a bacterium that can cause Listeriosis, a serious infection usually caused by eating contaminated food. The disease primarily affects older adults, pregnant women, newborns, and adults with weakened immune systems. Rarely, persons without these risk factors can also be affected. The risk may be reduced by following recommendations for safe food preparation, consumption, and storage.

¹⁰ *Salmonella* is a bacteria that can cause diarrhea, fever, and abdominal cramps. For more information, see <http://www.cdc.gov/salmonella/general/index.html>.

adaptive traits provide potential targets for preventive controls against *Salmonella* known to invade produce production. Other Foods Program accomplishments include:

- Analyzed foods that list live microbes as an ingredient (such as probiotics) to conduct genomic characterization and identify bacteria that may be a safety concern
- Implemented rapid detection methods to improve detection of adulterated food products such as oil and honey
- Developed advanced methods for detecting allergens and gluten in foods, improving FDA's capabilities to inform and protect sensitive individuals from severe adverse effects.

Developed Seafood Product Labeling Online Learning Module

To ensure the proper labeling of seafood products sold in the U.S., FDA developed an online learning module for seafood producers, retailers, state regulators, and others involved in the processing, distribution, sale, or regulation of seafood.

The module explains federal identity labeling requirements for seafood and lists the laws, regulations, guidance documents, and other materials relevant to the proper labeling of seafood. The module helps stakeholders better understand FDA's role in ensuring the proper labeling of seafood. The module also provides tips for identifying mislabeled seafood in the wholesale distribution chain or at the point of retail.



Instead of protein profiles, FDA uses DNA barcoding to identify seafood. Barcoding provides a DNA sequence that allows analysts to identify different seafood products. These sequences are accessible online in a curated FDA library. This allows FDA field staff to better identify potentially toxic species of imported puffer fish currently restricted to a single species from Japan.

Encouraged the Safe Production of Dietary Supplements

In FY 2016, FDA initiated several regulatory actions to address ingredient safety for marketed dietary supplements. Additionally, FDA field investigators completed 678 domestic and 99 foreign inspections of firms to enforce dietary supplement regulations, including current Good Manufacturing Practices (cGMPs) and labeling requirements. These inspections and initiatives resulted in:

- 83 warning letters
- 6 untitled letters
- 49 detentions
- 3 injunctions.

FDA worked closely with the Department of Justice, the Federal Trade Commission, and the U.S. Postal Inspection Service to identify potentially unsafe or tainted products. This resulted in civil injunctions and criminal actions against 117 manufacturers and distributors of dietary supplements and tainted products.

Mandatory premarket safety notifications on new dietary ingredients (NDIs) in dietary supplements are vital to FDA's knowledge of marketed dietary ingredients. In FY 2016, FDA received 58 NDI notifications. FDA objected to 67 percent of the notifications because of inadequate safety, incomplete information, or other issues.

To address this high objection rate FDA issued revised draft guidance to industry in August 2016. This revised draft guidance explained when an NDI notification is necessary and what it should include. To clarify expectations of the NDI notification to stakeholders, FDA initiated regulatory actions aimed at ingredients that did not go through proper FDA review before being marketed.

In FY 2016, FDA received more than 4,600 voluntary and mandatory adverse event reports associated with dietary supplements. FDA reviewed these reports to identify products or ingredients with possible safety implications for the consumer. This review allowed FDA to target inspections and regulatory actions against unsafe products, such as pure powdered caffeine products.

In early FY 2016, FDA announced the creation of the Office of Dietary Supplements¹¹ (ODSP) within CFSAN. Elevating the program's position from a division to a new independent office raises the profile of the dietary supplements program within the agency. The creation of ODSP further enhances the effectiveness of dietary supplement regulation by allowing ODSP to better compete for government resources and capabilities to regulate this rapidly expanding industry.

Enhanced Food Emergency Response Network Capacity

To prepare for food-related emergencies and high-profile events, FDA directly oversees the Food Emergency Response Network (FERN) in addition to using FDA's field, Center, and FERN laboratories. FERN grants provide state-of-the-art equipment, analytical platforms,

¹¹ For more information on the creation of the Office of Dietary Supplements, please visit: <http://www.fda.gov/Food/NewsEvents/ConstituentUpdates/ucm478303.htm>

methodology, training, and proficiency testing. These resources support surge capacity, outbreak sampling, and large surveillance assignments. FERN grants also support the FERN training program that provides courses for both federal and state laboratory analysts. FDA maintains the FERN Storeroom that provides reagents and supplies to federal and state laboratories to support analytical activities. This program increases the FERN capacity and analytical capability for chemical, microbiological, and radiological testing that enhances the response to food emergency events—including food safety and food defense.

Exercised Science-Based Compliance Actions

When firms violate FDA requirements, FDA monitors firms and encourages prompt voluntary corrective action to obtain full compliance. When firms do not comply with FDA regulations, or FDA identifies a safety risk, FDA pursues regulatory action to prevent unsafe or improperly labeled products from reaching U.S. consumers.

FDA monitors the recalls of food, cosmetic, and dietary supplement products and ensures the removal of violative products from commerce. In FY 2016, FDA classified 330 Class I (most serious), 315 Class II, and 46 Class III human food recall events.

FDA issues import controls when non-compliant food products are discovered or when food companies manufacture or ship non-compliant products. In FY 2016, FDA issued 785 import alert notices.

FDA created Import Alert # 54-17 in response to high levels of mercury, arsenic and lead found in Ayurvedic supplements manufactured in India. This Import Alert imposed import controls for dietary supplements with levels of heavy metals high enough to make the product injurious to health. Particularly vulnerable populations susceptible to heavy metal poisoning include infants, small children, pregnant women, and people with underlying kidney disorders.

Additionally, CFSAN worked with the FDA field offices to assist in 767 cases where the district needed CFSAN's technical expertise to determine import admissibility.

FDA protects the public from impure, adulterated, and misbranded food and acts as an industry-wide deterrent for regulated entities and criminal enterprises through its authority to initiate criminal cases. In FY 2016, FDA issued six injunctions and one suspension related to adulterated or misbranded food.

Implemented New Procedures to Address Food Recalls

In 2016, FDA created a senior leadership team to direct FDA's actions to address challenging recall situations. The team, Strategic Coordinated Oversight of Recall Execution (SCORE), supports FDA's field staff and district offices by evaluating the range of FDA's compliance and enforcement authorities. SCORE quickly decides the best action to take to protect consumers.

For example, in September 2016 SCORE suspended a company's facility registration because a food product from the company was contaminated with *Listeria monocytogenes*. At the FDA's request, the company agreed to a recall and briefly stopped operations to improve its cleaning and sanitation procedures. In follow-up inspections FDA identified contaminated food using environmental sampling, and FDA suspended the firm's food facility registration.

Selected Guidances Issued in 2016

Below are non-FSMA guidances issued by the Foods Program in the last calendar year. These guidances help address various issues. This list does not represent any degree of importance or priority ranking among the published guidances.¹²

Date	#	Title	Description
Jan 2017	FDA-2016-D-4414	Draft Guidance for Industry: Questions and Answers on the Nutrition and Supplement Facts Labels Related to the Compliance Date, Added Sugars, and Declaration of Quantitative Amounts of Vitamins and Minerals	Provides information related to compliance with FDA's final rule: "Food Labeling: Revision of the Nutrition and Supplement Facts Labels" and discusses labeling of added sugars
Nov 2016	FDA-2016-D-3401	Draft Guidance for Industry: Scientific Evaluation of the Evidence on the Beneficial Physiological Effects of Isolated or Synthetic Non-digestible Carbohydrates Submitted as a Citizen Petition	Explains current thinking on information needed when submitting a citizen petition and the scientific review approach we plan to use for evaluating scientific evidence

¹² For more information on guidance please visit <http://www.fda.gov/Food/GuidanceRegulation/>

Sep 2016	FDA-2016-D-2241	Draft Guidance for Industry: Substantiation for Structure/Function Claims Made in Infant Formula Labels and Labeling	Helps infant formula manufacturers and distributors comply with certain labeling requirements for infant formula products.
Sep 2016	FDA-2016-D-2335	Guidance for Industry: Use of the Term “Healthy” in the Labeling of Human Food Products	Advises manufacturers who wish to use the implied nutrient content claim “healthy” to label their food products as provided by our regulations.
Date	#	Title	Description
Aug 2016	FDA-2011-F-0171	Draft Guidance for Industry: Calorie Labeling of Articles of Food in Vending Machines	Provides vending machine operators and industry with better understanding of how to comply with the rule on Labeling of Articles of Food in Vending Machines.
June 2016	FDA-2014-D-0055	Draft Guidance for Industry: Voluntary Sodium Reduction Goals: Target Mean and Upper Bound Concentrations for Sodium in Commercially Processed, Packaged, and Prepared Foods	Helps Americans achieve the Dietary Guidelines-recommended sodium levels by encouraging food manufacturers, restaurants, and food service operations to reduce sodium in foods.
Apr 2016	FDA-2011-F-0172	Guidance for Industry: A Labeling Guide for Restaurants and Retail Establishments Selling Away-From-Home Foods - Part II	Helps restaurants and similar retail food establishments understand nutrition labeling requirements.

Mar 2016	FDA-2013-D-0715	Guidance for Industry: Acrylamide in Foods	Provides information to help growers, manufacturers, and food service operators reduce acrylamide levels in certain foods.
Apr 2016	FDA-2016-D-1099	Draft Guidance for Industry: Inorganic Arsenic in Rice Cereals for Infants: Action Level	Protects public health by limiting 100 parts per billion of inorganic arsenic in infant rice cereals.

Published Infant Formula Rule and Guidances

Infant formulas are intended for a vulnerable population and may serve as a sole or primary source of nutrition during a critical period of growth and development. Caregivers of babies fed infant formula products must be able to trust that the information on the label is truthful, not misleading, and scientifically supported.

In September 2016, FDA issued guidance for industry to help infant formula manufacturers and distributors comply with certain labeling requirements for infant formula products. In this guidance,¹³ FDA clarifies the following infant formula labeling requirements.

Issued Draft Guidance on Structure and Function Claims Made in Infant Formula Labels and Labeling

In September 2016, FDA's Foods Program issued draft guidance for industry to help infant formula manufacturers who make structure and function claims comply with the requirement that all claims in infant formula labels and labeling be truthful and not misleading. "Structure and function" claims are statements made about the effects of a product or its constituent on the normal structure or function of the body. An example of a structure and function claim in infant formula labeling is a statement that the formula "supports digestion."

In the draft guidance¹⁴, FDA describes its recommendations for the type and quality of scientific evidence that is appropriate to support structure and function claims made about an infant formula by the product's manufacturers or distributors. The draft guidance provides recommendations for all infant formulas, including formulas marketed for use by infants who have inborn errors of metabolism or low birth weight, or who otherwise have unusual medical or dietary problems.

Created Internet Resource for Sampling Programs for Food Safety

¹³ Guidance for Industry: Labeling of Infant Formula,

<http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm517113.htm>

¹⁴ Substantiation for Structure/Function Claims Made in Infant Formula Labels and Labeling,

<http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm514640.htm>

In FY 2015, FDA developed a new public website to share microbiological surveillance information to help predict and prevent bacterial contamination. In FY 2016, FDA sampled and tested cucumbers and hot peppers under this program and published the test results on the website.¹⁵ This resource helps FDA shift to a prevention-based model by providing information needed to identify hazards. This resource also will help determine if contamination occurs due to factors such as season, region, or import status (domestic vs import).

Arsenic in Rice

In FY 2016, FDA continued to work with stakeholders to understand and address the risks associated with arsenic in food. Arsenic is a naturally occurring substance found in water, air, food, and soil in both an organic and the more toxic inorganic form. Arsenic can be found in many foods – including grains, fruits, and vegetables – due to absorption from the soil and water. Recently, FDA conducted more sophisticated sample analyses to quantify the presence of inorganic arsenic in foods. FDA’s sampling and risk analyses focused on rice and rice products for the following reasons:

- Rice has higher average levels of inorganic arsenic than other foods measured by FDA.
- Rice is an ingredient in a variety of foods and beverages, including foods for infants and young children.

In April 2016, FDA published proposed draft guidance to industry on the limit or “action level” recommended for inorganic arsenic in infant rice cereal. The proposed limit stems from the following FDA actions:

- extensive testing of rice and non-rice products
- scientific studies showing an association between adverse pregnancy outcomes and neurological effects in early life with inorganic arsenic exposure
- evaluation of the feasibility of reducing inorganic arsenic in infant rice cereal.

Launched Food Defense Plan Builder

In FY 2016, FDA published the final rule on “Focused Mitigation Strategies to Protect Food Against Intentional Adulteration” as part of its implementation of FSMA. The rule requires food facilities to develop and implement food defense plans.

FDA plans to update the Food Defense Plan Builder – a user-friendly software program that helps owners and operators of food facilities develop personalized food defense plans for their facilities. This user-friendly tool harnesses existing FDA tools, guidance, and resources for food

¹⁵Source: Microbiological Surveillance Sampling: FY16 Cucumbers and Hot Peppers, <http://www.fda.gov/Food/ComplianceEnforcement/Sampling/ucm473115.htm>

defense into one single application. The tool guides users through a series of sections, which include:

- Company Information
- Broad Mitigation Strategies
- Vulnerability Assessments
- Focused Mitigation Strategies
- Emergency Contacts
- Action Plan.

The information collected from each section automatically compiles a customized food defense plan for their facility. Since its launch in May 2013, the Food Defense Plan Builder received excellent reviews from industry. It has been downloaded more than 18,000 times by users from all over the world.

Improve and Safeguard Access

The Foods Program has statutory responsibility for the following premarket review activities that fall within the FDA goal of improving and safeguarding access:

- review and approval of all petitions for direct food additives
- review and approval of all new food contact substances, food contact materials, packaging, antimicrobials, and other indirect food additives
- review of Generally Recognized as Safe (GRAS) ingredients and products of biotechnology related to food.

Published Timely Food and Color Additive and Food Contact Substance Reviews

FDA has the primary legal responsibility for determining the safe use of food additives and color additives. To market a new food additive, color additive or food contact substance – or before using an additive already approved for one use in another manner not yet approved – a manufacturer or other sponsor must first petition FDA for its approval. This petition process is unique to FDA's regulatory mission. In FY 2016, FDA ensured safe access to the food supply by reviewing 7 Food and Color Additive Petitions, 73 GRAS notifications, and 111 premarket notifications for Food Contact Substances.

Updated Risk Assessment Capabilities

FDA Centers, led by CFSAN, continue to update FDA's Toxicological Principles for the Safety Assessment of Food Ingredients – also called the “Redbook” – so that it reflects the most recent science. FDA's overarching goal in this effort is to develop a framework that incorporates the assessment of ingredients in various products such as:

- food additives
- food contact substances
- ingredients that are generally regarded as safe (GRAS)
- new plant varieties
- dietary supplements and new dietary ingredients
- cosmetic ingredients.

The Centers plan to jointly develop a process to ensure use of consistent methodologies for safety and risk assessments throughout CFSAN, and between CFSAN and CVM.

Promote Informed Decisions

The Foods Program is responsible for ensuring that foods sold in the United States are safe, wholesome, and properly labeled. The Nutrition Labeling and Education Act (NLEA) requires most packaged foods to bear nutrition labeling. NLEA also requires food labels – that bear nutrient content claims and certain health messages – to comply with specific requirements.

The Foods Program serves as FDA's primary organization for directing, developing, and coordinating web communications, outreach, and consumer education. FDA has statutory responsibility for food safety, and has jurisdiction over all domestic and imported food except meat, poultry, and processed egg products that fall under the authority of the U.S. Department of Agriculture. Outreach is essential to ensure that consumers and food safety partners have the information needed to make informed decisions.

Provide Outreach and Education on FDA Regulated Products

FDA strives to provide consumers with material about healthy choices using the most up-to-date science. CFSAN's social scientists use scientific methods to learn about and understand human behavior to help FDA fulfill its public health mission. In FY 2016, CFSAN conducted consumer studies using a variety of methods such as focus groups, surveys, and eye tracking studies. In one study FDA surveyed 4,169 Americans ages 18 and older to learn more about consumers' attitudes, behaviors, and knowledge of food safety. Survey results inform FDA's efforts to

improve consumer food safety behaviors through targeted education outreach. Results are also used in the Healthy People 2020 initiative¹⁶.

In 2016, FDA released findings from its 2014 Health and Diet Survey. This survey helps FDA make informed regulatory, educational, and other decisions with a better understanding of consumer knowledge, attitudes, and practices about current and emerging nutrition and labeling issues¹⁷.

¹⁶ Food Safety Survey Shows Consumer Knowledge Up, Still Room to Grow, <http://www.fda.gov/Food/NewsEvents/ConstituentUpdates/ucm529604.htm>

¹⁷ FDA Releases 2014 Health and Diet Survey Findings, <http://www.fda.gov/Food/NewsEvents/ConstituentUpdates/ucm499141.htm>

Issued Final Guidance for Updates to the Nutrition Facts Label, Menu, and Vending Machine Labeling Requirements

In FY 2016, FDA finalized updates to the Nutrition Facts label that require declaration of the percent daily value for added sugars, and change the current footnote on the Nutrition Facts label to help consumers understand the percent daily value concept. FDA also finalized a 2014 proposal to update FDA's serving size requirements. These updates feature a fresh design to highlight key parts of the label such as calories and serving sizes. This information will help consumers to make healthy food choices. Most food manufacturers will be required to use the new label by July 2018.

In April 2016, FDA issued final guidance to help companies comply with the menu labeling final rule. The Menu Labeling Regulation requires certain restaurants and similar retail food establishments selling restaurant-type foods to disclose calorie information on their menus and menu boards for standard menu items and to disclose calorie information for foods on display and self-service foods that are standard menu items. Covered establishments must have the required additional written nutrition information available onsite upon consumer request. Throughout 2016, FDA hosted public workshops about menu labeling in three different geographic locations to help industry comply with these new requirements.

Issued Requests for Information and Draft Guidance on Fiber and Use of the term "Healthy" in Food Labeling

In November 2016, FDA's Foods Program issued a Request for Information (RFI) and Draft Guidance on Fiber on the Nutrition Facts Label. The request for information, along with the accompanying draft guidance, will help industry understand how FDA reviews the scientific evidence to determine whether other fibers beyond the seven identified in the rule should be added to the regulations. It also provides an opportunity for stakeholders to add to or comment on FDA's review of the science with respect to whether any of 26 additional types of fiber are beneficial to human health and therefore should be included in the fiber definition.

In September 2016, the Foods Program published a Request for Information (RFI) and Guidance for Industry on the Use of the term "Healthy" in the Labeling of Human Food Products. The guidance advises manufacturers who wish to use the implied nutrient content claim "healthy" to label their food products in accordance with FDA's regulations.

More specifically, this guidance is intended to advise food manufacturers of FDA's intent to exercise enforcement discretion relative to foods that use the implied nutrient content claim "healthy" on their labels which:

- Are not low in total fat, but have a fat profile makeup of predominantly mono and polyunsaturated fats; or

- Contain at least ten percent of the Daily Value (DV) per reference amount customarily consumed (RACC) of potassium or vitamin D.

Issued Draft Guidance for Industry Voluntary Sodium Reduction Goals

In June 2016, FDA issued voluntary guidance to help Americans meet the Dietary Guidelines' recommended sodium levels. This voluntary guidance encourages food manufacturers, restaurants, and food service operations to reduce sodium in foods and is intended to complement existing efforts by food manufacturers, restaurants, and food service operations to achieve these goals.

Approximately 75 percent of total sodium intake comes from processed and commercially prepared (e.g., restaurant) foods. FDA recognizes the important role of sodium in food for microbial safety, stability, and other functions. This guidance is not intended to undermine these functions. Instead the guidance is intended to provide measurable voluntary short-term (2 year) and long-term (10 year) goals for sodium content in commercially processed, packaged, and prepared foods to reduce excess population sodium intake.

FDA Developed Improved Method for Attributing Foodborne Illness (in Collaboration with Federal Partners)

FDA, working with the Centers for Disease Control and Prevention (CDC) and USDA's Food Safety Inspection Service, developed an improved method for analyzing outbreak data to determine which foods are responsible for illnesses related to four major foodborne bacteria.

The three agencies, operating as a partnership known as the Interagency Food Safety Analytics Collaboration (IFSAC), released a paper titled "Comparing Characteristics of Sporadic and Outbreak-Associated Foodborne Illnesses, United States, 2004-2011."

The results of this study provide evidence that *Campylobacter*, *Listeria monocytogenes*, and *E. coli* O157 outbreak illnesses are not significantly different from sporadic illnesses with respect to patients' illness severity, gender, and age. The study also provides evidence that *Salmonella* outbreak illnesses are not significantly different from sporadic illnesses with respect to illness severity and gender. Analyses, such as this study, help us better understand the relationship between sporadic foodborne illnesses and those that are identified as a part of an outbreak. Such analyses are essential to advancing scientific progress in this field.

Investigated Adverse Event Reports Related to the Use of Cosmetic Products

In an effort to protect consumers from potentially dangerous cosmetics products, FDA initiated an investigation on reports of hair loss, hair breakage, balding, itching, and rash associated with the use of WEN by Chaz Dean Cleansing Conditioner products. As of November 15, 2016, FDA received 1,386 adverse event reports directly from consumers with some reports occurring

after general outreach to consumers and health care professionals. Of note, FDA was made aware, during inspections of manufacturing and distribution facilities, of more than 21,000 complaints reported directly to Chaz Dean, Inc. and Guthy Renker, LLC. This is the largest number of adverse event reports associated within the category of cosmetic hair cleansing products. The FDA also has reached out to physicians and other health care providers asking them to notify their patients of hair loss and other complaints associated with the use of these products and to report adverse events to the agency. FDA encourages consumers to stop using these products if they have a reaction, contact their health care provider, and report the incident to FDA.

Developed Additional Education Materials Related to Risks Associated with Tattoo Inks

State and local authorities oversee the practice of tattooing. However, ink and color additives (such as pigments) used in tattoos are subject to FDA oversight. The CFSAN Adverse Event Reporting System (CAERS) database continues to receive adverse event reports associated with tattoo inks. These reports include infections from tattoo inks contaminated with microorganisms, and allergic reactions to ingredients in the inks.

FDA developed educational materials to alert consumers to potential problems from tattooing and difficulties with tattoo removals. FDA is continuing research projects on the safety and quality of tattoo inks and pigments.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2014 Actual	\$882,814,000	\$882,814,000	\$0
FY 2015 Actual	\$903,340,000	\$903,340,000	\$0
FY 2016 Actuals	\$998,230,000	\$998,230,000	\$0
FY 2017 Annualized CR	\$992,972,089	\$981,386,089	\$11,586,000
FY 2018 President's Budget	\$922,014,000	\$910,428,000	\$11,586,000

BUDGET REQUEST

The FY 2018 Budget Request for the Foods Program is \$922,014,000, of which \$910,428,000 is budget authority and \$11,586,000 is user fees. Budget authority decreases by -\$70,958,000 compared to the FY 2017 Annualized CR level and user fees remain flat. The Center for Food Safety and Applied Nutrition (CFSAN) amount in this request is \$277,643,000. The Office of Regulatory Affairs amount is \$632,785,000.

In FY 2018, the Foods Program will continue its most critical public health and safety activities. For CFSAN, these activities include: responding to outbreaks, working with industry to

implement FSMA regulations, reviewing infant formula notifications, helping to ensure the safety of dietary supplements, conducting reviews of food ingredients and packaging, and ensuring that foods are safe and properly labeled. ORA will maintain food manufacturing inspections conducted through state contracts and will be able to keep reductions to the Voluntary National Retail Food Regulatory Program Standards (VNRFRPS) to a minimum.

BUDGET AUTHORITY

Reductions (-\$70.9 million)

Center: -\$21.8 million (Food Safety)

CFSAN will absorb funding reductions by reducing FTE through attrition and reducing operating expenses. FDA will balance reducing the federal footprint with providing specialized staff expertise to inform the Agency's response to the large volume of incoming work from a diverse array of stakeholders. FDA's goal is to minimize the impact of these reductions on FDA's core mission activities.

CFSAN will continue support for partnerships with academic institutions, state and local health organizations, and other groups that play a key role in outreach, research, and training needed to support FDA's food safety mission at reduced levels. CFSAN's support will be at reduced levels overall, which may include the elimination of support for some partnerships, such as the Centers of Excellence.

CFSAN will continue research, cosmetics safety, and international outreach activities at reduced levels.

Field: -\$49.1 million (Food Safety)

The FY 2018 Budget continues partnerships, training, IT and lab equipment, and program office operations at reduced levels. Resources for operational activities including field exams, import entry review, investigations, sample analysis, and inspections for surveillance, compliance, and follow up activities, both domestically and abroad are a priority. ORA will reduce existing workforce levels through attrition. FDA will prioritize maintaining operational activity levels with its existing staff at the proposed levels in the FY 2018 Budget.

Reduced investments in IT and lab equipment, and its related maintenance and operating expenses will require FDA to reprioritize and refocus ORA's resources for analyzing samples for surveillance and compliance purposes and for detection of emerging threats or potential outbreaks from contamination or adulteration. In the event of a food related outbreak, FDA would readjust its prioritization and reallocate resources from other less urgent operational activities in order to respond to emerging issues. Other areas of decreased investments include partnerships and training.

ORA will continue state cooperative agreements at reduced funding levels; those include agreements for:

- the Food Emergency Response Network (FERN), a network able to respond to biological, chemical, or radiological food contamination emergencies
- the International Standards Organization (ISO) accreditation which supports non-FDA laboratories in achieving and maintaining this accreditation
- the Manufactured Food Regulatory Program Standards (MFRPS), which help develop and implement standards for federal and state programs to better direct regulatory activities toward reducing foodborne illness
- the retail food protection standardization program, which helps prevent foodborne illness associated with the preparation, service, and sale of foods in food service and retail establishments.

PERFORMANCE

The Foods Program's performance measures focus on premarket application review, incidence of foodborne pathogens, regulatory science activities, and postmarket inspection and import screening activities in order to ensure the safety and proper labeling of the American food supply and cosmetics, as detailed in the following table.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
<u>213301</u> : Complete review and action on the safety evaluation of direct and indirect food and color additive petitions, within 360 days of receipt. (Output)	FY 2016: 100% Target: 80% (Target Exceeded)	80%	80%	Maintain
<u>214101</u> : Number of state, local, and tribal regulatory agencies in the U.S. and its Territories enrolled in the draft Voluntary National Retail Food Regulatory Program Standards. (Outcome)	FY 2016: 711 enrolled Target: 682 enrolled (Target Exceeded)	697	712	+15
<u>212404</u> : Reduce the incidence of infection caused by key pathogens commonly transmitted by food: <i>Campylobacter</i> species. (Outcome)	CY 2015: 12.97 cases/100,000 CY 2015 Target: 11.0 cases/100,000 (Target Not Met)	10.2 cases/100,000	9.7	-0.5
<u>212405</u> : Reduce the incidence of infection caused by key pathogens commonly transmitted by food: Shiga toxin-producing <i>Escherichia coli</i> O157:H7. (Outcome)	CY 2015: 0.95 cases/100,000 CY 2015 Target: 0.95 cases/100,000 (Target Met)	0.83 cases/100,000	0.76	-0.07
<u>212407</u> : Reduce the incidence of infection caused by key pathogens commonly transmitted by food: <i>Salmonella</i> species. (Outcome)	CY 2015: 15.89 cases/100,000 CY 2015 Target: 13.6 cases/100,000 (Target Not Met)	12.8 cases/100,000	12.4	-0.4
<u>212410</u> : Reducing foodborne illness in the population. By December 31, 2017, working	CY 2015: .24 cases/100,000 (Historical Actual)	0.22 cases/100,000	0.22	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
with federal, state, local, tribal, and industry partners, improve preventive controls in food production facilities and reduce the incidence rate (reported cases per 100,000 population per year) of <i>Listeria monocytogenes (Lm)</i> infections by 8%. (Outcome)				
<u>214306</u> : The average number of working days to serotype priority pathogens in food (Screening Only) (Output)	FY 2016: 3 working days Target: 3 working days (Target Met)	3 working days	3 working days	Maintain
<u>214212</u> : Percentage of planned import food field exams (approximately 160,000 in total). (Output)	FY 2016: 172,449 Target: 160,158 (Target Exceeded)	99%	99%	Maintain
<u>214206</u> : Maintain accreditation for ORA labs. (Outcome)	FY 2016: 13 labs Target: 13 labs (Target Met)	13 labs	13 labs	Maintain
<u>214209</u> : As required by the FSMA Legislation, cover all of the High Risk domestic inventory (approximately 19,000 firms) every three years. (Output)	FY 2016: 99.8% Target: 100% (Target Not Met)	33%	66%	Maintain
<u>214305</u> : Increase laboratory surge capacity in the event of terrorist attack on the food supply. (Radiological and chemical samples/week). (Outcome)	FY 2016: 2,500 rad & 2,100 chem Target: 2,500 rad & 2,100 chem (Target Met)	2,500 rad & 2,100 chem	2,500 rad & 2,100 chem	Maintain

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

Food Additive and Color Additive Petition Review

The Foods Program conducts an extensive review as part of its Food Additive and Color Additive Petition review process, which includes a Chemistry, Toxicology and Environmental evaluation. The current measure requires FDA to complete review and action on the safety evaluation of direct and indirect food and color additive petitions within 360 days of receipt. FDA exceeded the FY 2016 target of 80 percent by reviewing and completing 100 percent of the petitions received within 360 days of receipt, a result consistent with the FY 2015 performance of 100 percent completed within the same timeframe.

Voluntary National Retail Food Regulatory Program Standards

Strong and effective regulatory programs at the state, local and tribal level are needed to prevent food borne illness and reduce the occurrence of food borne illness risk factors in retail and foodservice operations. The voluntary use of the Retail Program Standards by a food inspection program reflects a commitment toward continuous improvement and the application of effective risk-based strategies for reducing food borne illness. The FY 2016 target for enrollment of State, local and tribal agencies in the Retail Program Standards was far exceeded. Awareness of the value of the using the Retail Program Standards to drive program improvement continues to grow, particularly among local health departments. In addition, more retail food regulatory programs are recognizing that FDA cooperative agreement funds are available to jurisdictions that enroll in the Retail Program Standards and commit to achieving key milestones. The FY 2017 and FY 2018 targets reflect increases in the number of enrollees by 15 above the previous year's actual number of enrollees or target.

Foodborne Illness

FDA's Priority Goal to reduce foodborne illness is a long-term outcome goal that reflects FDA's efforts, along with our partners in CDC and NIH, to decrease the rate of *Listeria monocytogenes* (*L.m.*). *L.m.* infections are one of the leading causes of death from foodborne illness in the United States, resulting in an estimated 1,600 illnesses and 260 deaths each year. With enactment of the 2011 Food Safety Modernization Act (FSMA), Congress mandated a paradigm shift to prevention – to establishing a modern system of food safety protection based not on reacting to problems, but on preventing them from happening in the first place. Over the next two years, concentrated efforts to 1) improve preventative controls through inspections and technical guidance to industry, 2) improve surveillance and detection using whole genome sequencing of *L.m.* isolates, and 3) improve response by more accurately linking illnesses and outbreaks to the food that caused the illness, should lead to a reduction in the overall *L.m.* rate.

Pathogen Detection

FDA microbiologists are evaluating and integrating commercially available instrumentation into its microbiological testing workflow that is vastly improving the ability of FDA to more quickly and effectively detect and characterize foodborne pathogens such as Salmonella directly from the food supply. Improvements in sample throughput, along with the high degree of sensitivity and specificity built into new pathogen detection technologies, will dramatically improve FDA's foodborne response and traceback capabilities. When fully deployed, technologies such as next-generation whole-genome sequencing (WGS) and others will reduce the time to conduct these analyses from 14 days originally to just a few days. One updated technology which provides highly accurate and rapid Salmonella serotype results for FDA, known as the flow cytometry/fluorescence platform, has been validated extensively and is now deployed in nearly all FDA field laboratories, as well as in CFSAN and CVM laboratories. In FY 2016, FDA met the target of reducing the average number of days to serotype priority pathogens in foods to three days. The proposed targets for FY 2017 and FY 2018 are three days, maintaining the critically important downward progress in analytical return times achieved in FY 2016.

FSMA High Risk Domestic Inspection Coverage

FDA is committed to ensuring that the U.S. food supply continues to be among the safest in the world. ORA plays a critical role in the implementation of FSMA, and recognizes the importance of complying with high-risk domestic inspections mandated by FSMA legislation. FSMA legislation requires inspecting the entire high-risk domestic inventory every three years. This goal serves to cumulatively track the progress over the three-year period as the coverage of the high-risk domestic inventory approaches the FSMA-driven goal of 100 percent. FY 2016 marked the final year of a three-year cycle.

The identified inventory to be inspected at the beginning of the FY 2014 to F 2016 cycle was approximately 19,000 firms; however this inventory number does not remain static over the course of the inspection cycle. Therefore as the inventory changes over the three-year period, FDA must make adjustments to work plans to meet the 100 percent target. Upon completion of FY 2016, the cumulative percentage reached 99.8 percent, very nearly achieving the 100 percent target. This high level of accomplishment was achieved despite the dynamic and uncertain conditions facing FDA. For example, given that this goal tracks the inspections of the high-risk inventory there are more likely to be issues uncovered during these inspections. This requires ORA to redirect resources to conduct follow-up actions and reinspections, which use resources that otherwise would be deployed for inspecting the rest of the required inventory. The near-miss of the 100 percent target in FY 2016 resulted from a combination of changes in the inventory and utilization of resources for follow up or reinspections conducted within the domestic foods high-risk inventory that count as inspections but do not count toward additional

coverage of the inventory, as these are inspections conducted at the same firm more than once.

FY 2017 marks the beginning of a new cycle and the target returns to 33 percent to signify that FDA is targeting the first third of the inventory for the new three-year cycle. FDA came very close to meeting our FY 2016 goal of 100 percent, and most of the remaining FSMA high risk firm inspections were completed in early FY 2017.

PROGRAM ACTIVITY DATA TABLES**Foods Program Activity Data**

CFSAN Workload and Outputs	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
Food and Color Additive Petitions			
Petitions Filed ¹	7	7	7
Petitions Reviewed ²	7	7	7
Premarket Notifications for Food Contact Substances			
Notifications Received	99	130	130
Notifications Reviewed ³	111	128	128
Infant Formula Notifications			
Notifications Received ⁴	23	22	22
Notifications Reviewed ⁵	19	18	18
FDA Review Time	90 days	90 days	90 days
New Dietary Ingredient Notifications			
Notifications Received ⁶	58	66	66
Notifications Reviewed ⁷	56	66	66
FDA Review Time	75 days	75 days	75 days

¹ This number is for the cohort of petitions filed in the FY.

² Number reviewed includes petitions approved, withdrawn, or placed in abeyance due to deficiencies during the FY.

³ Number reviewed includes notifications that became effective or were withdrawn.

⁴ A notification may include more than 1 infant formula.

⁵ Number of submissions reviewed includes some submissions that were received in the previous FY.

⁶ Number of submissions received in current FY includes some received late in the FY that are expected to be completed in the next FY when the due date occurs.

⁷ Number of submissions reviewed in the current FY includes some submissions that were received in the previous FY when the due date occurred in the current FY.

Field Foods Program Activity Data (PAD)

Field Foods Program Workload and Outputs	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	7,933	8,000	8,000
Domestic Food Safety Program Inspections	5,783	Activities no longer planned to this level due to enactment of FSMA and alignment of resources into only high and low risk categories.	Activities no longer planned to this level due to enactment of FSMA and alignment of resources into only high and low risk categories.
Imported and Domestic Cheese Program Inspections	182		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	249		
Domestic Fish & Fishery Products (HACCP) Inspections	716		
Import (Seafood Program Including HACCP) Inspections	321		
Juice HACCP Inspection Program (HACCP)	161		
Interstate Travel Sanitation (ITS) Inspections	922		
Domestic Field Exams/Tests	2,398	2,500	2,500
Domestic Laboratory Samples Analyzed	16,927	13,000	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS	1,269	1,400	1,400
All Foreign Inspections	1,269	1,400	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	9,202	9,400	9,400
IMPORTS			
Import Field Exams/Tests	252,766	168,200	168,200
Import Laboratory Samples Analyzed	23,736	35,300	35,300
Import Physical Exam Subtotal	276,502	203,500	203,500
Import Line Decisions	13,952,537	14,650,164	15,382,672
Percent of Import Lines Physically Examined	1.98%	1.39%	1.32%
Prior Notice Security Import Reviews (Bioterrorism Act Mandate)	87,817	80,000	80,000
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	8,952	9,088	9,088
UNIQUE COUNT OF STATE PARTNERSHIPS FOOD ESTABLISHMENT INSPECTIONS	676	100	100
State Contract Food Safety (Non HACCP) Inspections	7,897	8,000	8,000
State Contract Domestic Seafood HACCP Inspections	964	1,000	1,000
State Contract Juice HACCP	91	100	100
State Contract LACF	110	100	100
State Partnership Inspections	676	100	100
State Contract Foods Funding	\$13,283,752	\$13,682,265	\$14,092,732
Number of FERN State Laboratories	19	19	19
Number of Food Safety State Laboratories	15	15	15
Annual FERN State Cooperative Agreements/Operations Funding	\$19,038,534	\$17,705,837	\$16,466,428
Total State & Annual FERN Funding	\$32,322,286	\$31,388,101	\$30,559,161
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	18,830	18,588	18,588

Field Cosmetics Program Activity Data (PAD)

Field Cosmetics Program Workload and Outputs	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget
<i>FDA WORK</i>			
DOMESTIC INSPECTIONS			
<i>UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS</i>	<i>133</i>	<i>100</i>	<i>100</i>
Domestic Inspections	133	100	100
FOREIGN INSPECTIONS			
<i>UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS</i>	<i>3</i>	<i>0</i>	<i>0</i>
Foreign Inspections	3	0	0
IMPORTS			
Import Field Exams/Tests	12,036	1,600	1,600
Import Laboratory Samples Analyzed	393	400	400
Import Physical Exam Subtotal	12,429	2,000	2,000
Import Line Decisions	2,939,034	3,085,986	3,240,285
Percent of Import Lines Physically Examined	0.42%	0.06%	0.06%
<i>GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS</i>	<i>136</i>	<i>100</i>	<i>100</i>

¹ The FY 2016 actual unique count of foreign inspections includes 178 OIP inspections (147 for China, 9 for India, & 22 for Latin America).

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HUMAN DRUGS

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
Human Drugs.....	1,390,656	1,451,570	1,324,422	1,611,504	287,082
<i>Budget Authority.....</i>	<i>487,332</i>	<i>487,299</i>	<i>486,398</i>	<i>179,139</i>	<i>-307,259</i>
<i>User Fees.....</i>	<i>903,324</i>	<i>964,271</i>	<i>838,024</i>	<i>1,432,365</i>	<i>594,341</i>
Center.....	1,185,398	1,267,547	1,119,903	1,414,764	294,861
Budget Authority.....	351,163	351,135	350,488	94,353	-256,135
User Fees.....	834,235	916,412	769,415	1,320,411	550,996
Prescription Drug (PDUFA).....	601,643	617,004	533,134	795,071	261,937
Generic Drug (GDUFA).....	215,867	286,312	219,018	451,771	232,753
Biosimilars (BsUFA).....	16,298	12,007	16,706	72,976	56,270
Outsourcing Facility.....	427	1,089	557	593	36
Field.....	205,258	184,023	204,519	196,740	-7,779
Budget Authority.....	136,169	136,164	135,910	84,786	-51,124
User Fees.....	69,089	47,859	68,609	111,954	43,345
Prescription Drug (PDUFA).....	12,276	8,662	10,878	37,391	26,513
Generic Drug (GDUFA).....	55,167	38,403	55,973	71,717	15,744
Biosimilars (BsUFA).....	1,382	400	1,416	2,485	1,069
Outsourcing Facility.....	264	394	342	361	19
FTE.....	5,681	5,681	5,935	6,472	537

Authorizing Legislation: Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321-399); Public Health Service Act of 1944 (42 U.S.C. 201); Federal Advisory Committee Act (FACA) of 1972 as amended; Orphan Drug Act of 1983 (21 U.S.C. 360ee); Drug Price Competition and Patent Term Restoration Act of 1984 (Section 505(j) 21 U.S.C. 355(j)) (a.k.a. "Hatch Waxman Act"); Prescription Drug Marketing Act (PDMA) of 1987 (21 U.S.C. 353); Anti-Drug Abuse Act of 1988; Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 201); Orphan Drug Amendments of 1988; Generic Drug Enforcement Act of 1992; Prescription Drug User Fee Act (PDUFA) of 1992; FDA Export Reform and Enhancement Act of 1996; Food and Drug Administration Modernization Act (FDAMA) of 1997; Public Health Security and Bioterrorism Preparedness and Response Act of 2002; Best Pharmaceuticals for Children Act (BPCA) of 2002; Freedom of Information Act (FOIA) as amended in 2002 (5 U.S.C. § 552); Pediatric Research Equity Act (PREA) of 2003; Project Bioshield Act of 2004 (21 U.S.C. 360bbb-3); Food and Drug Administration Amendments Act (FDAAA) of 2007; Public Health Service Act of 2010 (42 U.S.C. 262); Protecting Patients and Affordable Care Act of 2010; Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA); Drug Quality and Security Act (2013); Sunscreen Innovation Act (2014); Adding Ebola to the FDA Priority Review Voucher Program Act (2014); 21st Century Cures Act (Cures Act) (2016)

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

FDA's Human Drugs Program is responsible for ensuring the safety and efficacy of new, generic, and over-the-counter (OTC) drug products,



monitoring marketed drug products to ensure patient safety, and monitoring drug quality. The Center for Drug Evaluation and Research (CDER) and the Office of Regulatory Affairs (ORA) field drugs program are the components of FDA's Human Drugs Program, which operates with funding from budget authority and user fees.

The Program's mission is to promote and protect public health by helping to ensure that human drugs are safe and effective for their intended use, that they meet established quality standards, and that they are available to patients. The Human Drugs Program supports the FDA priorities of improving health care quality and reducing health care costs.

The following selected accomplishments demonstrate the Human Drugs Program's delivery of its regulatory and public health responsibilities within the context of current priorities.

Improve and Safeguard Access

Within this Goal area, the Human Drugs Program addresses the FDA Strategic Priorities including Regulatory Science, Globalization, Safety and Quality, and Smart Regulation.

The goal of the Human Drugs Program is to promote the public health by ensuring that prescription and OTC human drug products, including brand-name and generic products, are safe and effective. In addition, FDA aims to ensure that novel prescription drugs become available in a timely manner without compromising high standards of safety and efficacy.

In calendar year 2016, CDER approved 22 novel new drugs. From 2007 through 2015, CDER has averaged about 30 novel new drug approvals per year. Novel new drugs are often innovative products that serve previously unmet medical needs or otherwise significantly help to advance patient care and public health.

The Human Drugs Program employs a variety of regulatory tools including FDA's expedited development and review programs – fast track, priority review, accelerated approval, and new breakthrough therapy designation. Early and repeated communications with sponsors have also been helpful in expediting these products to market.

FDA is working to increase the speed and efficiency in several areas in the clinical trial phase of drug development. FDA's efforts include:

- accepting flexible clinical development designs
- meeting frequently and working closely with industry sponsors throughout the development process to plan efficient clinical trial programs and agree on needed data

- helping create clinical trial networks and “master protocols,” where appropriate, to greatly reduce the cost of conducting clinical trials and reduce the time needed to carry them out.

FDASIA Implementation

FDA’s recent accomplishments include implementing several components of the Food and Drug Safety and Innovation Act of 2012 (FDASIA). This authority allows FDA to protect the public health by providing an administrative process for the description of certain drugs refused for import into the United States, thus increasing the integrity of the drug supply chain.

Drug Shortages

Drug shortages can delay or deny needed care for patients. Drugs in short supply may also lead health care professionals to rely on alternative drug products, which may be less effective or associated with higher risks than the drug in shortage. With the passage of FDASIA, regulations were put in place which allowed FDA to begin to gain control over these staggeringly high numbers and effectively hold industry accountable to require early notification of discontinuances or interruptions in manufacturing of all covered prescription drugs. These requirements have helped FDA to work with industry early on to address problems before shortages occur and have resulted in decreasing numbers of new shortages in recent years.

FDA continues to make significant progress in reducing the number of drug shortages, from a high of 251 new shortages in 2011 to just 23 new shortages in 2016. Currently, FDA is working to resolve over 46 shortages that began prior to 2016 and persisted through the end of 2016, which is a decrease from over 64 ongoing shortages tracked at the end of 2015.

During 2016, FDA launched an external collaboration portal for industry. The CDER Direct NextGen Collaboration Portal enables sponsors to submit drug shortage notifications to FDA based on FDA-validated product information, such as National Drug Code (NDC), active ingredient, and product name. The Portal allows industry users to log in, enter their shortage information, and submit notifications directly into the CDER Shortage Tracker. This online capability will help to minimize manual data entry and track notifications for better drug shortage monitoring and mitigation.

User Fees

FDA has continued implementation of two user fee programs under FDASIA – the Generic Drug User Fee Amendments (GDUFA) and the Biosimilars User Fee Act (BsUFA) – as well as the fifth authorization of the Prescription Drug User Fee Act (PDUFA V). GDUFA and BsUFA continue to deliver tremendous public health benefits resulting from the availability of generic drugs and biosimilar biological products which provide patients with more affordable treatments. PDUFA V ensured FDA continued to receive consistent funding from FY 2013 through FY 2017,

enhancing its capacity to fulfill its mission of bringing novel drug products for patients to the market.

New Drug Review

One of the key programs under PDUFA V has been the new molecular entity (NME) review program (the Program). Under PDUFA V, FDA has established a modified review program for NME New Drug Applications (NDAs) and original Biologics License Application (BLAs) received from October 1, 2012, through September 30, 2017. The goals of the Program are to increase the efficiency and effectiveness of the first review cycle and decrease the number of review cycles necessary for approval. The Program provides new opportunities for communication between applicants and the FDA review team during the FDA's review of these highly complex applications and additional review time for FDA and applicants to address review activities that occur late in the review cycle.

As of September 30, 2016 FDA has received 216 applications through this Program since its inception, which involves a more interactive review with applicants. All of the FY 2015 program cohort applications that received actions by September 30, 2015, were acted on within the goal date. The FY 2015 program cohort is nearly closed, and 95 percent of applications were acted on within the goal date. FDA will continue to focus on these highly innovative products that represent important new medicines for the American people.

Generic Drug Review

Generic drug review is a high priority for the Human Drugs Program, and the review function supports the larger FDA mission of promoting and protecting public health. With increasing healthcare costs, many Americans face challenges in accessing medically necessary drug products.

The passage of the GDUFA brought high expectations for the timely review of human generic drug applications, creating risk-based parity between inspections of domestic and foreign firms, and reducing the backlog (i.e., applications pending prior to the implementation of GDUFA on October 1, 2012) of human generic drug applications. Pursuant to GDUFA's design, FDA executed a deep, foundational restructuring of the generic drug program including the hiring and training of many new employees, replacing fragmented information technology systems with a new integrated system, and substantially enhancing review and business processes.

FDA's efforts to lay the foundation for a modern generic drug program have positioned the Agency to meet goals through the end of GDUFA I, September 30, 2017. FDA is on track to

meet and in many cases exceed its GDUFA goals.¹⁸ For example, FDA achieved GDUFA's 90 percent goal well ahead of schedule. 2016 marked the highest number of generic drug approvals and tentative approvals ever – more than 800.

FDA will continue modernizing the generic drug program by focusing efforts on improving the efficiency, quality, and predictability of the human generic drug program ensuring that Americans have timely access to safe, effective, high quality, and low cost human generic drugs.

Biosimilars

BsUFA supports the review process for biosimilar biological products. The Biosimilar Product Development (BPD) Program was created as a part of BsUFA to provide a mechanism and structure for the collection of development-phase user fees to support FDA's biosimilar review program activities. BsUFA also includes the collection of original and supplemental application user fees, and product and establishment fees.

As of April 21, 2017, 66 programs were in the BPD Program. CDER has received meeting requests to discuss the development of biosimilar products for 23 different reference products. (Note: A biosimilar product is no longer in the BPD program after a 351(k) BLA is accepted for review (i.e., filed). FDA has licensed five biosimilar products to date: Zarxio (filgrastim-sndz), which has been determined to be biosimilar to Neupogen; Inflectra (infliximab-dyyb) and Renflexis (infliximab-abda), which have been determined to be biosimilar to Remicade; Erelzi (etanercept-szzs), which has been determined to be biosimilar to Enbrel; and Amjevita (adalimumab-atto) which has been determined to be biosimilar to Humira. These significant accomplishments represent the next step to increasing treatment options for patients.

In April 2015, FDA finalized three guidances: "Scientific Considerations in Demonstrating Biosimilarity to a Reference Product;" "Quality Considerations in Demonstrating Biosimilarity of a Therapeutic Protein Product to a Reference Product;" and "Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009." In December 2016, FDA finalized the guidance, "Clinical Pharmacology Data to Support a Demonstration of Biosimilarity to a Reference Product." These guidances are part of the series to implement the BPCI Act. FDA also issued draft guidance in May 2015, "Biosimilars: Additional Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009," providing new and revised questions and answers from sponsors interested in developing proposed biosimilar products.

¹⁸ For a full description of the FDA's goals see the GDUFA Commitment Letter. For a full description of FDA's performance under GDUFA, see <http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/default.htm>.

FDA also issued draft guidance for industry in April 2016, “Labeling for Biosimilar Products,” which, when finalized, will assist applicants in developing draft labeling for submission in applications for proposed biosimilar products under section 351(k) of the PHS Act.

In addition, in January 2017 FDA finalized the guidance for industry, “Nonproprietary Naming of Biological Products,” which describes how biological products licensed under the Public Health Service Act (PHS Act) should be named. The final guidance describes the FDA’s current thinking and intention to designate a nonproprietary name for originator (reference) biological products, related biological products, and biosimilar products licensed under the PHS Act (351(a) and 351(k)) that includes a suffix composed of four lowercase letters attached with a hyphen to the core name each product. As stated in the final guidance, FDA is continuing to consider the appropriate suffix format for interchangeable products.

FDA issued a proposed rule in August 2015, “Designation of Official Names and Proper Names for Certain Biological Products.” This proposed rule would designate nonproprietary names that include a suffix for six previously licensed biological products. FDA is continuing to consider comments on the proposed rule, including comments on the appropriate timeframe for implementing the changed nonproprietary name in product labeling.

On January 17, 2017, the FDA issued a Draft Guidance for Industry: “Considerations in Demonstrating Interchangeability With a Reference Product.” The guidance provides an overview of important scientific considerations in demonstrating interchangeability of a proposed therapeutic protein product with a reference product for the purposes of submitting a marketing application or supplement under section 351(k) of the PHS Act. This guidance is specific to interchangeable products.

21st Century Cures

The Cures Act supports the Agency’s innovation and evidence framework to expedite the delivery, discovery, development, and evaluation of beneficial new medical products for the American public. The Cures Act authorizes FDA to prioritize and enhance ongoing activities including efforts to facilitate greater patient engagement in drug development, advance innovative clinical trials through the adoption of adaptive designs and novel statistical modeling, foster the generation of evidence derived from clinical experience and evaluate its applicability to drug development, and qualify new drug development tools. Additionally, it provides the Agency authority to increase public engagement, enhance internal and external communications, and expedite clinical decision-making.

By providing new hiring authorities to FDA, the Cures Act greatly improves the Agency’s ability to compete with industry and academia in hiring and retaining scientific experts. One of FDA’s ongoing challenges has been recruiting and retaining the experts it needs in specialized areas to

get its work done rapidly and in a consistent manner and to meet its growing list of responsibilities. This is an especially important need given the tremendous advances in biological sciences, engineering, information technology, and data science.

Opioids

Opioids are powerful medications that can help manage pain when prescribed for the right condition and used properly. But when physicians prescribe these medications to patients who should not receive them, or when they are used improperly, such as for recreational purposes, they can cause serious harm including overdose and death. FDA has many ongoing activities aimed at reducing these harms, including continued efforts to improve opioid prescribing practices through prescriber training and better labeling, work to broaden access to overdose treatments such as naloxone, and work to encourage the development of opioid products with abuse-deterrent properties.

In February 2016, FDA announced its comprehensive [action plan](#) for reducing the impact of opioid misuse and abuse on American families and communities. As part of this plan, FDA will work more closely with its advisory committees before making critical product and labeling decisions; enhance safety labeling; require new data on long-term opioid use; and seek to improve treatment of both addiction and pain. At the same time, FDA will re-examine the risk-benefit paradigm for opioids and ensure that the Agency continues to consider appropriately the wider public health effects of prescription opioids. FDA is committed to taking all of these steps transparently and in close cooperation with other Federal agencies and stakeholders, and participates actively in the groups coordinating those activities both within HHS and across all the relevant agencies of the U.S. government.

Successfully confronting the ongoing epidemic is challenging. Throughout the year, through concerted efforts to take swift regulatory action in support of the Action Plan, engage the public and key opinion leaders in open discussion on key issues, we continue to reexamine the agency's policies in the regulation of opioids. The role of the agency continues to include the thoughtful regulation of the drugs and devices used in the treatment of pain, as well as opioid addiction and overdose, to assure that the actions we take are in the best interest of public health.

Combating Antibiotic Resistant Bacteria

Antibiotic resistance continues to erode our therapeutic armamentarium due to the selective pressure from the use of existing antibacterial drugs. Over the last few decades, there has been a marked decline in innovative antibacterial drug development. Patients and clinicians are increasingly confronting infections caused by pathogens resistant to many or all antibacterial drugs in both the inpatient and outpatient settings. Antibacterial products are challenging to

develop because of the need to study a new therapy in the setting of an acute serious disease and the limited economic returns from an antibacterial drug. For example, patients with serious infections are likely to be acutely ill and in need of urgent therapy, which results in challenges obtaining informed consent and timely completion of trial enrollment procedures. In addition, many patients with serious infections have significant comorbidities that may render them less likely to be enrolled in a clinical trial.

Advancing the science of clinical trials for antibacterial drugs can have an impact facilitating as well as stimulating development of needed, new therapies. CDER is supporting the following research:

- A clinical study and development of tools to improve enrollment in clinical trials of new drugs in patients with hospital acquired / ventilator associated bacterial pneumonia
- Clinical studies needed for the final step in the development of Patient Reported Outcome questionnaires for use in pneumonia and skin infection clinical trials
- The development of a method using electronic medical records from patients with blood infections to update laboratory standards for reporting drug resistance
- Clinical and animal model studies to more quickly develop antibacterial drug dosing recommendations for newborns with meningitis and other serious infections
- Animal model studies that should help in the development of new antibacterial drugs targeting high priority resistant pathogens

The work being performed addresses some important gaps in knowledge for antibacterial drug development. There are still other important areas of work that are needed to provide dependable pathways for studying new antibacterial drugs. Sustained funding would allow CDER to continue efforts to advance the science of clinical trials for new antibacterial drugs. This is the type of work that is essential to the field, but will not be performed by a single drug company.

Guidances

Below are notable guidances recently issued by FDA. These guidances help address various issues. This list reflects the guidances published most recently and does not represent any degree of importance or priority ranking among the published guidances.¹⁹

Date	#	Title	Description
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¹⁹ For more information on guidance please visit <http://www.fda.gov/RegulatoryInformation/Guidances/>.

Oct 2016	<u>FDA-2015-D-3990</u>	Sunscreen Innovation Act: Section 586C(c) Advisory Committee Process	Explains the process by which FDA intends to convene advisory committees to provide recommendations on requests submitted under the SIA.
Oct 2016	<u>FDA-2008-D-0530</u>	Tropical Disease Priority Review Vouchers	Explains to stakeholders how FDA is implementing the provisions of the priority review voucher section in the Federal Food, Drug, and Cosmetic Act.
Nov 2016	<u>FDA-2015-D-4021</u>	Nonprescription Sunscreen Drug Products – Safety and Effectiveness Data	Addresses FDA's thinking on data needed to determine whether nonprescription sunscreen active ingredient or combination of active ingredients is generally recognized as safe and effective.
Nov 2016	<u>FDA-2012-D-0880</u>	Generic Drug User Fee Amendments of 2012: Questions and Answers Related to User Fee Assessments	Provides updated answers to common questions from the generic drug industry and other interested parties involved in the development and/or testing of generic drug products.

Product Approvals

Below are some of CDER's recent product approvals. This list does not represent any degree of importance or priority ranking of products.²⁰

Disease State	Approved	Generic Name	Reference Listed Drug	FDA-approved use on approval date
Cancer	Mar 2016	Bendamustine Injection	Treanda	To treat chronic lymphocytic leukemia (CLL)
	Jun 2016	Dasatinib Tablets	Sprycel	To treat Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML)
Heart Disease	Apr 2016	Rosuvastatin Tablets	Crestor	To treat high cholesterol
	Jun 2016	Dofetilide Capsules	Tikosyn	To treat atrial fibrillation/flutter
	Oct 2016	Olmesartan Tablets	Benicar	To treat high blood pressure
Mental Health	Sept 2016	Memantine Extended-Release Capsules	Namenda	To treat moderate to severe dementia of the Alzheimer's type
	Nov 2016	Quetiapine Extended-Release Tablets	Seroquel XR	To treat schizophrenia; bipolar disorder, manic or mixed episodes; bipolar disorder, depressive episodes; or major depressive disorder
Infectious Disease	Feb 2016	Efavirenz Tablets	Sustiva	To treat human immunodeficiency virus (HIV)
	Aug 2016	Oseltamivir Capsules	Tamiflu	To treat uncomplicated flu in patients who have are symptomatic for less than 48 hours
Other Diseases	Mar 2016	Sildenafil Tablets	Viagra	To treat erectile dysfunction
	Mar 2016	Mometasone Nasal Spray	Nasonex	To treat nasal symptoms of seasonal allergies

²⁰ For more information on product approvals and designations visit <http://www.fda.gov/NewsEvents/ProductsApprovals/>

	Apr 2016	Lacosamide Tablets	Vimpat	To treat partial-onset seizures as an Adjunctive therapy
	May 2016	Rufinamide Tablets	Banzel	To treat seizures associated with Lennox-Gastaut Syndrome (LGS) as an Adjunctive therapy

Rules

Below are rules recently published by FDA. Rules help address various issues. This list does not represent any degree of importance or priority ranking among the published rules.²¹

Date	#	Purpose or Benefit
Sep 2016	FDA-1975-N-0012	Safety and Effectiveness of Consumer Antiseptics; Topical Antimicrobial Drug Products for Over-the-Counter Human Use - Consumer Wash
Oct 2016	FDA-2011-N-0830	Abbreviated New Drug Applications and 505 (b)(2) Applications
Oct 2016	FDA-2015-N-1355	Use of Ozone Depleting Substances - Sterile Aerosol Talc and Metered Dose Atropine Sulfate
Nov 2016	FDA-2011-N-0697	Amendments to Regulations on Citizen Petitions, Petitions for Stay of Action and Submission of Documents to Dockets
Nov 2016	FDA-2005-N-0343	Medical Gas Containers and Closures; Current Good Manufacturing Practice Requirements

Enhance Oversight

Within this Goal area, the Human Drugs Program addresses the FDA Strategic Priorities on Globalization, Safety and Quality, and Smart Regulation.

The Human Drugs Program provides comprehensive regulatory coverage of the production and distribution of drug products and manages inspection programs designed to minimize consumer exposure to defective or harmful drug products. FDA evaluates the findings from inspections and examines the conditions and practices in facilities where drugs are manufactured, packed, tested, and stored. FDA also monitors the quality of finished drug products in distribution through sampling and analysis.

FDA's postmarket safety surveillance activities exist to monitor the safety of drugs that are currently available to consumers. FDA aims to identify and communicate risks associated with approved drugs. The ongoing postmarket safety activities allow FDA to discover risks associated with drug products that could not have been discovered during premarket review. The goal of safety activities is to protect patients from adverse events or improper use of drug products that could result in potentially harmful effects.

²¹ For more information on FDA rules please visit <http://www.fda.gov/RegulatoryInformation/RulesRegulations/default.htm>.

Sentinel

The 2007 Food and Drug Administration Amendments Act (FDAAA) required FDA to establish a postmarket risk identification and analysis (ARIA) system to analyze drug and biologic safety data from multiple sources. In response to this requirement, FDA launched the Sentinel Initiative in 2008, which led to the development and implementation of the Sentinel System. The Sentinel Initiative provides significant public health benefits by developing new approaches and methods to actively monitor the safety of marketed medical products to complement existing FDA surveillance capabilities. The Sentinel System includes access to large quantities of electronic healthcare data and enhances the FDA's ability to detect and better understand safety signals to better inform patients and healthcare providers on the safe use of regulated medical products.

In FY 2016, the Sentinel System expanded surveillance to 193 million patients, which is an increase of 11 million patients from FY 2015. In February 2016, FDA held the Eighth Annual Sentinel Initiative Public Workshop to bring the stakeholder community together to discuss a variety of topics on active medical product surveillance and current and emerging Sentinel projects. Additionally, FDA formally announced the transition of the Mini-Sentinel Pilot to the Sentinel System and the official launch of its ARIA subcomponent. To date, the Sentinel Initiative has contributed to multiple safety communications and labeling changes to better inform patients and providers about safe use of drugs and vaccines.

Drug Quality and Security Act

In November 2013, after a fungal meningitis outbreak linked to contaminated compounded drugs caused more than 60 deaths and 750 cases of illness, the Drug Quality and Security Act (DQSA) was enacted, providing FDA with additional authorities to oversee compounding. The DQSA added a new section 503B to the Federal Food, Drug, and Cosmetic Act (FD&C Act), creating a new category of compounders known as outsourcing facilities. As of March 23, 2017, 62 firms are registered with FDA as outsourcing facilities. The DQSA also amended section 503A of the FD&C Act to remove provisions that the U.S. Supreme Court held to be unconstitutional in 2002.

Following the enactment of the DQSA, FDA has acted quickly to increase its drug compounding oversight through inspections and enforcement, develop policies regarding the compounding provisions of federal law, convene and obtain input from an advisory committee, collaborate and coordinate with state regulators, and conduct stakeholder outreach.

Inspections and Enforcement: FDA has conducted over 350 inspections since enactment of the DQSA. Many of these inspections have been for-cause, generally based on reports of serious adverse events or product quality issues. Following these inspections, FDA has issued more than 130 warning letters describing significant violations of the law that could put patients at

risk and more than 30 letters referring inspectional findings to state regulatory agencies. FDA also has overseen about 100 recalls involving compounded drugs. In addition, FDA has worked with the Department of Justice on civil and criminal enforcement actions.

Policy Development: Between enactment of the DQSA and March 23, 2017, FDA has issued 21 draft guidance documents (11 of which have been finalized), three proposed rules (one of which has been finalized), and a draft memorandum of understanding that, when finalized, FDA would enter into with individual states. The policy documents address many significant compounding provisions of the FD&C Act and are an important part of FDA's efforts to communicate with stakeholders about its regulatory policies, and to protect patient health from the risks associated with compounded drugs.

Advisory Committee: FDA re-established the Pharmacy Compounding Advisory Committee, which provides advice on scientific, technical, and medical issues concerning drug compounding under sections 503A and 503B of the FD&C Act. As of March 23, 2017, FDA has held six Committee meetings.

State Collaboration and Coordination: FDA has held four intergovernmental working meetings with states in addition to numerous one-on-one meetings and interactions. FDA also invites state regulators to accompany its investigators on inspections.

Stakeholder Outreach: FDA has held four sets of listening sessions with more than 75 stakeholders, including pharmacy, hospital, long-term care, and other medical organizations; consumer and patient advocacy groups; insurers; and outsourcing facilities.

These efforts, which are ongoing, are critical to protect the public health. FDA continues to receive reports of serious adverse events associated with compounded drugs and to identify poor drug production practices that could cause widespread patient harm.

Title II of the DQSA, the Drug Supply Chain Security Act (DSCSA), outlines critical steps to build an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed in the United States. Since enactment of the DSCSA, FDA has issued five draft guidance documents and four final guidances, and FDA is working to develop standards, policy, and programs to implement the law. Along with FDA, prescription drug manufacturers, wholesale distributors, repackagers, and many dispensers (primarily pharmacies) will collaborate toward the development of the new system for enhanced drug distribution security by 2023. The new system will continuously evolve toward an ultimate goal of identification of each individual prescription drug package, enabling better methods for verification of product legitimacy, detection and notification of illegitimate products in the supply chain, and facilitation of recalls.

Rules

Below are rules recently published by FDA. These rules help address various issues. This list does not represent any degree of importance or priority ranking among the published rules.²²

Date	#	Purpose or Benefit
Mar 2016	FDA-2016-N-0001	Advisory Committee: Pharmaceutical Science and Clinical Pharmacology Advisory Committee
Aug 2016	FDA-2005-N-0464	Requirements for Foreign and Domestic Establishment Registration and Listing for Human Drugs; Including Drugs that are Regulated Under a Biologics License Application and Animal Drugs
Nov 2016	FDA-2016-N-0543	Food and Drug Administrative Review and Action on Over-the-Counter Time and Extent Applications

Promote Informed Decisions

Within this Goal area, the Human Drugs Program addresses the FDA Strategic Priority on Safety and Quality.

FDA is responsible for protecting the public health by assuring prescription drug information that healthcare professionals and consumers receive is truthful, balanced, and accurate. This is accomplished through a comprehensive surveillance, enforcement, and education program, and by fostering better communication of labeling and promotional information directed to both healthcare professionals and consumers.

²² For more information on FDA rules please visit <http://www.fda.gov/RegulatoryInformation/RulesRegulations/default.htm>.

Strengthen Organizational Excellence

Within this Goal area, the Human Drugs Program addresses the FDA Strategic Priority on Stewardship.

The Human Drugs Program supports FDA's objective to recruit, develop, retain, and strategically manage a world-class workforce, improving the overall operation and effectiveness of FDA. Specifically, CDER employs a lean management approach to streamline operations in order to meet public health responsibilities and uphold CDER's public health mission with limited resources. CDER analyzes business operations and processes to maximize business modernization to accomplish as much as possible within budget constraints.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2014 Actual	\$1,210,709,000	\$466,303,000	\$744,406,000
FY 2015 Actual	\$1,338,599,000	\$482,243,000	\$856,356,000
FY 2016 Actuals	\$1,451,570,000	\$487,299,000	\$964,271,000
FY 2017 Annualized CR	\$1,324,422,000	\$486,398,000	\$838,024,000
FY 2018 President's Budget	\$1,611,504,000	\$179,139,000	\$1,432,365,000

BUDGET REQUEST

The FY 2018 Budget Request for the Human Drugs Program is \$1,611,504,000, of which \$179,139,000 is budget authority and \$1,432,365,000 is user fees. This level provides a net increase of \$287,082,000. Budget authority decreases by \$307,259,000 compared to the FY 2017 Annualized CR level and user fees increase by \$594,341,000. The Center for Drug Evaluation and Research (CDER) amount in this request is \$1,414,764,000. The Office of Regulatory Affairs amount is \$196,740,000.

The FY 2018 Budget allows the Human Drugs Program to uphold its public health mission of ensuring that new, generic, biosimilar, and OTC drugs are safe and effective. The FY 2018 Budget will enable FDA to continue to carry out rigorous science-based premarket drug reviews of new, generic, and biosimilar biological drug products. Identifying and developing new scientific methods, models, and tools to improve the quality, safety, predictability, and efficiency of new drug development is a core mission of FDA. FDA will continue to promote patient and health professional awareness of drug benefits and risks through effective communication of drug information.

FDA will continue to conduct postmarket surveillance to enable early detection of drug safety signals. FDA oversees drug promotion and marketing to help ensure that marketed drug labeling and advertising are truthful and not misleading. FDA will also continue its efforts related to opioids with abuse-deterrent properties. FDA is committed to making progress on setting and applying appropriate regulatory incentives and expectations regarding opioids with abuse- deterrent properties.

FDA will continue oversight of human drug compounding through inspections and enforcement, policy development and implementation, obtaining input from an advisory committee, state collaboration and coordination, and stakeholder outreach. The FY 2018 Budget will also support FDA's ability to improve the integrity of the drug supply chain. FDA will continue to establish the regulatory framework to support the implementation of the Drug Supply Chain Security Act by developing policy and programs, drafting proposed rules, drafting guidance documents and conducting public meetings.

The FY 2018 Budget will support FDA's efforts to minimize public health risks associated with counterfeit and substandard drugs. FDA is educating consumers and the health care community about the risks of, and minimizing exposure to, counterfeit and substandard drug products in addition to implementing regulatory and enforcement tools to improve the security of the drug supply chain.

BUDGET AUTHORITY

Reductions (-\$17.8 million)

Center: -\$11.2 million (Medical Product Safety & Availability)

Proposed budget reductions will require CDER to reprioritize and refocus how it promotes and protects public health. These proposed budget reductions will include some contracts that promote drug safety and research studies, investments in innovation and research, and training and development opportunities for personnel. It is FDA's goal to minimize the impact of these reductions on FDA's core mission activities.

Field: -\$6.6 million (Medical Product Safety & Availability)

ORA will apply strategic reductions to its programs in order to preserve the highest priority activities and operations in support of protecting public health. ORA will reduce existing workforce levels through attrition.

In order to continue operations under the FY 2018 request levels, ORA will apply the necessary program reductions to areas such as training, IT and lab equipment, and across all program office operating budgets while protecting resources for inspections and compliance activities.

Medical Product Budget Authority Recalibration (-\$289.4 million)**Center: -\$244.9 million / Field: -\$44.5 million (Medical Product Safety & Availability)**

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees.

USER FEES**Medical Product User Fee Recalibration and Regulatory Efficiencies (+\$594.3 million)****Center: +\$551.0 million / Field: +\$43.3 million (Medical Product Safety & Availability)**

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees. The budget also includes a package of administrative actions designed to achieve greater regulatory efficiency and speed the availability of innovative, safe, and effective medical products in the market. These actions include the improvements are described in the PDUFA VI, GDUFA II, and BSUFA II commitment letters submitted to Congress in January 2017.

In FY 2018, CDER will work closely with the Agency to effectively implement and leverage the Cures Act which aims to help accelerate medical product innovation while reducing regulatory and administrative burden. The Breakthrough Therapy program is one of the most popular components of the human drug review program with requests and designations far exceeding expectations and has been instrumental in bringing forward innovative therapies for patients. CDER will continue to leverage the breakthrough therapy designation efforts with the goal of expediting the development and review of drug and biological products, alone or in combination, for serious or life-threatening diseases or conditions when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies.

PERFORMANCE

The Human Drugs Program's performance measures focus on premarket and post market activities, generic drug review actions, and drug safety in order to ensure that human drugs are safe and effective and meet established quality standards, as detailed in the following table.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
<u>223210</u> : Review and act on 90 percent of standard NME NDA and original BLA submissions within 10 months of the 60 day filing date. <i>(Output)</i>	FY 2015: 100% Target: 90% (Target Exceeded)	90%	90%*	Maintain
<u>223211</u> : Review and act on 90 percent of priority NME NDA and original BLA submissions within 6 months of the 60 day filing date. <i>(Output)</i>	FY 2015: 92% Target: 90% (Target Exceeded)	90%	90%*	Maintain
<u>223212</u> : Review and act on 90 percent of standard non-NME original NDA submissions within 10 months of receipt. <i>(Output)</i>	FY 2015: 95% Target: 90% (Target Exceeded)	90%	90%*	Maintain
<u>223213</u> : Review and act on 90 percent of priority non-NME original NDA submissions within 6 months of receipt. <i>(Output)</i>	FY 2015: 100% Target: 90% (Target Exceeded)	90%	90%*	Maintain
<u>223215</u> : Review and act on 90 percent of standard original Abbreviated New Drug Application (ANDA) submissions within 10 months of receipt. <i>(Output)</i>	FY 2015: 97% Target: 60% (Target Exceeded)	90%	90%*	Maintain
<u>223216</u> : Review and act on 90 percent of priority	New Goal	N/A	90%*	N/A

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
original Abbreviated New Drug Application (ANDA) submissions within 8 months of receipt. (Output)				
<u>224211</u> : Percentage of planned foreign and domestic high-risk human drug inspections (approximately 560 in total). (Output)	FY 2016: 698 Target: 560 (Target Exceeded)	64%	64%	Maintain
<u>292202</u> : Number of people for whom FDA is able to evaluate product safety through Mini-Sentinel/Sentinel system. (Outcome)	FY 2016: 193 million Target: 182 million (Target Exceeded)	195 million	198 million	+3 million

* Anticipated performance targets under PDUFA VI or GDUFA II

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

Review Goals

The New Drug Review performance measures focus on ensuring that the public has access to safe and effective new treatments as quickly as possible. The goal of the PDUFA program is to increase the efficiency and effectiveness of the first review cycle and decrease the number of review cycles necessary for approval. The Agency will continually work to meet or exceed the review performance goals when possible moving forward. The Generic Drug Review performance measure focuses on process enhancements resulting from the GDUFA program. The goal of the GDUFA program is to enhance efficiency in the generic drug review process, promote transparency between FDA and generic drug sponsors, and enhance access to high-quality, lower cost generic drugs. This investment in the Generic Drug Review program is reflected in the performance target which increases from 75 percent of Abbreviated New Drug Application (ANDA) submissions reviewed in 15 months in FY 2016 to 90 percent reviewed in 10

months in FY 2017 and FY 2018. The anticipated FY 2018 targets for the review goals align to the PDUFA VI and GDUFA II performance commitments.

Sentinel

The FDA's Sentinel Initiative provides essential public health benefits by enabling FDA to quickly assess the safety of FDA-approved medical products in near real time. Through the Sentinel System the FDA is able to evaluate drug safety issues that may require regulatory action. In FY 2016, FDA expanded surveillance to 193 million patients, which is an increase of 11 million patients from FY 2015. During the February 3rd, 2016 8th Annual Sentinel Initiative Public Workgroup Public Meeting, the FDA announced the transition from the Mini-Sentinel pilot to a sustained active surveillance system, the Sentinel System. The Sentinel System ensures FDA will continue to have the tools necessary to conduct active safety surveillance work.

PROGRAM ACTIVITY DATA TABLES

CDER Workload and Outputs	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
New Drug Review			
Workload – Submissions/Filings/Requests			
New Drug Applications/Biologic Licensing Applications (NDA/BLA)	124	124	124
Efficacy Supplements	170	170	170
Manufacturing Supplements	1,669	1,669	1,669
Commercial INDs (Drugs and Biologics) with Activity	6,831	6,831	6,831
Sponsor Requests: IND-Phase Formal Meetings	2,547	2,547	2,547
Sponsor Requests: Review of Special Study Protocols	212	212	212
Submissions of Promotional Materials	97,780	102,000	106,000
Outputs – Reviews/Approvals			
Reviews: Priority NDA/BLA	40	40	40
Reviews: Standard NDA/BLA	150	150	150
Approvals: Priority NDA/BLA	30	30	30
Approvals: Standard NDA/BLA	86	86	86
Mean time from Receipt to Approval: Priority NDA/BLAs (in months)	12.8	12.8	12.8
Mean time from Receipt to Approval: Standard NDA/BLAs (in months)	15.3	15.3	15.3
Median time from Receipt to Approval: Priority NDA/BLAs (in months)	8.0	8.0	8.0
Median Time from Receipt to Approval: Standard NDA/BLAs (in months)	10.3	10.3	10.3
Reviews: NDA Supplementals	2,851	2,851	2,851
Reviews: Clinical Pharmacology/ Bio-Pharmaceutic	4,593	4,823	5,064
Biologic Therapeutics Review			
Workload – Submissions/Filings/Requests			
Receipts: Commercial IND/IDE (Biologics Only)	119	119	119
Receipts: IND/IDE Amendments (Biologics Only)	28,010	28,010	28,010
Outputs – Reviews/Approvals			
Reviews: Total Original License Application (PLA/ELA/BLA)	14	14	14
Approvals: PLA/BLA	13	13	13
Reviews: License Supplement (PLA/ELA/BLA)	329	329	329
Generic Drug Review			
Workload – Submissions/Filings/Requests			
Receipts: Abbreviated New Drug Applications (ANDA)	852	750	850
Outputs – Reviews/Approvals			
Actions – ANDA	2,808	2,900	3,000
Approval Actions - ANDA (both Tentative and Full Approvals)	835	850	875
Median Review Time from ANDA Receipt to Approval (months)	39.42	38.25	37.00
Actions - ANDA Supplementals (Labeling and Manufacturing)	6,554	6,750	7,000
Over-the-Counter Drug Review			
OTC Monographs Under Development*	25	25	25
OTC Monographs Published*	3	4	4
*Category includes Proposed Rules, Final Rules, and Proposed and Final Orders under the Sunscreen Innovation Act			

CDER Workload and Outputs	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
Best Pharmaceuticals for Children Act			
Labels Approved with New Pediatric Information	4	11	11
New Written Requests Issued	20	18	19
Pediatric Exclusivity Determinations made	3	7	7
Post Exclusivity Safety Report	7	8	8
Patient Safety			
Workload – Submissions/Filings/Requests			
Submissions: Adverse Event Reports	1,709,290	1,807,356	1,911,048
Electronic Submissions: % of Total Adverse Drug Reaction Reports	97%	97%	97%
Electronic Submissions: % of Serious/Unexpected Adverse Drug Reaction Reports	97%	97%	97%
Submissions: Drug Quality Reports	13,763	14,000	14,400
Outputs – Reviews/Approvals			
Safety reviews completed by Office of Surveillance & Epidemiology	7,100	7,455	7,828
Number of drugs with Risk Communications	250	260	270
Administrative/Management Support			
Workload			
Number of Advisory Committee Meetings	36	35	35
Number of FOI Requests	3,221	3,000	3,000
Number of FOI Requests Processed	3,239	3,025	3,025
Number of Citizen Petitions Submitted (excluding suitability petitions and OTC monograph-related petitions)	90	83	83
Number of Citizen Petitions Pending on Last Day of Fiscal year (excluding suitability petitions and OTC monograph-related petitions)	164	170	170
Number of Citizen Petitions Completed ¹ (excluding suitability petitions and OTC monograph-related petitions)	101	90	90

¹ Citizen Petitions completed may include petitions filed in prior years.

Field Human Drugs Program Activity Data (PAD)

Field Human Drugs Program Workload and Outputs	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS	1,846	1,767	1,767
Pre-Approval Inspections (NDA)	88	135	135
Pre-Approval Inspections (ANDA)	92	215	215
Bioresearch Monitoring Program Inspections	616	550	550
Drug Processing (GMP) Program Inspections	805	650	650
Compressed Medical Gas Manufacturers Inspections	97	50	50
Adverse Drug Events Project Inspections	88	88	88
OTC Monograph Project and Health Fraud Project Inspections	51	70	70
Compounding Inspections ¹	135	130	130
Domestic Laboratory Samples Analyzed	1,301	1,300	1,300
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS	1,231	1,275	1,275
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	100	98	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	173	190	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	214	255	255
Foreign Drug Processing (GMP) Program Inspections	909	900	900
Foreign Adverse Drug Events Project Inspections	7	10	10
TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS	3,077	3,042	3,042
IMPORTS			
Import Field Exams/Tests	10,053	10,000	10,000
Import Laboratory Samples Analyzed	<u>1,009</u>	<u>620</u>	<u>620</u>
Import Physical Exam Subtotal	11,062	10,620	10,620
Import Line Decisions	739,309	776,274	815,088
Percent of Import Lines Physically Examined	1.50%	1.37%	1.30%
STATE WORK			
UNIQUE COUNT OF STATE PARTNERSHIP HUMAN DRUG ESTABLISHMENT INSPECTIONS²	0	0	0
State Partnership Inspections: Compressed Medical Gas Manufacturers Inspections	0	0	0
State Partnership Inspections: GMP Inspections	0	0	0
GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS	3,077	3,042	3,042

¹ The number of compounding inspections includes inspections of compounders that are and are not registered with FDA as outsourcing facilities.

² The FY 2016 actual unique count of foreign inspections includes 82 OIP inspections (41 for China, 35 for India, & 6 for Latin America).

³ The State inspections that are funded by the FDA are now being obligated via formal contract funding vehicles.

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OFFICE OF ORPHAN PRODUCTS DEVELOPMENT²³

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
Office of Orphan Products Development (BA Only).....	26,099	26,099	26,099	26,099	---
FTE.....	27	27	27	27	---

Authorizing Legislation: Federal Food, Drug and Cosmetic Act (21 U.S.C. 321-399); PHS Act (42 U.S.C. 241) Section 301; Safe Medical Device Act of 1990 (as amended) (21 U.S.C. 351-353, 360, 360c-360j, 371-375, 379, 379e, 381); Pediatric Medical Devices Safety and Improvement Act of 2007, Section 305; Food and Drug Administration Safety and Innovation Act of 2013, Sections, 510, 620 and 908.

Allocation Method: Direct Federal/Extramural Grants

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The public health programs of the Office of Orphan Products Development (OOPD) have promoted and advanced the development of innovative products – drugs, biologics, medical devices, and medical foods – that demonstrate promise for the prevention, diagnosis, and/or treatment of rare diseases or underserved populations. There are an estimated 7,000 rare diseases, with a public health impact that affects more than 25 million Americans and many millions more of family members in the United States. Between 85 and 90 percent of these cases are serious or life-threatening.

Improve and Safeguard Access

OOPD administers major provisions of the 1983 Orphan Drug Act (ODA), relevant sections of the 1990 Safe Medical Devices Act, and other statutes, where Congress sought to provide incentives to promote the development of products for the treatment of rare diseases and underserved populations. OOPD's program activities directly support the Health and Human Services' strategic goal to advance scientific knowledge and innovation.²⁴ Further, OOPD activities support FDA's strategic goal to improve access to FDA regulated products that benefit health by enhancing the process of developing promising new products into safe, effective, and accessible treatments for rare disease patients. OOPD programs facilitate product development through collaboration with private, public, and academic entities.

Orphan Product Grants Activity

²³ The Office of Orphan Products Development is shown for illustrative purposes and is not contained as a separate line item in the All Purpose Tables.

²⁴ <http://www.hhs.gov/about/strategic-plan/strategic-goal-2/index.html>

The Orphan Drug Act created the Orphan Product Clinical Trial Grants Program, which is administered by OOPD, to stimulate the development of promising products for rare diseases and conditions. Orphan product grants are a proven method of fostering and encouraging the development of new safe and effective medical products for rare diseases and conditions. These grants support new and continuing extramural research projects that test the safety and efficacy of promising new, drugs, biologics, devices, and medical foods through human clinical trials in very vulnerable populations often with life-threatening conditions.

Over 590 new clinical trials have been funded by the Orphan Products Grants Program to date. This OOPD Grants Program has supported the marketing approval of more than 60 orphan products for serious or life threatening orphan indications. This program has funded approximately 10 percent of all orphan product approvals. In FY 2016, OOPD funded 21 new grant awards – out of 76 grant applications – and provided funding or continued support for approximately 85 other ongoing clinical study projects.

These grants are a modest investment to better ensure that product development occurs in a timely manner. However, FDA grant funds are covering less and less of the total cost for conducting clinical trials, which continue to increase far faster than the rate of medical cost inflation. Increases in the costs of clinical trials have reduced the capacity of the program to provide the needed monetary support to researchers actively conducting clinical trials that increase the number of new, safe and effective diagnostic and therapeutic options for patients with rare diseases.

Natural History Grant Program

OOPD launched its new grant program in FY 2016 intended to support studies that advance rare disease medical product development through characterization of the natural history of rare diseases/conditions, identification of genotypic and phenotypic subpopulations, and development and/or validation of clinical outcome measures, biomarkers and/or companion diagnostics. OOPD received 89 applications for this new program in FY 2017 and plans to fund approximately \$2 million in FY 2017 to award three to five grants for natural history studies targeted on expediting the development of products for these rare conditions.

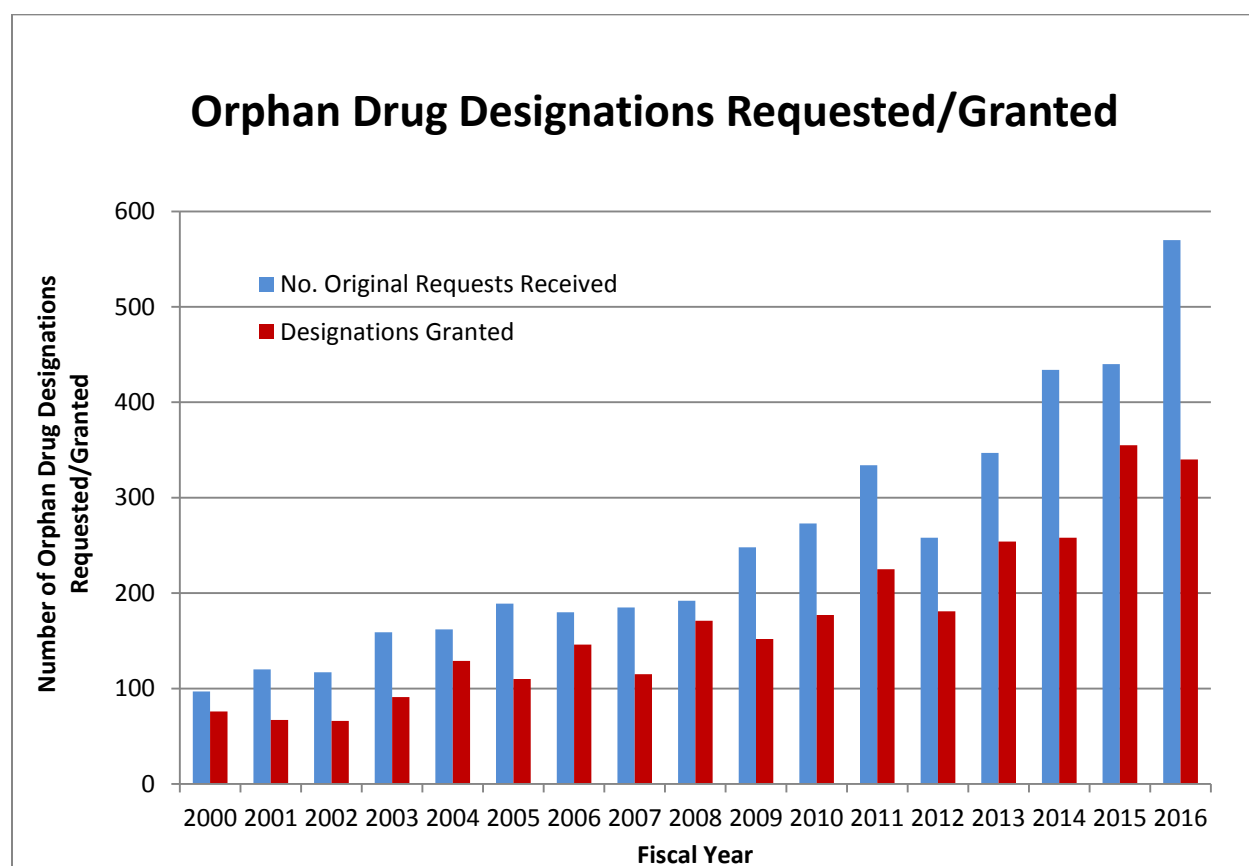
Orphan Drug Designation Activity

The Orphan Drug Act also created the orphan drug designation program to provide financial incentives to sponsors for developing drugs and biologics for rare diseases and conditions, which is, in part, defined as one affecting fewer than 200,000 persons in the United States. OOPD evaluates applications from sponsors who are developing drugs to treat rare diseases to determine eligibility for orphan drug designation. Sponsors whose drugs are designated as

orphan are eligible for significant tax credits for clinical trial costs, user fee waiver of marketing applications and, upon approval, consideration for seven years of marketing exclusivity.

The approximately 3,900 orphan drug designations OOPD issued since 1983 have resulted in over 550 marketing approvals, the vast majority having been awarded orphan exclusivity. In contrast, the decade prior to 1983 saw fewer than ten such products developed by industry make it into the market. During FY 2016, OOPD received a record 569 new applications for orphan drug designation. These included potential treatments for many kinds of rare cancers, sickle cell disease, and Ebola. OOPD designated 340 orphan drugs in FY 2016. FDA approved 52 orphan designated drugs for marketing in FY 2016.

The number of requests for orphan designation has quintupled since FY 2000. Not only are the requests rapidly increasing, but the complexity of the science associated with these orphan drugs is increasing due, in part, to advances in pharmacogenomics and precision medicine.



Product Designations

Below are examples of noteworthy orphan drug designated products that received approval in 2016.²⁵

Date	Product	Purpose or Benefit
March 2016	Defibrotide	Treatment of adult and pediatric patients with hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), with renal or pulmonary dysfunction following hematopoietic stem cell transplantation (HSCT). First FDA approval for this indication.
October 2015	Asfotase alfa	To provide long-term enzyme replacement therapy for infantile-and juvenile-onset hypophosphatasia, a serious and sometimes fatal bone disease
December 2015	Sebelipase alfa	To treat lysosomal acid lipase deficiency, a rare inherited genetic disorder that does not allow the body to produce an enzyme responsible for breaking down fats, which can lead to life-threatening organ damage.

²⁵ For more information on designations and product approvals, visit <http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm>

Rare Pediatric Disease Priority Review Voucher Designation

Food and Drug Administration Safety and Innovation Act (FDASIA) added Section 529 to the FD&C Act to encourage development of new drug and biological products (“drugs”) for the prevention and treatment of qualifying rare pediatric diseases. This legislation created the Rare Pediatric Disease Priority Review Voucher (PRV) program wherein the sponsor of an approved drug to prevent or treat a rare pediatric disease may receive a voucher for a priority review of a subsequent drug.

Sponsors who are interested in receiving a rare pediatric disease priority review voucher may first request a “rare pediatric disease” designation through OOPD. While such designation is not required to receive a voucher, requesting designation in advance may expedite a sponsor’s future request for a priority review voucher. In FY 2016, OOPD received 43 new rare pediatric disease designation requests plus 2 consults from submitted marketing applications needing rare pediatric disease determinations. Of these, OOPD determined that 20 met the definition of a “rare pediatric disease.” On September 29, 2016, the Advancing Hope Act revised the definition of a “rare pediatric disease,” and was implemented immediately thereafter. By the end of 2016, a total of seven rare pediatric disease priority review vouchers had been issued.

On December 13, 2016, Congress extended the designation aspect of the program to September 30, 2020.

Humanitarian Use Device (HUD) Designation Activity

The HUD program, created from provisions of the Safe Medical Devices Act, encourages the development of devices for rare diseases and is administered by OOPD.

OOPD reviews applications from sponsors requesting HUD designation. A device that has received HUD designation is eligible for Humanitarian Device Exemption (HDE) approval if, among other criteria, the device will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from use of the device outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of available devices or alternative forms of treatment. FDA approval of an HDE application authorizes the applicant to market the device. This marketing approval is subject to certain profit and use restrictions set forth in Section 520(m) of the FD&C Act. Since 1990, 69 HUD devices have been approved for marketing through the HDE pathway.

Except in certain circumstances, a HUD approved under an HDE cannot be sold for an amount that exceeds the costs of research and development, fabrication, and distribution of the device (for profit). Under Section 520(m)(6)(A)(i) of the FD&C Act, as amended by FDASIA, a HUD is eligible to be sold for profit after receiving HDE approval if the device meets certain criteria. As of the end of FY2016 twelve manufacturers have received approval to market their devices for

profit and other sponsors have submitted requests to qualify for the exemption from profit prohibition.

In FY 2016, OOPD received 18 new HUD applications and designated 14 devices. Of the 14 devices that were designated, six designations were based on HUD applications originally submitted in prior years. In FY 2016, three devices received an HDE approval from CDRH. Also, in FY 2016, two manufacturers who previously had HDE approval were authorized to market their devices for profit.

Pediatric Device Consortia Grants Activity

There is a significant public health need for medical devices designed specifically for children. This need is due in part to the lack of commercial incentives and market forces to drive pediatric medical device development, as well as the challenges of pediatric device development including differences in size, growth, development, and body chemistry that impact pediatric device requirements. Section 305 of the Pediatric Medical Device Safety and Improvement Act of 2007 (part of the 2007 FDAAA legislation) mandates demonstration grants for improving pediatric device availability through pediatric device consortia.

The FDA Pediatric Device Consortia Grant Program, administered in OOPD, supports nonprofit consortia that promote the development of pediatric medical devices. In FY 2016, the consortia funded in this program are based out of Ann Arbor, MI; Atlanta, GA; Boston, MA; Washington, DC; Lebanon, NH; Los Angeles, CA; Philadelphia, PA; and San Francisco, CA.

Since the program's inception in 2009, a total of \$24.4 million has been awarded to the consortia. Collectively, the consortia have supported the development of more than 650 potential pediatric devices, many of which are in the early stages of development. Over 10 new devices are now available for use in pediatric patients as a result of advisory assistance received from the consortia, including the "Buzzy" device for relief of pain associated with needlesticks; the Rhinoguard to assist in nasotracheal intubation; and an external compressor brace for pectus carinitum. The consortia collectively have also raised more than \$95 million of additional non-FDA funds to support pediatric device development research.

Promote Informed Decisions

OOPD participates in significant communication and outreach activities by:

- providing information on incentives available to develop products for rare diseases to external stakeholders including industry, the patient community, advocacy groups, and international regulatory agencies
- speaking at meetings and conferences on the FDA designation and approval processes, the OOPD grant programs, and the science of developing therapeutic products for rare diseases and conditions
- assisting patients and advocacy groups on issues of concern related to rare diseases and orphan products, such as pediatric device needs and orphan drug shortages
- providing web-based rare disease and orphan product resources and information to various stakeholders such as industry, the patient community, advocacy groups, and international regulatory agencies

In FY 2016, OOPD participated in 117 individual industry outreach meetings. In addition, OOPD received more than 56 invitations to speak and participate at orphan product stakeholder meetings and conferences to discuss different rare disease issues. OOPD made presentations and participated in 33 of these meetings both nationally and internationally, often to explain how orphan drugs and humanitarian devices could be developed with ODA incentives and HDE provisions, as well as FDASIA requirements for rare diseases.

At these meetings, the missions of OOPD and FDA were explained, and questions and concerns from stakeholders were addressed. Examples of public health related OOPD outreach activities in FY 2016 include conducting training courses for researchers and reviewers, and presentations to national and international rare disease patient groups. In FY 2017 through FY 2018, OOPD will continue the outreach efforts to enhance all stages of the development and approval process for products to treat rare disease patients.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2014 Actual	\$23,599,000	\$23,599,000	\$0
FY 2015 Actual	\$23,599,000	\$23,599,000	\$0
FY 2016 Actuals	\$26,099,000	\$26,099,000	\$0
FY 2017 Annualized CR	\$26,094,000	\$26,094,000	\$0
FY 2018 President's Budget	\$26,094,000	\$26,094,000	\$0

BUDGET REQUEST

The FY 2018 Budget Request is \$26,099,000 in budget authority. With this funding level, OOPD will fund a total of 12-18 new clinical trials grant awards and provide funding or continued support for approximately 75 other ongoing clinical study projects.

In addition, OOPD plans to fund approximately \$2 million in FY 2017 to award three to five grants for natural history studies targeted on expediting the development of products for these rare conditions. These natural history studies will assist in drug development and identification of treatment options in many ways like formulating sensitive clinical outcome measures, identifying appropriate subpopulations or developing biomarkers. Despite their importance, funding to conduct such studies is sorely lacking.

In FY 2018, OOPD plans to continue to sustain the awarded three to five grants for targeted natural history studies and hold a second receipt date for grant applications.

PROGRAM ACTIVITY DATA TABLE

	Office of Orphan Products Development			
Program Workload and Outputs	FY 2015 Actuals	FY 2016 Actuals	FY 2017 Estimate	FY 2018 Estimate
Grant Programs				
Total Orphan Product Grant (New and Continuations)	85	85	90	95
Total Pediatric Consortia Grants (New and Continuations)	8	8	8	8
Orphan Drug Designation Requests/Designations Granted/Orphan Drug Approvals				
New Orphan Drug Designation Requests	440	569	650	700
Drug Designations Granted	355	340	350	375
FDA Orphan Drug Marketing Approvals	41	52	60	60
HUD Requests and Designations				
New HUD Designation Requests	21	18	25	25
HUD Designations	10	14	14	14
Rare Pediatric Disease Priority Review Voucher Designation/Consultation Requests	31	57	65	65

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BIOLOGICS

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
Biologics	354,775	329,156	339,082	366,230	27,148
<i>Budget Authority</i>	<i>215,317</i>	<i>215,308</i>	<i>214,907</i>	<i>95,893</i>	<i>-119,014</i>
<i>User Fees</i>	<i>139,458</i>	<i>113,848</i>	<i>124,175</i>	<i>270,337</i>	<i>146,162</i>
Center.....	311,094	286,622	295,735	325,101	29,366
<i>Budget Authority</i>	173,937	173,929	173,606	61,398	-112,208
<i>User Fees</i>	137,157	112,693	122,129	263,703	141,574
<i>Prescription Drug (PDUFA)</i>	<i>123,801</i>	<i>102,934</i>	<i>109,704</i>	<i>226,459</i>	<i>116,755</i>
<i>Medical Device (MDUFA)</i>	<i>11,475</i>	<i>9,731</i>	<i>10,508</i>	<i>34,010</i>	<i>23,502</i>
<i>Generic Drug (GDUFA)</i>	<i>1,072</i>	<i>26</i>	<i>1,088</i>	<i>1,502</i>	<i>414</i>
<i>Biosimilars (BsUFA)</i>	<i>809</i>	<i>2</i>	<i>829</i>	<i>1,732</i>	<i>903</i>
Field.....	43,681	42,534	43,347	41,129	-2,218
<i>Budget Authority</i>	41,380	41,379	41,301	34,495	-6,806
<i>User Fees</i>	2,301	1,155	2,046	6,634	4,588
<i>Prescription Drug (PDUFA)</i>	<i>2,084</i>	<i>1,152</i>	<i>1,847</i>	<i>5,311</i>	<i>3,464</i>
<i>Medical Device (MDUFA)</i>	<i>217</i>	<i>3</i>	<i>199</i>	<i>1,323</i>	<i>1,124</i>
FTE	1,341	1,341	1,379	1,409	30

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, 21st Century Cures Act of 2016 (Cures Act)

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.

The mission of CBER is to ensure the safety, purity, potency, and effectiveness of biological products including vaccines, allergenics, blood and blood products, and cells, tissues, and gene therapies for the prevention, diagnosis, and treatment of human diseases, conditions, or injury. Through our mission, we also seek to protect the public against the threats of emerging infectious diseases and bioterrorism. CBER uses sound science and regulatory expertise to:

- Protect and improve public and individual health in the United States and, where feasible, globally
- Facilitate the development, approval of, and access to safe and effective biological products and promising new technologies
- Strengthen CBER as a preeminent regulatory organization for biological products.

CBER has developed an interim strategic plan for 2017-2019 to contribute to the improvement of public health and to provide a framework for how CBER can most effectively allocate its fiscal and human resources to successfully navigate the challenges and opportunities of 21st Century medicine,. This plan aligns with FDA's Strategic Priorities and the Department of Health and Human Services' strategic plan and reflects new legislative mandates, expanded roles in addressing global health needs, recent innovations in regulatory science and technology, and expanded opportunities for collaboration. The CBER goals include:

- Increase the nation's preparedness to address threats as a result of terrorism, pandemic influenza, and emerging infectious diseases.
- Improve global public health through international collaboration including research and information sharing.
- Utilize advances in science and technology to facilitate development of safe and effective biological products.
- Ensure the safety of biological products.
- Advance regulatory science and research.
- Manage for organizational excellence and accountability.

During 2016, the Biologics Program contributed to the improvement of public health with the following accomplishments:

- In response to the Zika virus outbreak, FDA contributed with the development of blood and tissue safety guidances and took rapid steps to help ensure safety of the blood supply.
- FDA approved noteworthy biological products including Imlygic, the first FDA-approved oncolytic virus therapy to treat melanoma lesions that cannot be removed completely by surgery.
- FDA issued a Warning Letter regarding three stem cell treatment centers for operating without a valid biologics license or investigational new drug application in effect.

The following selected accomplishments demonstrate the Biologics Program's delivery of its regulatory and public health responsibilities within the context of current priorities.²⁶

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 committed to facilitating the development of new biological products for a broad range of complex and life-threatening diseases. The program seeks to expedite the development of innovative and complex biological products, including those representing the exciting medical promise of precision medicine; additional vaccines against pandemic influenza and other infectious diseases; cellular and gene therapies; and new technologies to enhance the safety and availability of blood and blood products.

Facilitate Product Development through Regulatory Science

FDA contributes to, and draws on, advances in science and technology to design better ways of predicting the safety, purity, potency and effectiveness of biological products early in their life cycle and conducts mission-related research to facilitate product development. The Biologics Program has a cadre of scientific experts who understand the regulatory process to conduct proactive research to address regulatory science gaps and provide effective regulatory responses to public health emergencies and new technologies. FDA leverages this considerable scientific expertise to develop new methods and technologies designed to expedite product development.

FDA conducted research to model the impact of removing risk assessment questions for HIV and rely solely on HIV nucleic acid testing in order to protect the blood supply. The study found these changes would potentially increase the risk of exposure to HIV four-fold to blood recipients.²⁷

In response to the Zika virus outbreak, FDA participated in the 7th meeting of the World Health Organization (WHO) Collaborating Centers to support development of WHO Biological Reference Preparations, including the Zika virus for the development of blood products and in vitro diagnostics devices used to test blood and blood components in March of 2016.

²⁶ Please visit [FDA.gov](https://www.fda.gov) for additional program information and detailed news items.

²⁷ Modeling complete removal of risk assessment questions in the USA predicts the risk of HIV exposure in blood recipients could increase despite the use of nucleic acid testing. Vox Sanguinis 2016 May (Epub 2016 Jan 14); Yang H, Anderson SA, Forshee R, Williams A, Epstein JS, Marks PW.

FDA also supported Zika diagnostic test development to help ensure diagnostic tests for Zika virus provide accurate and reliable results. FDA created Zika Virus RNA reference materials that were distributed to manufacturers to qualify blood screening methods.



To address potential bottlenecks in the production of seasonal and pandemic influenza vaccines, FDA has developed novel alternative methods to generate reagents needed to measure vaccine potency for lot release testing of vaccines. When the avian influenza viruses (H7N9) emerged in China in 2013, FDA overcame an unexpected bottleneck in the preparation of H7N9 vaccine reagents with the first use of an alternative approach to the standard procedure for producing an influenza vaccine potency reagent. Since the results were less than optimal with the traditional method, scientists used a method developed in FDA laboratories where the influenza H7N9 hemagglutinin (HA) glycoprotein is expressed as a virus-like particle and used to generate the H7-specific antiserum needed for potency testing.

FDA scientists are studying how to define the key properties of stem cell-derived therapies that would correlate with safety, potential for efficacy, and product quality in the clinical application of these cells. The scientists are testing the feasibility of innovative methodological approaches to characterize the cells. One recent example is the development of a new method to predict the ability of human mesenchymal stem cells (also known as multipotent mesenchymal stromal cells) to differentiate into bone cells (a term referred to scientifically as osteogenic induction).

In November 2016, two FDA scientists were awarded the Patent for Humanity award from the US Patent and Trademark Office for developing an improved meningitis vaccine production process that has been used to produce a vaccine for African countries to protect against meningococcal type A disease. 235 million people in high-risk Africa countries have been immunized with this vaccine, and thereby tens of thousands of deaths have been prevented.

In June 2016, FDA released a study on multiplex detection and identification of viral, bacterial, and protozoan pathogens in human blood and plasma using a high-density resequencing pathogen microarray platform, published in *Transfusion*. The results indicate that the technology has potential for use in blood safety to identify nucleotide changes in the target pathogen and its potential utility in confirmatory testing for a wide variety of blood-borne pathogens.

In January 2016, the Allergenic Products Advisory Committee met in open session to discuss approaches to establish the safety and effectiveness, including challenge study endpoints, to support the licensure of food allergy immunotherapy products and the clinical development of aeroallergen immunotherapy products for the prevention of respiratory allergic disease.

Improve the Development of Advanced Technologies and Methods

Advances in science and technology show great promise for the development of safe and effective biological products. The Biologics Program is working to expedite the use of advanced technologies and methods, such as newly identified clinical biomarkers, innovative clinical trial designs, and genomics, through the development of regulatory policy and guidances for industry. FDA is also identifying opportunities to expand the use of new scientific technologies in genomics, proteomics, and structural biology to strengthen science-based regulatory review.

Building on the FDA's existing expedited programs available to regenerative medicine products, the Regenerative Medicine Advanced Therapy (RMAT) Designation was established through the Cures Act, signed into law in December of 2016. Drugs that are regenerative medicine therapies may obtain the RMAT designation if the drug is intended to treat serious or life-threatening diseases or conditions and if there is preliminary clinical evidence indicating that the drug has the potential to address unmet medical needs for that disease or condition. RMAT-designated products are eligible for increased interactions with the FDA, similar to those interactions available to sponsors of breakthrough-designated therapies. In addition, they may be eligible for priority review and accelerated approval.

To improve the effectiveness of the product development process, FDA convened the public workshop "Scientific Evidence in the Development of Human Cells, Tissues, and Cellular and Tissue-Based Products Subject to Premarket Approval" on September 8, 2016, to identify and discuss scientific considerations and challenges to help inform the development of human cells, tissues, and cellular and tissue-based products (HCT/Ps) subject to premarket approval, including stem cell-based products. The importance of



Complex Therapies

rigorous science for the development of stem cell therapies and product review and approval, risk-based approaches to review or change a product, and correct identification of stem cells were discussed.

FDA also held a Part 15 hearing, on September 12-13, 2016, to obtain feedback from stakeholders on four draft guidances relating to the regulation of HCT/Ps with over 90 presenters and close to 500 attendees. This feedback will be used to clarify and finalize Agency guidance on these complex yet critical issues related to the regulation of HCT/Ps.

Additionally, FDA hosted the 19th US-Japan Cellular and Gene Therapy Conference, on March 10, 2016, in conjunction with Japan's Ministry of Education, Culture, Sports, Science and Technology, under the US-Japan Cooperative Research Program. The theme of this meeting

was three-dimensional (3D) modeling and printing of tissues and organs. The goal of the conference was to exchange ideas on cutting-edge areas of biomedical research, discuss the innovations in 3D bioprinting of various anatomical structures and their potential use in regenerative medicine, and enhance opportunities for collaborations among scientists from the U.S. and Japan.

Efficiently Provide Access for Safe and Effective Products

FDA continuously evaluates and improves its business processes so that mission-critical work is performed in an effective and efficient manner. FDA also continues to provide scientific and regulatory advice to sponsors and stakeholders and to collaborate with other agencies and international regulatory authorities to advance the clinical development and licensure of biological products. To expedite the development and review of innovative products, established FDA programs such as fast track, breakthrough therapy, accelerated approval, and priority review are used for products that address an unmet medical need of a serious condition.

The Biologics Program exceeded its performance target by completing 100 percent of the standard and priority Biologics License Application/New Drug Application reviews, and standard and priority Efficacy Supplement reviews, within the specified review timeframes for the FY 2015 receipt cohort.

To improve efficiency in the review process, the Electronic Managed Review Process information technology system was developed and launched in September 2016. This system provides comprehensive workload, workflow, and regulatory information on Biologic License Application (BLAs) to supervisors, reviewers, and regulatory project managers to increase efficiency and reduce costs.

Selected Product Approvals in 2015 – 2017

FDA's Biologics Program has reviewed and approved an array of biological products to treat and prevent diseases. Below are selected recent Biological product approvals in date order.

Disease	Approved	Trade Name	Proper Name	Purpose or Benefit
Dust Mite Allergy	Mar 2017	Odactra	House Dust Mite Allergen Extract	The first allergen extract to be administered under the tongue to treat house dust mite induced nasal inflammation in people 18 through 65 years.
Full-thickness cartilage defects of the knee	December 2016	MACI	Autologous cultured chondrocytes on porcine collagen	First FDA-approved product that applies the process of tissue engineering to grow cells on scaffolds using healthy cartilage tissue from the patient's own knee for repair.

			membrane	
Cholera	June 2016	Vaxchora	Cholera Vaccine Live Oral	Only FDA-approved vaccine for the prevention of cholera for adults traveling to cholera-affected areas. (Fast Track designation, Priority Review Status and Tropical Disease Priority Review Voucher)
von Willebrand disease	Dec 2015	Vonvendi	von Willebrand factor (Recombinant)	For adults, 18 years of age and older, diagnosed with von Willebrand disease. The first FDA-approved recombinant von Willebrand factor approved for the on-demand treatment and control of bleeding episodes. (Orphan Drug designation)
Influenza	Nov 2015	Fluad	Influenza vaccine, adjuvanted	The first adjuvanted trivalent seasonal influenza vaccine persons 65 years of age and older against influenza virus subtypes A and B. (Accelerated approval)
Disease	Approved	Trade Name	Proper Name	Purpose or Benefit
Melanoma lesions in the skin and lymph nodes	Oct 2015	Imlygic	talimogene laherparepvec	First FDA-approved genetically modified live oncolytic virus therapy used to treat melanoma lesions that cannot be removed completely by surgery.
Hereditary Factor X deficiency	Oct 2015	Coagadex	Coagulation Factor X (Human)	The first coagulation factor replacement therapy for treatment of adults and adolescents with hereditary Factor X deficiency for control of bleeding episodes. (Fast track designation, Priority Review Status, and Orphan Drug designation)

Enhance Oversight

Within this Goal area, FDA's 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, combined with surveillance of postmarket product use, plays a critical role in assuring the safety of FDA-regulated products.

As a part of regulatory oversight, FDA develops standards; assists industry in reducing risks in the manufacturing, production, and distribution of FDA-regulated products; strengthens the detection and surveillance of potential problems; and improves the response to identified and emerging problems with FDA-regulated products.

Compliance and Oversight

FDA's field work plays an integral role in helping to assure the safety of FDA-regulated products. The field staff provides additional 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 2016, FDA issued a Warning Letter regarding three stem cell treatment centers for operating without a valid biologics license or investigational new drug application in effect. The treatment centers had recovered adipose tissue and processed into adipose-derived stem cells intended to treat a variety of medical conditions. The Warning Letter also identified violations of current Good Manufacturing Practice (cGMP) and current Good Tissue Practice (CGTP).

Develop Guidance to Ensure Product Safety

FDA is responsible for ensuring that blood, blood components, and HCT/Ps remain free of infectious agents and contamination, which may be spread, through contact with infected individuals, travel to endemic areas, arthropod vectors, contaminated food, risk behaviors and many other mechanisms. FDA plays a critical role in the United States' preparedness for and response to infectious diseases including issuing guidance documents to help protect the safety of FDA regulated biological products. FDA also works proactively to prepare for and respond to threats and potential problems, collaborating with Department of Health and Human Services (DHHS) agencies, federal government partners, the World Health Organization (WHO), National Regulatory Authorities, and stakeholders from the private and public sector.

For example, FDA has been working aggressively to combat the Zika virus outbreak. In February 2016, FDA issued guidance recommending the deferral of individuals from donating blood



Mosquito Borne Virus

if they have been to areas with active Zika virus transmission, may have been exposed to the Zika virus, or had a confirmed Zika virus infection.²⁸ In August 2016, revised guidance was issued, recommending nationwide testing of individual units of blood components for Zika virus or the use of a pathogen reduction device for plasma and platelet products.²⁹

FDA also issued guidance in March 2016, providing “Donor Screening Recommendations to Reduce the Potential Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps).” This guidance addresses donation of HCT/Ps from both living and deceased donors, including donors of reproductive cells/tissue (semen, oocyte, embryos) and gestational tissues such as umbilical cord blood, placenta, and amniotic membrane.

In January of 2017, FDA issued the final guidance for industry, “Recommendations for Assessment of Blood Donor Suitability, Donor Deferral and Blood Product Management in Response to Ebola Virus.” This guidance provides blood establishments recommendations for assessing blood donor eligibility, donor deferral and blood product management in the event that an outbreak of Ebola virus disease.

In December 2015, FDA published the final guidance “Revised Recommendations for Reducing the Risk of Human Immunodeficiency Virus Transmission by Blood and Blood Products,” changing the blood donor deferral period for men who have sex with men from an indefinite deferral to 12 months. AABB and Plasma Protein Therapeutics Association developed revised donor history questionnaires to facilitate blood establishments’ implementation of the final guidance. FDA reviewed the questionnaires and recognized them as acceptable mechanisms for collecting donor history information in FDA guidance issued in May, 2016, “Implementation of Acceptable Full-Length and Abbreviated Donor History Questionnaires and Accompanying Materials for Use in Screening Donors of Blood and Blood Components.”

FDA is committed to reevaluating and updating its blood donor deferral policies to reduce the risk of HIV transmission as new scientific data become available. In July 2016, FDA established a public docket for comment on the Agency's blood donor deferral recommendations described in the December 2015 guidance. FDA invited the submission of scientific evidence on the feasibility of moving from the existing time-based deferrals related to risk behaviors to alternate options, including the use of individual risk assessments.

Collaboration with Industry and Public Health Organizations

²⁸ Guidance for Industry: Recommendations for Donor Screening, Deferral, and Product Management to Reduce the Risk of Transfusion-Transmission of Zika Virus, Feb 2016

²⁹ Guidance for Industry: Revised Recommendations for Reducing the Risk of Zika Virus Transmission by blood and Blood Components

Each year, the FDA, WHO, CDC and other public health experts collaborate on the review of influenza disease surveillance and laboratory data collected from around the world in an effort to identify influenza strains that may cause the most illness in the upcoming season. Based on that information and the recommendations of the FDA's Vaccines and Related Biological Products Advisory Committee, which met on March 9, 2017, FDA selected the strains that should be included in the influenza virus vaccines for the 2017-2018 influenza season.

FDA participated in meetings with WHO to facilitate regulatory capacity building of national regulatory authorities in developing countries. In May 2016, FDA participated in a consultation meeting on the development of a guideline for Ebola vaccine development.

FDA continues to engage with trade organizations to discuss the concerns from the blood collection industry over the sustainability of the blood collection industry due to decreased demand for red blood cells for transfusion, causing significant reductions in collections of Whole Blood and Red Blood Cells. FDA representatives also participate as ex officio members of the HHS Advisory Committee on Blood and Tissue Safety and Availability to discuss the sustainability of the blood collection industry.

Guidances

Below are selected recent guidances issued by CBER, listed in date order. These guidances help address various issues.³⁰

Date	#	Title	Description
Nov 2016	FDA-2016-D-3750-0001	Revised Recommendations for Determining Eligibility of Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products Who Have Received Human -Derived Clotting Factor Concentrates	Supplements the August 2007 guidance. FDA no longer considers FDA licensed Human-Derived Clotting Factor Concentrates a risk factor for HIV, HBV, or HCV.
Sep 2016	FDA-2013-D-1143-0097	Use of Nucleic Acid Tests to Reduce the Risk of Transmission of West Nile Virus (WNV) from Living Donors of Human Cells,	Makes recommendations for eligibility determinations for HCT/Ps, for testing living donors for WNV. Supplements recommendations and supersedes the "WNV"

³⁰ 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
		Tissues, and Cellular and Tissue-Based Products (HCT/Ps)	section in the August 2007 guidance.
Aug 2016	FDA-2016-D-0545-00010049/0050	Revised Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components	Supersedes February 2016 “Recommendations for Donor Screening, Deferral, and Product Management to Reduce the Risk of Transfusion-Transmission of Zika Virus” guidance and March 2016 Q&A.
Mar 2016	FDA-2013-D-0811-0022	Donor Screening Recommendations to Reduce the Risk of Transmission of Zika Virus by Human Cells, Tissues, and Cellular and Tissue-Based Products	Identifies Zika virus as a relevant communicable disease agent or disease and provides recommendations to reduce the risk of transmission of the virus by HCT/Ps.
Jan 2016	FDA-2012-D-0307-0007	Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease and Variant Creutzfeldt-Jakob Disease by Blood and Blood Products	Provides manufacturers of plasma-derived products with revised recommendations for how to report labeling that accurately reflects the potential risk for vCJD in products.

Monitor the Safety, Quality, and Availability of Licensed Biological Products

The Biologics Program’s vision for postmarket safety monitoring entails expanding access to information regarding patients’ use of a biological product and health outcomes in automated databases, enabling optimal detection and analysis of potential biologics safety concerns. FDA is working to expand the use of large databases from healthcare providers, insurers, and other partners to identify safety problems associated with biologic product use. Using large datasets that reflect real life experiences of consumers treated with the product allows a comprehensive approach to product safety surveillance. Combined with enhanced scientific tools such as genomics, advanced statistics, and mathematical modeling, FDA is using powerful tools of bioinformatics to develop new scientific data and methods to evaluate safety signals. Recent accomplishments are highlighted below.

FDA has launched initiatives to facilitate new “real time” surveillance of vaccines and blood products. In September 2016, FDA in collaboration with the National Heart, Lung and Blood Institute, and the DHHS Office of the Assistant Secretary for Health, launched the Transfusion-Transmissible Infections Monitoring System (TTIMS). This system provides invaluable data for estimating the incidence and prevalence of HIV, hepatitis B virus, and hepatitis C virus infection. TTIMS is actively assessing transfusion-transmitted infection markers, behavioral risk factors, and other epidemiologic variables among voluntary U.S. blood donors that may be used to reflect changes in future blood safety policies. FDA has awarded multi-year contracts to US blood centers for data and provides a sample collection representing more than 50 percent of the total US blood supply.

The Blood Safety Continuous Active Surveillance Network (BloodSCAN), a component of the Sentinel System, is an active surveillance system used to evaluate recipient safety of FDA-regulated blood components and plasma-derived products, utilizing billing electronic health record data and other electronic data to assess the risk of adverse health outcomes among large populations. In 2016, FDA expanded the data within BloodSCAN to include inpatient electronic health record data from Hospital Corporation of America. This assessment, which is the first Sentinel utilization of this new inpatient data source, examines the feasibility of utilizing this information to capture exposure to blood components and the outcome of transfusion-related acute lung injury (TRALI), identify potential risk factors and estimate the incidence rates of TRALI subsequent to blood component exposure.

In September 2016, FDA issued the protocol and study report for the pilot study of TreeSCAN utilizing PRISM data for the HPV4 vaccine. The TreeSCAN method allows a wide range of unsuspected but potential adverse reactions to be simultaneously evaluated, helping to identify adverse events that may merit additional, careful epidemiologic investigation. FDA is also applying this method in the first protocol-based study designed to mine healthcare data in Sentinel to detect whether there are any serious, unexpected adverse events after vaccination for Gardasil 9.

In December, 2016, FDA held a public workshop entitled “The Sentinel Post-Licensure Rapid Immunization Safety Monitoring (PRISM) Program” to describe the Sentinel Initiative, illustrate how PRISM is used by FDA for regulatory responsibilities including the integration into FDA’s regulatory review process, and discuss the future expansion and integration of PRISM.

Under FDASIA and the Drug Quality and Security Act, FDA gained additional authorities to enhance product safety through monitoring of drug shortages. From January 1 to September 30, 2016, the Biologics Program has documented 1 new drug product shortage, 9 prevented shortages, 2 ongoing shortages, 24 notifications of potential or actual shortages from 17

different manufacturers. CBER has used regulatory flexibility to prevent or mitigate 1 shortage, and expedited 6 reviews to prevent or mitigate a shortage.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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 Actuals	\$329,156,000	\$215,308,000	\$113,848,000
FY 2017 Annualized CR	\$339,082,000	\$214,907,000	\$124,175,000
FY 2018 President's Budget	\$366,230,000	\$95,893,000	\$270,337,000

BUDGET REQUEST

The FY 2018 Budget Request for the Biologics Program is \$366,230,000, of which \$95,893,000 is budget authority and \$270,337,000 is user fees. This level provides a net increase of \$27,148,000. Budget authority decreases by -\$119,014,000 compared to the FY 2017 Annualized CR level and user fees increase by \$146,162,000. The Center for Biologics Evaluation and Research (CBER) amount in this request is \$325,101,000. The Office of Regulatory Affairs amount is \$41,129,000.

The FY 2018 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 the American public. FDA will continue to facilitate the development of new biological products for a broad range of complex and life-threatening diseases. FDA will work to reduce review times and regulatory burden by continuing to make every effort to enhance FDA-sponsor communications in its user fee programs and conducting Expedited Reviews to promote timely access for critically needed therapies for patients that meet an important public health need, without compromising FDA's high standards for demonstrating the safety, efficacy, and quality of new medicines. The Biologics Program will continue to leverage all of the expedited medical programs, including Breakthrough Therapy designation, Regenerative Medicine Advanced Therapy Designation, Fast Track designation, Priority Review Status, and Accelerated approval, when appropriate. Building on the FDA's existing expedited programs available to regenerative medicine products, CBER will continue implementation of the Regenerative Medicine Advanced Therapy (RMAT) Designation, which was established through the Cures Act.

The regulatory science and research program will continue to engage in forward-looking priority setting to allocate its resources towards efforts that best support FDA's ability to

respond to public health needs, use science to address the complexity of products and ever-changing scientific and technological advancements.

To foster manufacturing innovation, flexibility, and adaptation in the increasingly global regulatory environment, FDA works to modernize existing regulations and guidance. These guidances range from protecting the blood and tissue supply in the face of an emerging infectious disease, to addressing recent statutory mandates, to expediting the use of advanced technologies, such as newly identified clinical biomarkers, innovative clinical trial designs, and genomics. FDA continues to collaborate with federal partners and regulated industry when developing or updating new guidance, rules, and standards that provide important direction to manufacturers and distributors of regulated biological products. The Biologics Program will continue early engagement with manufactures through participation in workshops to identify and discuss scientific considerations and challenges to help inform the development of biological products subject to premarket approval.

FDA collaborates and establishes relationships with other regulators and health agencies in the U.S. and throughout the world to respond quickly to public health threats resulting from outbreaks of emerging infectious diseases, pandemic influenza, and terrorism. FDA also strategizes to harmonize existing regulatory standards and works with international scientific efforts to establish and maintain reference materials and standards for biologics.

FDA continues to expand the use of large databases from healthcare providers, insurers, and other partners using real time data and population-based systems to identify and then address safety problems associated with biologic product use. Working with others in FDA, CBER will also support the advancement and use of systematic approaches to collect and utilize robust and meaningful patient and caregiver input that can more consistently inform drug development and, as appropriate, regulatory decision making.

BUDGET AUTHORITY

Reductions (-\$7.5 million)

Center: -\$4.8 million (Medical Product Safety & Availability)

CBER will reduce its applied scientific research, which supports the development of innovative products, in order to preserve critical regulatory oversight of its non-user fee programs that address blood components, tissues, and allergenic products. Spending on equipment upgrades and maintenance will be reduced, as will the number of research fellows hired to support the regulatory science program. Research fellows bring innovative ideas, talents, and skills to FDA and fill gaps in emerging and targeted regulatory science areas. FDA's goal is to minimize the impact of these reductions on FDA's core mission activities.

CBER will also reduce work on the development of laboratory standards, including reference materials, assays, and methodologies that improve product quality and provide standards and guidance to address new technologies and emerging diseases.

Additionally, CBER will reduce staff through attrition in its non-user fee activities that include the regulation of blood components, tissues, and allergenic products. Not backfilling critical positions will require CBER to reprioritize how it provides advice to sponsors and reduce resources dedicated to the review of blood components for transfusion and allergenic extracts as well as the ability to provide advice to sponsors of tissues that do not require premarket review. CBER may no longer be able to exceed its performance target to complete review and action on 90% of complete blood bank and source plasma Biologic License Application supplements within 12 months after submission date. CBER will also limit proactive work to respond to infectious disease outbreaks globally, including limiting its active participation in international collaboration activities.

Field: -\$2.7 million (Medical Product Safety & Availability)

ORA will apply strategic reductions to its programs in order to preserve the highest priority activities and operations in support of protecting public health. ORA will reduce existing workforce levels through attrition.

In order to continue operations under the FY 2018 request levels, ORA will apply the necessary program reductions to areas such as training, IT and lab equipment, and across all program office operating budgets while protecting resources for inspections and compliance activities.

Medical Product Budget Authority Recalibration (-\$111.5 million)

Center: -\$107.4 million / Field: -\$4.1 million (Medical Product Safety & Availability)

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees.

USER FEES

Medical Product User Fee Recalibration and Regulatory Efficiencies (+\$146.2 million)

Center: +\$141.6 million / Field: +\$4.6 million (Medical Product Safety & Availability)

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees. The budget also includes a package of administrative actions designed to achieve greater regulatory efficiency and speed the availability of innovative, safe, and effective medical products in the market. These actions include the improvements are described in the PDUFA VI, MDUFA IV, GDUFA II, and BSUFA II commitment letters submitted to Congress in January 2017.

CBER will strive to reduce review times and regulatory burden by continuing efforts to enhance FDA-sponsor communications and conducting Expedited Reviews with the goal of promoting patients' timely access to life-saving therapies consistent with FDA's high standards and public health mission. CBER is also working to enhance the use of real world evidence to incorporate meaningful patient and caregiver input, as appropriate, into FDA's regulatory decision making on behalf of patients. As part of our commitment to being a global leader at the forefront of medical advances and bringing forward cutting-edge therapies for patients, CBER will continue implementation of the Regenerative Medicine Advanced Therapy (RMAT) Designation, which was established through the 21st Century Cures Act. RMAT-designated products, cell therapy, therapeutic tissue engineering products, human cell and tissue products, and combination products, are eligible for increased interactions with the FDA, similar to those interactions available to sponsors of breakthrough-designated therapies and may be eligible for priority review and accelerated approval. The Center will also work in collaboration with federal partners and regulated industry to address infectious diseases that may emerge to threaten public health, such as novel influenza viruses.

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.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
<u>233207</u> : 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 2015: 100% Target 90% (Target Exceeded)	90%	90%	Maintain
<u>233208</u> : Review and act on priority NME NDA and original BLA submissions within 6 months of the 60 day filing date. (Output)	FY 2015: NA (No submissions received)	90%	90%	Maintain
<u>233209</u> : Review and act on standard non-NME original NDA submissions within 10 months of receipt. (Output)	FY 2015: NA (No submissions received)	90%	90%	Maintain
<u>233210</u> : Review and act on priority non-NME original NDA submissions within 6 months of receipt. (Output)	FY 2015: NA (No submissions received)	90%	90%	Maintain
<u>233205</u> : Complete review and action on complete blood bank and source plasma BLA submissions within 12 months after submission date. (Output)	FY 2015: NA (No submissions received)	90%	90%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
<u>233206</u> : Complete review and action on complete blood bank and source plasma BLA supplements within 12 months after submission date. <i>(Output)</i>	FY 2015: 100% Target: 90% (Target Exceeded)	90%	90%	Maintain
<u>233211</u> : Review and act on new non-user fee, non-blood product applications within 12 months of receipt. <i>(Output)</i>	FY 2015: 100% Target: 60% (Target Exceeded)	60%	60%	Maintain
<u>234101</u> : Increase manufacturing diversity and capacity for influenza vaccine production. <i>(Output)</i>	FY 2016: 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	Maintain
<u>231301</u> : Percentage of Lot Distribution Reports that were entered into the Regulatory Management System – Biologics License Applications (RMS-BLA) within 7 Days. <i>(Output)</i>	FY 2016: 96% Target 85% (Target Exceeded)	85%	85%	Maintain
<u>234212</u> : Percentage of registered domestic blood bank and biologics manufacturing inventory inspected (approximately 900 in total). <i>(Output)</i>	FY 2016: 992 Target: 900 (Target Exceeded)	99%	99%	Maintain
<u>234213</u> : Percentage of planned human foreign and domestic tissue establishment inspections (approximately 570 in total). <i>(Output)</i>	FY 2016: 703 Target: 570 (Target Exceeded)	82%	82%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017

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. In FY 2016, 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 comparing several alternative methods and involving multiple manufacturers and regulatory agencies was completed. Most of the newer methods demonstrated feasibility in this study and a follow-up study is being planned for FY 2017 that will continue to evaluate and compare these alternative potency methods, with an emphasis on evaluating the capability of each technique to distinguish and quantify sub-potent vaccine.

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 was completed in FY 2016. In additional studies at FDA, designed to increase the yields of candidate vaccines by targeted manipulation, FDA produced and optimized potentially pandemic influenza vaccine viruses, such as H7N9 vaccine reference virus. H7N9 candidate vaccine viruses produce a relatively low protein yield when compared with other seasonal or pandemic viruses for the influenza vaccine production. The protein yield of a H7N9 vaccine reference virus was enhanced by multiple passaging in cells and eggs. The substitution mutations in the high yield virus will be confirmed by introduction of the mutation into the other low yield viruses and assessment their protein yield in FY 2017.

PROGRAM ACTIVITY DATA TABLES

CBER Workload and Outputs	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
Original Biologics License Applications (BLA)			
Workload ¹	40	40	40
Total Decisions ²	36	36	36
Approved	12	12	12
BLA Efficacy Supplements			
Workload ¹	27	27	27
Total Decisions ²	35	35	35
Approved	19	19	19
BLA Manufacturing Supplements			
Workload ¹	1,403	1,403	1,403
Total Decisions ²	1,230	1,230	1,230
Approved	1,054	1,054	1,054
BLA Labeling Supplements			
Workload ¹	145	145	145
Total Decisions ²	161	161	161
Approved	152	152	152
Original New Drug Application (NDA)			
Workload ¹	0	0	0
Total Decisions ²	0	0	0
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	28	28	28
Total Decisions ²	26	26	26
Approved	24	24	24
NDA Labeling Supplements			
Workload ¹	3	3	3
Total Decisions ²	6	6	6
Approved	6	6	6
Original Abbreviated New Drug Application			
Workload ¹	1	1	1
Total Decisions ²	0	0	0
Approved	0	0	0
ANDA Efficacy Supplements			
Workload ¹	0	0	0
Total Decisions ²	0	0	0
Approved	0	0	0

CBER Workload and Outputs	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
ANDA Manufacturing Supplements			
Workload ¹	2	2	2
Total Decisions ²	3	3	3
Approved	2	2	2
ANDA Labeling Supplements			
Workload ¹	0	0	0
Total Decisions ²	0	0	0
Approved	0	0	0
Device 510Ks			
Workload ¹	44	44	44
Total Decisions ²	80	80	80
Final Decision - SE	31	31	31
Device Premarket Applications (PMA)			
Workload ¹	1	1	1
Total Decisions ²	3	3	3
Approved	1	1	1
Device Premarket Applications (PMA) Supplements			
Workload ¹	48	48	48
Total Decisions ²	29	29	29
Approved	26	26	26
Investigational New Drugs (IND)			
Receipts: IND (new)	402	402	402
Receipts: IND Amendments	9,898	9,898	9,898
Total Active IND ³	2,421	2,421	2,421
Investigational Device Exemptions (IDE)			
Receipts: IDE (new)	20	20	20
Receipts: IDE Amendments	292	292	292
Total Active IDE ³	153	153	153
Patient Safety			
Adverse Event Reports Received ⁴	73,720	78,000	80,000
Biological Deviation Reports Received	51,230	51,000	51,000
Sponsor Assistance Outreach			
Meetings	481	481	481
Final Guidance Documents ⁵	37	30	30
Admin/Management Support			
Advisory Committee Meetings Held	10	13	13
FOI Requests Processed	334	360	360

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 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget
<i>FDA WORK</i>			
DOMESTIC INSPECTIONS			
<i>UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>1,875</i>	<i>1,909</i>	<i>1,909</i>
Bioresearch Monitoring Program Inspections	80	100	100
Blood Bank Inspections	895	900	900
Source Plasma Inspections	180	190	190
Pre-License, Pre-Market Inspections	61	55	55
GMP Inspections	38	28	28
GMP (Device) Inspections	4	7	7
Human Tissue Inspections	638	650	650
FOREIGN INSPECTIONS			
<i>UNIQUE COUNT OF FDA FOREIGN BIOLOGICS</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>68</i>	<i>47</i>	<i>47</i>
Bioresearch Monitoring Program Inspections	17	11	11
Foreign Human Tissue Inspections	2	0	0
Blood Bank Inspections	7	7	7
Pre-License, Pre-market Inspections	7	7	7
GMP Inspections (Biologics & Device)	34	20	20
<i>TOTAL UNIQUE COUNT OF FDA BIOLOGIC</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>1,943</i>	<i>1,956</i>	<i>1,956</i>
IMPORTS			
Import Field Exams/Tests	155	45	45
Import Line Decisions	151,911	162,545	173,923
Percent of Import Lines Physically Examined	0.10%	0.03%	0.03%
<i>GRAND TOTAL BIOLOGICS ESTABLISHMENT</i>			
<i>INSPECTIONS</i>	<i>1,943</i>	<i>1,956</i>	<i>1,956</i>

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ANIMAL DRUGS AND FEEDS

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
Animal Drugs and Feed.....	188,615	188,042	190,540	183,280	-7,260
<i>Budget Authority.....</i>	<i>158,635</i>	<i>158,629</i>	<i>158,333</i>	<i>107,606</i>	<i>-50,727</i>
<i>User Fees.....</i>	<i>29,980</i>	<i>29,413</i>	<i>32,207</i>	<i>75,674</i>	<i>43,467</i>
Center.....	122,508	122,848	124,497	121,749	-2,748
Budget Authority.....	94,005	94,001	93,826	49,117	-44,709
User Fees.....	28,503	28,847	30,671	72,632	41,961
<i>Animal Drug (ADUFA).....</i>	<i>20,125</i>	<i>20,459</i>	<i>20,879</i>	<i>57,775</i>	<i>36,896</i>
<i>Animal Generic Drug (AGDUFA).....</i>	<i>8,378</i>	<i>8,388</i>	<i>9,792</i>	<i>14,857</i>	<i>5,065</i>
Field.....	66,107	65,194	66,043	61,531	-4,512
Budget Authority.....	64,630	64,628	64,507	58,489	-6,018
User Fees.....	1,477	566	1,536	3,042	1,506
<i>Animal Drug (ADUFA).....</i>	<i>411</i>	<i>378</i>	<i>427</i>	<i>1,665</i>	<i>1,238</i>
<i>Animal Generic Drug (AGDUFA).....</i>	<i>259</i>	<i>188</i>	<i>302</i>	<i>570</i>	<i>268</i>
<i>Food and Feed Recall.....</i>	<i>---</i>	<i>---</i>	<i>---</i>	<i>---</i>	<i>---</i>
<i>Food Reinspection.....</i>	<i>807</i>	<i>---</i>	<i>807</i>	<i>807</i>	<i>---</i>
FTE.....	925	925	948	920	-28

Authorizing Legislation: Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321-399); Public Health Service Act (42 U.S.C. 201, *et seq.*); Animal Drug Amendments (1968) (21 U.S.C. 360b); Generic Animal Drug and Patent Term Restoration Act (1988); Animal Medicinal Drug Use Clarification Act of 1994; Animal Drug Availability Act of 1996; FDA Export Reform and Enhancement Act of 1996; Food and Drug Administration Modernization Act of 1997; Antimicrobial Regulation Technical Corrections Act of 1998; Public Health Security and Bioterrorism Preparedness and Response Act of 2002; Animal Drug User Fee Act of 2003 (21 U.S.C. 379j-11 - 379j-12); Minor Use and Minor Species Animal Health Act of 2004; Sanitary Food Transportation Act of 2005; Food and Drug Administration Amendment Act of 2007; Animal Drug User Fee Amendments of 2008 (P.L. 110-316); Animal Generic Drug User Fee Act of 2008 (P.L. 110-316); Patient Protection and Affordable Care Act; FDA Food Safety Modernization Act (P.L. 111-353); FDA Safety and Innovation Act (P.L. 112-144); Animal Drug User Fee Reauthorization Act of 2013 (P.L. 113-14); Animal Generic Drug User Fee Reauthorization Act of 2013 (P.L. 113-14); Drug Quality and Security Act (2013)

Allocation Methods: Competitive grant; Contract; Direct Federal/intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The Animal Drugs and Feeds Program began in 1968 with an amendment to the Federal Food, Drug, and Cosmetic (FD&C) Act to include new authorities for regulating animal drugs, devices, and feed. The Animal Drugs and Feeds Program protects and promotes the health of humans and animals by ensuring the safety of the American food supply, the safety of animal feed and devices, and the safety and effectiveness of animal drugs.

The Center for Veterinary Medicine (CVM) is a scientific and regulatory organization and one component under the Foods and Veterinary Medicine (FVM) Program that works to fulfill the

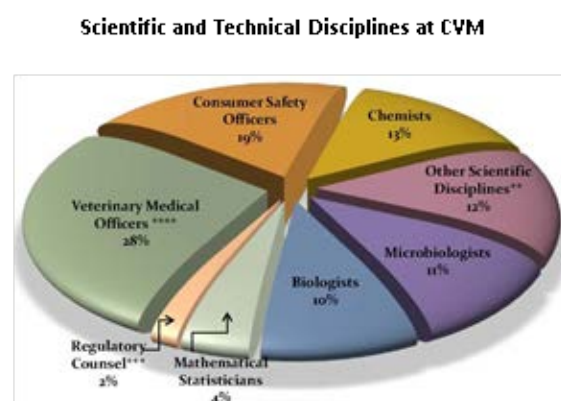
U.S. Food and Drug Administration's (FDA) public health mission. The other component, the Foods Program, described in another section, is administered by the Center for Food Safety and Applied Nutrition (CFSAN). These two component programs collaborate with the Office of Regulatory Affairs (ORA), which performs field activities, including inspections, sample collections, and import exams. The Office of Foods and Veterinary Medicine provides leadership and strategic direction to the FVM Program.

The Animal Drugs and Feeds Program fosters human and animal health by evaluating animal products for safety and efficacy and by enforcing applicable provisions of the Federal Food, Drug, and Cosmetic Act and other legal authorities. These include animals from which human foods are derived, and pet (or companion) animals.

The Animal Drugs and Feeds Program reviews animal drug applications for safety and effectiveness, monitors animal drugs, animal foods, and devices on the market, reviews food additives for safety and utility, and conducts research that helps FDA ensure the safety of animal drugs, food for animals, and food products made from animals. The Animal Drugs and Feeds Program also helps to make more animal drugs legally available for minor species, such as fish, pet rodents, and birds, and for minor (infrequent and limited) uses in major species, such as cattle, turkeys, and dogs.

Congress recognized the unique challenges FDA faces in the area of food safety in the 21st Century and gave FDA a legislative mandate to meet these challenges by enacting the FDA Food Safety Modernization Act (FSMA). FSMA directs FDA to build a food and feed safety system based on the public health principles of comprehensive prevention, enhanced focus on risk-based resource allocation, and partnerships across the public and private sectors to minimize hazards from farm to table.

FDA's FVM Program Strategic Plan³¹ provides a framework for implementing FSMA. The plan



places a high priority on preventing foodborne illness of known and unknown origins. FVM also regulates the safety and effectiveness of animal drugs. In support of this endeavor, the Animal Drugs and Feeds Program is aligned with the FVM Strategic Plan goals for food safety, nutrition, animal health, and organizational excellence.

To achieve the goals of the FVM Strategic Plan, the

³¹ The strategic plan can be found at: <http://www.fda.gov/aboutfda/centersoffices/officeoffoods/ucm273269.htm>.

Animal Drugs and Feeds Program focuses on:

- timely premarket review of new animal drugs,
- appropriate use of approved animal drugs,
- scientific research solutions for the safety of animal-derived food and health products,
- minimizing the illegal sale of unapproved and compounded drugs,
- prevention of marketing of unsafe products, and
- compliance and enforcement actions to remove unsafe products from market.

Appropriations and user fee programs fund the regulatory process to ensure product safety and effectiveness. User fees are authorized under the Animal Drug User Fee Act (ADUFA), the Animal Generic Drug User Fee Act (AGDUFA), and the FDA Export Reform and Enhancement Act (Export Certificate program).

ADUFA and AGDUFA supplement the appropriated portion of the animal drug review processes. By supplementing funding for the animal drug review processes, ADUFA and AGDUFA support the quality and timeliness of new (pioneer) and generic animal drug reviews.

The Export Certificate program helps international trade and promotes the export of U.S.-made products by assuring that exported products can be marketed in the U.S., or meet specific U.S. regulations.

The following selected accomplishments demonstrate the Animal Drugs and Feeds Program's delivery of its regulatory and public health responsibilities within current priorities.³²

Improve and Safeguard Access

The Animal Drugs and Feeds Program regulates animal drugs and feeds. Premarket responsibilities include ensuring the effectiveness and efficiency of the product review process; and working collaboratively with partners in the private sector, public sector, and academia to facilitate product development. Within this goal area, the Program addresses the following FDA Strategic Priorities:

- Safety and Quality
- Regulatory Science
- Globalization.

Animal Drug Review

³² Please visit <https://www.fda.gov/AnimalVeterinary/default.htm> for additional program information and detailed news items.

The Animal Drugs and Feeds Program increases the availability and variety of safe and effective products, including antimicrobials, to relieve animal pain and suffering and to support their health. The animal drug user fee acts require FDA to meet timeframes for review and action on 90 percent of new animal drug applications each fiscal year.

In FY 2016, FDA exceeded all animal drug review performance goals. FDA completed the review and action on 99.8 percent of original New Animal Drug Applications (NADAs) and other ADUFA sentinel submissions within timeframes specified by ADUFA. FDA also exceeded the animal drug review performance goals and completed the review and action on 100 percent of original Abbreviated New Animal Drugs Applications (ANADAs) for generic drugs, Reactivations (resubmissions), and other AGDUFA sentinel submissions within the timeframes for applications received and reviewed in FY 2016.

Selected Product Approvals in 2016

Below are the most recent Animal Drugs and Feeds Program significant product approvals during calendar year 2016. The term “Significant Approvals” means the approval of an original or supplemental NADA or ANADA that required FDA’s review of safety or effectiveness data. This type of approval applies to new animal drug products, new chemical entities, or changes such as:

- additions to the indication section of the label of a new target species,
- a new significant class of target animals,
- a new disease indication,
- a new route of administration, and
- a new tolerance or withdrawal period.

This list does not represent any degree of importance or priority ranking of products.³³

Date	Product Name	Purpose or Benefit
Sep 2016	Amoxicillin Trihydrate and Clavulanate Potassium Tablets	Indicated in the treatment of: Dogs: Skin and soft tissue infections and canine periodontal disease. Cats: Skin and soft tissue infections and urinary tract infections.
Jul 2016	BRAVECTO	For the treatment and prevention of flea infestations and the

³³ For more information on product approvals and designations visit <http://www.fda.gov/NewsEvents/ProductsApprovals/>.

		treatment and control of tick infestations for dogs.
Mar 2016	GALLIPRANT	For the control of pain and inflammation associated with osteoarthritis in dogs.
Mar 2016	Imrestor	For reduction in incidence of clinical mastitis in first 30 days of lactation in dairy cows and replacement dairy heifers that recently birthed a calf.
Jan 2016	Thyro-Tabs Canine	For replacement therapy for diminished thyroid function in dogs.

Genetic Engineering

In January 2017, FDA released *Draft Guidance for Industry #236, Regulation of Mosquito-Related Products*, which clarifies which mosquito-related products FDA regulates and which such products EPA regulates. FDA is accepting public comments through June 19, 2017. This draft guidance is consistent with the FDA's commitments outlined in the *National Strategy for Modernizing the Regulatory System for Biotechnology Products*, which sets forth a vision for ensuring that the federal regulatory system is equipped to assess efficiently the risks, if any, associated with future products of biotechnology. FDA is reviewing information in an Investigational New Animal Drug (INAD) file involving a genetically-engineered (GE) mosquito designed to reduce disease-transmitting mosquito populations. The *Aedes aegypti* species of mosquito is common in southern U.S. States and known to transmit potentially debilitating human viral diseases, including Zika, dengue, yellow fever, and chikungunya. As part of the INAD file review, in August 2016, the FDA completed an environmental review for a proposed field trial in Key Haven, Florida. Based on the results of a public referendum held in November 2016, the Florida Keys Mosquito Control District decided not to move forward with the trial in Key Haven. The sponsor of the GE mosquito will need to submit to FDA an environmental assessment for the new trial location.

CVM reviews applications related to GE animals as described in Guidance for Industry #187, *Regulation of Intentionally Altered Genomic DNA in Animals*. Applicants must demonstrate safety to the target animal and the lineage derived from it, food safety if the animal is from a food-producing species, and that the intended change is as claimed, such as effectiveness. With regard to animals that result from genome editing, FDA recently issued a draft revised version of its Guidance #187 that expands the scope of that guidance to include animals developed using that technology. The comment period on that guidance document is open until June 19, 2017.

In December 2015, FDA approved Kanuma (sebelipase alfa) – the first treatment for humans with a rare disease known as lysosomal acid lipase (LAL) deficiency. This drug comes from contained GE chickens. Patients with LAL deficiency have no or little LAL enzyme activity. This results in a build-up of fats within the tissue cells and can lead to liver disease, cardiovascular disease, and other complications. The approval of Kanuma resulted from collaboration between FDA's CVM and FDA's Center for Drug Evaluation and Research (CDER).

In November 2015, FDA approved an application for AquAdvantage Salmon, an Atlantic salmon for human consumption that is genetically-engineered to grow faster than its non-GE counterpart. FDA regulates GE animals under the new animal drug provisions of the FD&C Act. This is because the recombinant DNA (rDNA) construct transplanted into the animal meets the definition of a drug.³⁴ In this case, the rDNA construct introduces a trait that makes the AquAdvantage Salmon reach a key growth point faster. FDA found that AquAdvantage Salmon is safe for consumption, the rDNA construct is safe for the fish itself, and the salmon meets the sponsor's claim about faster growth. FDA also found that there are no material differences between this GE salmon and its non-GE counterpart that would require additional labeling.

Selected Guidances Issued 2016

Below are final guidances issued by the Animal Drugs and Feeds Program in 2016. These guidances help address various issues. This list does not represent any degree of importance or priority ranking among the published guidances.³⁵

Date Issued	#	Title	Description
Jun 2016	FDA-2015-N-4563	Modified Release Veterinary Parenteral Dosage Forms: Development, Evaluation, and Establishment of Specifications	Recommendations on submission of chemistry, manufacturing, and controls, pharmacokinetic information, and procedures, for approval of modified release parenteral drug products for use in veterinary species.
Apr 2016	FDA-2003D-0061	Comparability Protocols - Chemistry, Manufacturing, and Controls Information for New Animal Drugs	Recommendation for preparing and using comparability protocols for post-approval changes in chemistry, manufacturing, and controls of both NADAs and ANADAs.

Animal Drug Inspections

³⁴ A DNA construct is an artificially constructed segment of nucleic acid that is intended to be "transplanted" into a target tissue or cell.

³⁵ For more information on guidance please visit <http://www.fda.gov/RegulatoryInformation/Guidances/>.

FDA's field force conducts preapproval inspections to support the review of premarket applications for pioneer and generic animal drugs. To help ensure the integrity of scientific testing and the reliability of test data, FDA also conducts bioresearch monitoring (BIMO) inspections of study facilities, clinical investigators, institutional review boards, or contract research organizations that submit data to FDA.

After animal drug products are on the market, the field continues to inspect manufacturing establishments to determine their ability to manufacture products to the specifications stated in their applications, and to ensure product quality.

FDA also inspects non-clinical laboratories that collect data to determine whether Good Laboratory Practices have been followed. Accurate data is essential to the review and approval of new animal drugs, and helps to ensure that the rights and welfare of animals are protected.

Minor Use Minor Species

The Minor Use and Minor Species (MUMS) Animal Health Act, passed in 2004, helps FDA ensure that innovative treatments are available for small populations of animals. This law helps to increase the availability of drugs for minor species, such as ferrets and fish, and for minor uses in a major species, such as to treat certain types of cancer in dogs. Greater access to these "MUMS drugs" gives veterinarians more options in treating unique species and uncommon conditions.

One main provision created a new pathway called conditional approval to bring MUMS drugs to the marketplace faster. The conditional approval is valid for one year (and renewable for another four, for a total of five years of conditional approval) and allows the drug company to legally sell the animal drug before proving it meets the "substantial evidence" standard of effectiveness for full approval. Before conditional approval is granted, a sponsor can apply for Designation status for MUMS drugs, which is a status similar to "orphan drug" status for human drugs. As of November 25, 2016, FDA granted 137 MUMS drug designations.

In some cases, a minor species drug is intended for use in species that are too rare or too varied to be the subject of adequate and well-controlled studies in support of a drug approval, and therefore cannot reasonably go through the standard drug approval process. In such cases, FDA may add the drug to the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species (the Index). As of December 1, 2016, FDA had a total of 13 animal drugs on the Index.

FDA published a direct final rule effective December 1, 2016 to ensure that drugs used in animal feed remain available for therapeutic purposes in food-producing minor species after

changes are made to remove the production claims from these drugs. This direct final rule will ensure that these drugs can still be produced by both licensed and unlicensed feed mills.

International Activities

The Animal Drugs and Feeds Program engages in international partnerships that promote and protect animals, as well as the humans who are exposed to them, and develops harmonized product standards and conformity assessment procedures, which help regulators ensure that health, safety, or environmental conditions are met.

FDA partners with the European Food Safety Authority (EFSA) on the Animal Feed Cluster, which allows feed safety experts from both FDA and EFSA to discuss issues of joint interest, such as reviews of safety assessments of various animal feed ingredients.

FDA also partners with Health Canada through the U.S.- Canada Regulatory Cooperation Council (RCC), a council that works to reduce unnecessary regulatory differences. In FY 2016, CVM and RCC have simultaneously reviewed and approved four applications under the RCC program.

The Veterinary Drug Initiative (VDI), a part of the RCC that enhances the premarket evaluation of veterinary drugs, encourages the U.S. and Canada to seek greater alignment in regulatory approaches to:

- remove duplicative requirements
- reduce costs
- provide timely access to animal drug products.

In FY 2016 import field investigators performed more than 7,935 field and label examinations on entry lines of animal drugs and feeds. These activities were performed to identify violations, such as the product not matching the information transmitted electronically, or the product labeling not meeting applicable compliance requirements.

Enhance Oversight

The Animal Drugs and Feeds Program provides critical oversight of production, manufacturing, and the global supply chain for regulated products. The Program also provides surveillance of postmarket product use and assures the safety of FDA-regulated products. Within this goal area, the following FDA Strategic Priorities are addressed:

- Safety,
- Quality
- Regulatory Science.



Selected Rules Published 2016

Below are rules published by the Animal Drugs and Feeds Program in 2016. These rules help address various issues and are further described in the attached links and narratives in this section. This list does not represent any degree of importance or priority ranking among the published rules.³⁶

Date Issued	#	Title	Purpose or Benefit
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³⁶ For more information on FDA rules please visit <http://www.fda.gov/RegulatoryInformation/RulesRegulations/default.htm>.

Dec 2016	FDA-2016-N-1896	New Animal Drugs for Use in Animal Feed; Category Definitions (Direct final rule)	Revising definitions of two categories of new animal drugs used in medicated feeds to base category assignment only on approved uses in major animal species.
Nov 2016	FDA-2016-N-1487	Submission of Food and Drug Administration Import Data in the Automated Commercial Environment (Final Rule)	Establish requirements for electronic filing of entries of FDA-regulated products in electronic system authorized by U.S. CBP, to help FDA in determining admissibility of product.
Aug 2016	FDA-2016-19164	Substances Generally Recognized as Safe (Final rule)	Clarifies criteria for when use of substance in food not subject to premarket approval requirements because generally recognized as safe under conditions of intended use.
Aug 2016	FDA-2011-N-0079	Disqualification of a Clinical Investigator (Final rule)	Amend regulations for new animal drugs for investigational use to expand scope of clinical investigator disqualification to include ineligibility to conduct nonclinical laboratory studies.
May 2016	FDA-2012-N-0447	FDA issues rule for data collection of antimicrobial sales and distribution by animal species	Revises FDA's annual reporting requirements for drug sponsors of all antimicrobials sold or distributed for use in animals intended for human consumption or food-producing animals.

Additional rules address the critical need to establish preventative controls for Animal Food, promote safety standards for industry, and combat antimicrobial resistance.

Preventive Controls for Animal Food

The FSMA final rule on “Current Good Manufacturing Practice and Hazard Analysis and Risk-Based Preventive Controls for Food for Animals” published in September 2015 is foundational to implementing the modern prevention-focused food safety mandate granted to FDA under FSMA. Under this rule, facilities that manufacture, process, pack, or hold food for animals, including pet food, would be required to adhere to current good manufacturing practices and implement hazard analysis and risk-based preventive controls.

In May 2016, FDA issued draft guidance to allow qualified facilities, such as small businesses, to comply with a set of modified requirements of the FSMA Preventive Controls rule. In July 2016, FDA finalized a rule to improve the accuracy of the food facility registration database. This final rule will support the FDA's efforts to act quickly in response to food-related emergencies and will help the FDA to use its inspectional resources more efficiently.

Safety Standards

FDA evaluates industry compliance with safety standards throughout the production and handling stages of the global food – including pet food – and feed supply chain. Under FSMA, FDA received the authority to suspend a facility’s registration if FDA determines that human food or animal feed manufactured, processed, packed, received, or held by a registered facility has a reasonable probability of causing serious adverse health consequences or death to humans or animals. In August 2016, FDA issued draft Guidance for Industry (GFI) #235, “*Current Good Manufacturing Practice (CGMP) Requirements for Food for Animals*,” that provides information on complying with CGMP in areas throughout the facility (i.e., sanitation and water safety), and draft GFI #239, “*Human Food By-Products for Use as Animal Food*,” that provides guidance on determining what requirements in the Preventive Controls for Animal Food rule apply to human food by-products for use as animal food. In April 2016, FDA finalized a food safety rule under FSMA that will help to prevent food contamination during transportation.

Antimicrobial Resistance

The Animal Drugs and Feeds Program continues to take important steps to support antimicrobial stewardship and address public health concerns associated with antimicrobial resistance and the use of antimicrobial drugs in animals.

FDA’s judicious use strategy is intended to curb the emergence of antimicrobial resistance associated with the use of antimicrobial drugs in veterinary settings. The strategy includes GFI #209, which established a framework for ending production uses (e.g., growth promotion) of medically important antimicrobials and bringing the remaining therapeutic uses of such drugs in food-producing animals under veterinary oversight. It also includes GFI #213, which provided detailed guidance to drug sponsors for voluntarily removing production claims for medically important antimicrobials. In January 2017, FDA announced the successful completion of the 3-year plan (outlined in GFI #213) to transition the use of medically important antimicrobial drugs in the feed or drinking water of food-producing animals to veterinary oversight and eliminate their use for production (e.g. growth promotion) purposes. There are 292 affected applications. Judicious use limits antimicrobial drugs used in food-producing animals to those necessary for the animal’s health and are administered under the oversight or consultation of veterinarians.³⁷

FDA published the Veterinary Feed Directive (VFD) final rule in June 2015³⁸ and issued revised GFI #120 in September 2015, two critical pieces of the overall strategy to promote the judicious

³⁷ FDA’s judicious use strategy includes GFI #209, which established a framework for ending production uses (e.g., increased rate of weight gain and improved feed efficiency) of medically important antimicrobials and bringing the remaining therapeutic uses of such drugs in food-producing animals under veterinary oversight. It also includes GFI #213, which provided detailed guidance to drug sponsors for removing production claims for medically important antimicrobials and established an implementation timeline

³⁸ The veterinary feed directive final rule can be found at: <http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm482110.htm>

use of antimicrobials in food producing animals, bringing the use of medically important antimicrobials in feed under veterinary supervision. The VFD final rule defines the process for authorizing use of VFD drugs - animal drugs intended for use in or on animal feed that require the supervision of a licensed veterinarian - and provides veterinarians in all states with a framework for authorizing the use of medically important antimicrobials in feed when needed for specific animal health purposes.

FDA revised the annual summary of the amount of antimicrobials sold or distributed for use in food-producing animals reported under Section 105 of the Animal Drug User Fee Act to include additional data tables. The added data tables provide more detailed information and improve transparency. In December 2016, FDA published its seventh annual report under Section 105 providing a summary of sales and distribution data for 2015.³⁹

In May 2016, FDA released a final rule that established a new requirement for animal drug sponsors to provide species-specific antimicrobial drug sales estimates for the major food-producing species - cattle, swine, chickens, and turkeys. The additional data will improve understanding about how antimicrobials are sold or distributed for use in major food-producing species and help FDA further target its efforts to ensure judicious use of medically important antimicrobials.

In September 2016, FDA announced it was entering the next phase of its efforts to mitigate antimicrobial resistance by focusing for the first time on medically important antimicrobials (i.e., those important for treating human disease) used in animal feed or water that have at least one therapeutic indication without a defined duration of use.

National Antimicrobial Resistance Monitoring System (NARMS)

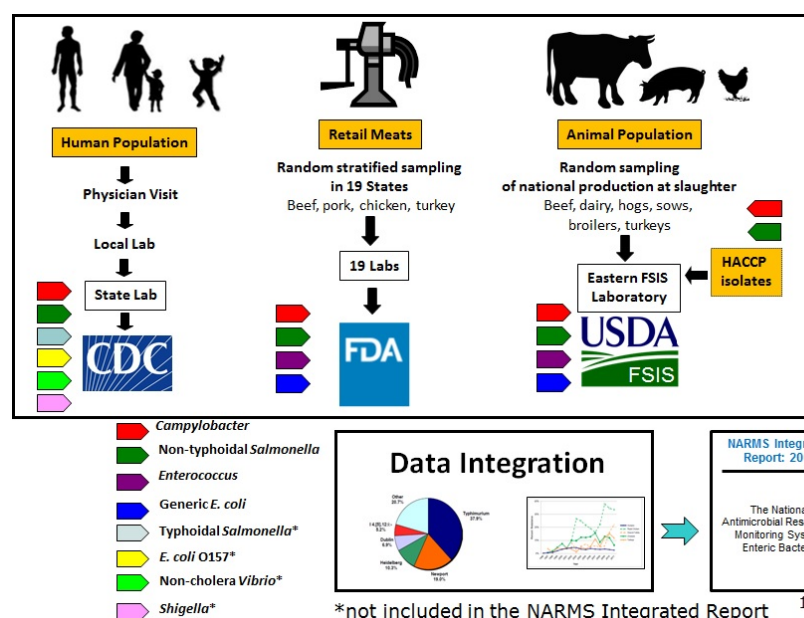
The Animal Drugs and Feeds Program monitors antimicrobial resistance among enteric (intestinal) bacteria via NARMS. FDA uses data from NARMS and other sources to reach an overall risk estimation for the proposed use of an antimicrobial drug in food-producing animals. This risk estimation is used to guide FDA's decision to approve or deny the use of an antimicrobial drug in food-producing animals. FDA may also limit a drug's conditions of use based on this risk estimation to lessen the risk of antimicrobial resistance development. This risk estimation is used to guide FDA's decision to approve or deny the use of an antimicrobial drug in food-producing animals. FDA may also limit a drug's conditions of use based on this risk estimation to lessen the risk of antimicrobial resistance development. Because NARMS data has played key roles in various regulatory activities, the Animal Drugs and Feeds Program must

³⁹ The 2015 Sales and Distribution Data Report can be found at:

<https://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM534243.pdf>

continue to re-evaluate its sampling approach to assure that the data being generated can withstand scrutiny from both a scientific and regulatory perspective. NARMS implemented a new sampling design within the collaborative surveillance framework that is more statistically representative, scientifically sound, and better supports FDA regulatory activities.

Through an interagency agreement with FDA, the USDA's Food Safety Inspection Service (FSIS) implemented a greatly improved food animal sampling scheme for federally inspected slaughter houses that is designed to generate a more representative data set for the purposes of NARMS.



In March 2016, FDA won a U.S. Department of Health and Human Services Ventures Program Award to design a public health surveillance mobile application that will improve the collection of retail food surveillance data that are used for resistance monitoring. The mobile application will advance the collection, management, and transfer of NARMS retail

meat sample data collected in the field by creating an electronic system. The mobile app will allow partners to report surveillance data to FDA faster to support time-sensitive regulatory decision-making and provide information needed to address food related outbreaks.

In November 2016, FDA published the 2014 NARMS Integrated Report⁴⁰. The report highlights antimicrobial resistance patterns in bacteria isolated from humans, retail meats, and animals at slaughter. The Integrated Report now has interactive data displays online to allow users to explore trends in resistance to antimicrobial agents by various factors and, for the first time, it includes Whole Genome Sequencing (WGS) data. This WGS data provides definitive information on the nature, origin, and spread of resistant bacteria in foods.

⁴⁰ The NARMS 2014 Integrated Report can be found at:

<http://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/UCM528861.pdf>

In April 2016, FDA published the 2014-2015 NARMS Retail Meat Interim Report.⁴¹ These reports measure antimicrobial resistance in certain bacteria isolated from raw meat and poultry collected through NARMS.

In August 2015, FDA published online, for the first time, raw NARMS data collected over the past 18 years, enabling the scientific community to contribute ideas and expertise about combating antibiotic-resistant bacteria.

Research Studies Encompassing Microorganisms

FDA provides scientific research solutions that ensure the safety of human and animal health. Whole Genome Sequencing (WGS) is a critical tool that helps FDA to provide such solutions. The high capacity and low costs of rapid DNA sequencing technology and advances in analysis software have made it affordable and easier to routinely determine and interpret the complete DNA sequence obtained from microorganisms. Advancements in WGS represent a revolution in infectious disease diagnosis and surveillance because this technique provides a complete picture of acquired traits that are present in a microorganism, such as known virulence and antibiotic resistance traits.

Further, FDA is using a technique developed at the University of Georgia to switch from traditional, labor intensive, expensive, *Salmonella* serotyping to rapidly identifying the most commonly occurring 200 serotypes of *Salmonella* from the WGS data obtained from cultured bacteria. During FY 2015, FDA sequenced 5,100 isolates and, in the first half of FY 2016, sequenced an additional 918 isolates of *Salmonella* sp. and *Campylobacter* sp. These numbers include the 2013 NARMS *Campylobacter* isolates recovered from retail meat and about 2,500 sequences from various pilot projects for *Escherichia coli*, *Salmonella* sp., and *Campylobacter* sp. that have been submitted to the National Institutes of Health's National Center for Biotechnology Information (NCBI) and are available to the public. The data from the *Salmonella* isolates are publically available via the NARMS interim report for *Salmonella* and NCBI.

FDA continues to work with scientists at the University of Georgia to improve the accuracy of serotyping *Salmonella* via the use of WGS data. FDA is providing sequence data derived from rare *Salmonella* serotypes to improve the serotyping algorithm for *Salmonella*.

Selected Guidances Issued 2016

Below are guidances issued by the Animal Drugs and Feeds Program in 2016. These guidances help address various issues and can be further described in the attached links and narratives in

⁴¹ The NARMS 2014-2015 Retail Meat Interim Report can be found at:

<http://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/UCM498134.pdf>

this section. This list does not represent any degree of importance or priority ranking among the published guidances.⁴²

Date Issued	#	Title	Description
Nov 2016	FDA-2011-N-0922	Small Entity Compliance Guide - Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Food for Animals	To inform domestic and foreign animal food facilities about the PCAF regulations and enable them to better understand the requirements of the rule.
Sep 2016	FDA-2010-N-0155	Veterinary Feed Directive Common Format Questions and Answers	Following comments on the VFD Q&A (GFI #120), FDA is issuing guidance to recommend a common VFD format.
Mar 2016	FDA-2003-D-0432	Use of Material from Deer and Elk in Animal Feed	FDA's recommendations regarding use in animal feed of material from deer and elk that are positive or at high risk for Chronic Wasting Disease (CWD).
Mar 2016	FDA-2014-D-1180	Ensuring Safety of Animal Feed Maintained and Fed On-Farm	To help animal producers develop procedures and practices to ensure the use of safe feed in animal production. Applies to all feed for farm animals.

Unapproved and Compounded Animal Drug Products

In addition to providing timely premarket review of new animal drugs, FDA leads the effort to combat the growing problem of unapproved and compounded animal drug products being marketed and sold.

FDA expanded its Animal and Veterinary compliance and enforcement webpage to include a page dedicated to: Inspections, Recalls, and Other Actions with Respect to Firms that Engage in Animal Drug Compounding.⁴³ FDA is working to reduce the risk of harm to humans and animals from substandard or illegally marketed animal drugs.



Medicated Feed Drugs

⁴² For more information on guidance please visit <http://www.fda.gov/RegulatoryInformation/Guidances/>.

⁴³ The webpage can be accessed at:

<http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/ComplianceEnforcement/UnapprovedAnimalDrugs/ucm417562.htm>

In November 2016, FDA finalized its report on proposed changes to improve the efficiency of approvals for the use of multiple new animal drugs in combination drug medicated feeds, while still protecting public health. This report is consistent with a performance goal in the Animal Drug User Fee Amendments of 2013 (ADUFA III) goals letter and are based on public comment. This report will be used in discussions concerning the reauthorization of the animal drug user fee program for FY 2019 – FY 2023 (ADUFA IV).

Postmarket Animal Drug Safety

In April 2016, FDA proposed to withdraw approval of all new animal drug applications (NADAs) providing for use of carbadox in medicated swine feed, based on FDA's determination that the approved use of carbadox results in residues of carcinogenic concern in the edible tissues of treated swine. Currently, there are three approved NADAs for use of carbadox in medicated swine feed, either by itself or in combination with other approved new animal drugs.

FDA believes that continued approval of carbadox would expose humans to concentrations of total residues of carcinogenic concern that are between 11 to 30 times higher than the allowed concentration of total residues that are considered safe.

Enforcement Strategies

The Animal Drugs and Feeds Program protects human and animal health by developing and implementing appropriate enforcement strategies, such as inspections, to ensure the compliance of marketed products. FDA identified and addressed policy and process changes to implement an inspection program that targets high-risk food and feed establishments and products.

When firms violate the FDA requirements of the FD&C Act, FDA takes regulatory action and assists the firms in reaching full compliance while ensuring that products of concern do not reach U.S. consumers. When firms refuse to comply with FDA regulations, FDA takes further enforcement action to ensure unsafe products do not reach U.S. consumers and requests the firm's potential shut down of operations. FDA issued 59 warning letters in FY 2016 based on violative inspection findings.

FDA also monitors recalls of veterinary products and feed and ensures the effectiveness of the firm's recall to remove the defective product from commerce. In FY 2016, FDA classified 73 Class I (most serious), 35 Class II, and 13 Class III recalls of regulated animal products.

Adverse Drug Review

The Animal Drugs and Feeds Program received approximately 99,000 Adverse Drug Experience (ADE) reports for FY 2016.

The Program has the largest regulatory agency animal drug ADE database in the world, with over 694,000 cases. The effort to increase the functionality, utilization, and analysis of this pharmacovigilance database has improved animal drug safety. Over the past few years, the Animal Drugs and Feeds Program eliminated the paper submission backlog and made substantial improvements to the electronic portal, allowing for 99 percent of reports to be submitted electronically. This database provides the ability to analyze data for use in both premarket and postmarket animal drug evaluation. Signal detection and signal management strategies are under development to assist with early identification of potential safety and effectiveness issues. ADE data summary reviews for newly marketed products are developed that describe the postmarket product safety profiles.

PREDICT

Since FDA's completion of the full national rollout of Entry Review and the Predictive Risk-based Evaluation for Dynamic Import Compliance Targeting (PREDICT) to all 16 import districts, FDA has improved the rules that support a risk-based approach to import screening. PREDICT enhances the prevention for entry of adulterated, misbranded, or otherwise violative goods and expedites the entry of non-violative goods. PREDICT allows FDA to make efficient and accurate admissibility decisions and allows FDA field office staff to target the examination of higher risk imported products.

Vet-LIRN

The Animal Drugs and Feeds Program offers grant funds to bolster efforts to validate testing methods as part of the Veterinary Laboratory Investigation and Response Network (Vet-LIRN). Vet-LIRN is a network of state and university laboratories that receive funding from FDA to increase testing capabilities and assist FDA with investigations into potential problems with animal feeds, including pet foods, and animal drugs.

FDA has been actively investigating the cause of illnesses reported in pets which may be associated with the consumption of pet jerky treat products. In FY 2016, FDA continued to work on pet illnesses related to jerky-type pet treats by posting updates to the investigation results on the FDA website. Hundreds of samples were collected and analyzed, but no disease-causing contaminants were identified. FDA continues to perform inspections and collect samples both domestically and internationally, conduct tests on pet jerky treat products, and follow up on consumer complaints.

Food Additive Petition

FDA reviews food additive petitions, establishes standards for feed contaminants, and directs FDA's medicated feed and pet food programs. FDA monitors the safety and usefulness of food additives to ensure the health and safety of livestock, poultry, fish, and pets. FDA works with

stakeholders to promote responsibility through the identification, development, and implementation of new regulations and guidance to further support the production of safe food for animals.

FDA is committed to moving to an all-electronic work environment to support CVM's business processes. CVM is leveraging its pre-market Electronic Document Submission and Review (EDSR) system for pre-market Food Additive Petitions and Investigational Food Additive files.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2014 Actual	\$164,313,000	\$141,566,000	\$22,747,000
FY 2015 Actual	\$175,024,000	\$147,564,000	\$27,460,000
FY 2016 Actuals	\$188,042,000	\$158,629,000	\$29,413,000
FY 2017 Annualized CR	\$190,540,000	\$158,333,000	\$32,207,000
FY 2018 President's Budget	\$183,280,000	\$107,606,000	\$75,674,000

BUDGET REQUEST

The FY 2018 Budget Request for the Animal Drugs and Feeds Program is \$183,280,000, of which \$107,606,000 is budget authority and \$75,674,000 is user fees. Budget authority decreases by \$50,727,000 to the FY 2017 Annualized CR level and user fees increase by \$43,467,000. The Center for Veterinary Medicine (CVM) amount in this request is \$121,749,000. The Office of Regulatory Affairs amount is \$61,531,000.

The Animal Drugs and Feeds Program will strive to uphold its pre-approval activities by continuing to enhance the availability and diversity of safe and effective products that relieve animal pain and suffering, sustain their health, and not compromise human health. These activities include conducting preapproval inspections, ensuring safety and effectiveness of an animal drug before approval, reviewing feed additives for safety and effectiveness, and ensuring food for animals is safe, made under sanitary conditions, and properly labeled. The Animal Drugs and Feeds Program will continue to support the evolving regulatory framework for emerging technologies by clarifying the process for evaluating Genetically Engineered (GE) animals.

In addition, the Animal Drugs and Feeds Program will strive to continue the most critical postmarket efforts to protect human and animal health such as monitoring the safety and effectiveness of animal drugs on the market, reviewing Adverse Drug Experience reports, monitoring the safety of animal devices, investigating pet illnesses, enforcing compliance actions, and ongoing efforts to reduce the availability of illegally marketed unapproved animal

drugs, including compounded animal drugs. Unapproved animal drugs pose a public health risk because they may not meet the agency's strict standards for safety and effectiveness and may not be properly manufactured or labeled.

The Animal Drugs and Feeds Program will continue the Food Safety Modernization Act (FSMA) efforts by implementing a modern, prevention-focused, science- and risk-based food and feed safety system.

The Animal Drugs and Feeds Program will continue surveillance efforts such as monitoring antimicrobial resistance among enteric (intestinal) bacteria via the National Antimicrobial Resistance Monitoring System (NARMS). Response efforts will also continue such as utilizing laboratory capacity via the Veterinary Laboratory Investigation and Response Network (Vet-LIRN) to assist FDA with investigations into potential problems with animal feeds, including pet foods, and animal drugs.

The Animal Drugs and Feeds Program will also conduct field inspections, investigations, and enforcement activities to ensure the adherence of laws to protect and advance human and animal health.

These activities in the FY 2018 President's Budget Request support mission critical program activities and Presidential, HHS, and FDA human and animal health priorities.

BUDGET AUTHORITY

Reductions (-\$8.4 million)

Food Safety: -\$6.6 million

Center: -\$2.1 million

CVM will reduce FTE through attrition. Not back-filling critical positions will require FDA to reprioritize to ensure that the most essential issues of post-market animal food and feed safety, including surveillance and response are addressed. These reductions will require FDA to reevaluate how the agency responds to food and feed outbreaks affecting companion and food animals. Reductions could impact applied research, investments related to information technology and the level of engagement in international activities. FDA's goal is to minimize the impact of these reductions on FDA's core mission activities.

Field: -\$4.5 million

In order to continue operations under the FY 2018 request level, ORA will apply the necessary program reductions to areas such as partnerships, training, IT and lab equipment, and across all program office operating budgets. While protecting resources for inspections and compliance activities will be the priority, some reductions will occur due solely to reduced staff. ORA will

reduce existing workforce levels through attrition, which may result in fewer staff conducting field exams, import entry review, investigations, sample analysis, and inspections for surveillance, compliance, and follow up activities, both domestically and abroad.

These reductions are targeted to investments in IT and lab equipment, and its related maintenance and operating expenses. In addition, there will be decreased investments in partnerships and training.

ORA will also have to reduce cooperative agreements supporting the Animal Feed Regulatory Program Standards (AFRPS).

Medical Product Safety & Availability: -\$1.7 million**Center: -\$1.7 million**

CVM will reduce FTE through attrition, which will require FDA to reprioritize activities related to post-market veterinary medical product safety, including surveillance and the ability to respond to Adverse Experience Reports; research used to make evidence-based regulatory decision; combatting antimicrobial resistance; and international standards harmonization. FDA's goal is to minimize the impact of these reductions to FDA's core mission activities.

CVM will reprioritize to ensure that approved therapeutic uses of medically important antimicrobials in food animals are consistent with the principles of judicious use, including being labeled for an appropriately defined duration of use. FDA published a request seeking information on how to better target such antimicrobial use to address various diseases in livestock as well as on strategies for updating affected product labels. This effort represents an important next step in FDA's ongoing strategy to mitigate antimicrobial resistance by ensuring the judicious use of antimicrobials in food-producing animals. CVM will continue to prioritize this work to fight against antimicrobial resistance.

CVM will reduce minor use minor species (MUMS) grants distributed to support innovation and the development of new animal drugs intended for minor species or minor uses in major species. These grants are included as a provision in the MUMS Animal Health Act of 2004 and are leveraged to support safety and effectiveness testing for Designation status, similar to the "orphan drug" status for human drugs.

Medical Product Budget Authority Recalibration (-\$42.4 million)**Center: -\$40.9 million / Field: -\$1.5 million**

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees.

USER FEES**Medical Product User Fee Recalibration (+\$43.4 million)****Center: +\$42.0 million / Field: +\$1.5 million**

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees. As user fees are replacing budget authority, which supports both medical product and food safety, such as evaluating the human food safety aspect of animal drugs used in food producing animals, for the Animal Drugs and Feeds Program, the fee increases proposed in the final year of authorization for the Animal Drugs and Animal Generics programs will support both medical product and food safety.

PERFORMANCE

The Animal Drugs and Feeds Program's performance measures focus on premarket animal drug application review, high risk inspections including BSE, warning letter review, and lab coordination for detection and response, as detailed in the following table.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
<u>243201</u> : Complete review and action on original New Animal Drug Applications (NADAs) and reactivations of such applications received during the fiscal year. <i>(Output)</i>	FY 2016: 99.8% w/in 180 days Target: 90% w/in 180 days (Target Exceeded)	90% w/in 180 days	90% w/in 180 days	Maintain
<u>243202</u> : Complete review and action on Non-administrative original Abbreviated New Animal Drug Applications (ANADAs) and reactivations of such applications received during the fiscal year. <i>(Output)</i>	FY 2016: 100% w/in 270 days Target: 90% w/in 270 days (Target Exceeded)	90% w/in 270 days	90% w/in 270 days	Maintain
<u>244212</u> : Percentage of domestic and foreign high-risk animal drug and feed inventory inspected (approximately 225 in total). <i>(Output)</i>	FY 2016: 248 Target: 225 (Target Exceeded)	99%	99%	Maintain
<u>244203</u> : Percentage of planned targeted prohibited material BSE inspections. <i>(Output)</i>	FY 2016: 100% Target: 100% (Target Met)	99%	99%	Maintain
<u>244204</u> : Complete review and action on warning letters received to better safeguard our food supply by alerting firms to identified deviations in order to become compliant. <i>(Output)</i>	FY 2016: 42% w/in 15 working days Target: 60% w/in 15 working days (Target Not Met)	50% w/in 25 working days	50% w/in 25 working days	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
244301: Total number of collaborating laboratories that will provide coordinated response to high priority chemical and microbial animal feed including pet food contamination events. (Outcome)	FY 2016: 38 Target: 36 (Target Exceeded)	36	36	Maintain

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

New Animal Drug Application Review

CVM exceeded ADUFA performance goals, except for one submission, in eleven out of twelve years. Additionally, CVM exceeded AGDUFA performance goals, except for one submission, in six out of seven years. CVM completed review and action on 99.8 percent of original NADAs as well as other ADUFA sentinel submissions within the timeframes specified during FY 2016. CVM also completed review and action on 100 percent of original ANADAs as well as other AGDUFA sentinel submissions within the time frames specified in FY 2016.

Warning Letter Review

In FY 2016, CVM saw an increase in both the volume and complexity of warning letters, while also accommodating a reduction in subject-matter experts. Each warning letter requires a case-by-case development of enforcement policies, in-depth scrutiny, and collaboration with field inspectors. These factors contributed to CVM missing the performance target to complete review and action on 50 percent of warning letter packages within 15 days by eight percent and influenced the decision to adjust the targets for FY 2017 and FY 2018.

PROGRAM ACTIVITY DATA TABLES**Animal Drugs & Feeds Program Activity Data (PAD)**

CVM Workload and Outputs	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
New Animal Drug Applications (NADAs) ¹			
Received	30	31	31
Completed	20	20	20
Approved	16	16	16
Pending ²	13	24	35
New Animal Drug Application Supplements ^{1,3}			
Received	544	675	625
Completed	443	550	475
Approved	333	400	400
Pending ²	217	342	492
Abbreviated New Animal Drug Applications (ANADAs) ¹			
Received	22	50	60
Completed	23	45	32
Approved	20	20	20
Pending ²	9	14	42
Abbreviated New Animal Drug Application Supplements ^{1,3}			
Received	227	340	425
Completed	204	300	325
Approved	123	200	160
Pending ²	189	229	329
Investigational New Animal Drug (INAD) Files ⁴			
Received	3,198	3,500	3,600
Completed	3,156	3,250	3,250
Pending ²	627	877	1,227
Generic Investigational New Animal Drug (JINAD) Files ⁴			
Received	502	750	800
Completed	469	675	700
Pending ²	476	551	651
Food (Animal) Additive Petitions Completed	101	100	100
Investigational Food Additive Petitions Completed	90	120	120
Adverse Drug Event (ADE) ⁵			
ADE Reports Received	98,679	90,000	90,000
Post-Approval ADE Data Reviews	139	175	185

¹Includes originals applications and reactivations. If the application is not approvable, the sponsor may submit additional information until FDA is able to approve the application.

²Reflects submissions received during the fiscal year that still require review.

³A supplemental application is a sponsor request to change the conditions of the existing approval. Supplemental applications can be significant (such as a new species or indication), or routine (such as product manufacturing changes). The estimates do not include invited labeling change supplement applications because it is not possible to accurately project sponsor or CVM requests for this type of application.

⁴An INAD or JINAD file is established at the request of the sponsor to archive all sponsor submissions for a phased drug review including requests for interstate shipment of an unapproved drug for study, protocols, technical sections, data sets, meeting requests, memos of conference, and other information.

ANIMAL DRUGS AND FEEDS

Field Animal Drugs & Feeds Program Activity Data (PAD)

Field Animal Drugs and Feeds Program Workload and Outputs	FY 2016 Actuals			FY 2017 Annualized CR			FY 2018 President's Budget		
	Total	Animal Drugs	Feeds	Total	Animal Drugs	Feeds	Total	Animal Drugs	Feeds
FDA WORK									
DOMESTIC INSPECTIONS									
<i>UNIQUE COUNT OF FDA DOMESTIC ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS</i>	<i>1,822</i>	<i>255</i>	<i>1,589</i>	<i>1,664</i>	<i>298</i>	<i>1,398</i>	<i>1,664</i>	<i>298</i>	<i>1,398</i>
Pre-Approval /BIMO Inspections	39	39	0	79	79	0	79	79	0
Drug Process and New ADF Program Inspections	221	221	0	175	175	0	175	175	0
BSE Inspections	1,341	0	1,341	1,205	0	1,205	1,205	0	1,205
Feed Contaminant Inspections	13	0	13	25	0	25	25	0	25
Illegal Residue Program Inspections	397	0	397	450	0	450	450	0	450
Feed Manufacturing Program Inspections	250	0	250	200	0	200	200	0	200
Domestic Laboratory Samples Analyzed	1,555	8	1,547	1,560	20	1,540	1,560	20	1,540
FOREIGN INSPECTIONS									
<i>UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS</i>	<i>126</i>	<i>118</i>	<i>8</i>	<i>76</i>	<i>71</i>	<i>5</i>	<i>76</i>	<i>71</i>	<i>5</i>
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	13	13	0	40	40	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	109	109	0	33	33	0	33	33	0
Foreign Feed Inspections	7	0	7	5	0	5	5	0	5
BSE Inspections	5	0	5	0	0	0	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	1,948	373	1,597	1,740	369	1,403	1,740	369	1,403
IMPORTS									
Import Field Exams/Tests	7,935	796	7,139	3,795	495	3,300	3,300	495	3,300
Import Laboratory Samples Analyzed	894	4	890	867	2	865	867	2	865
Import Physical Exam Subtotal	8,829	800	8,029	4,662	497	4,165	4,167	497	4,165
Import Line Decisions	446,903	48,661	385,723	469,248			492,711		
Percent of Import Lines Physically Examined	1.98%	1.64%	2.08%	0.99%			0.85%		
STATE WORK									
<i>UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS</i>	<i>3,702</i>	<i>0</i>	<i>3,702</i>	<i>3,832</i>	<i>0</i>	<i>3,832</i>	<i>3,832</i>	<i>0</i>	<i>3,832</i>
<i>UNIQUE COUNT OF STATE PARTNERSHIPS ANIMAL FEEDS ESTABLISHMENT INSPECTIONS ¹</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>
<i>UNIQUE COUNT OF STATE COOPERATIVE AGREEMENT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS ²</i>	<i>2</i>	<i>0</i>	<i>2</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>
State Contract Inspections: BSE	3,694	0	3,694	3,500	0	3,500	3,500	0	3,500
State Contract Inspections: Feed Manufacturers	623	0	623	620	0	620	620	0	620
State Contract Inspections: Illegal Tissue Residue	134	0	134	130	0	130	130	0	130
State Partnership Inspections: BSE and Other	0	0	0	0	0	0	0	0	0
State Cooperative Agreement BSE Inspections	2	0	2	0	0	0	0	0	0
State Contract Animal Drugs/Feeds Funding	\$3,073,399	0	\$3,073,399	\$3,165,601	0	\$3,165,601	\$3,260,569	0	\$3,260,569
BSE Cooperative Agreement Funding	\$0	0	\$0	\$0	0	\$0	\$0	0	\$0
State Contract Tissue Residue Funding	<u>\$456,317</u>	<u>0</u>	<u>\$456,317</u>	<u>\$442,627</u>	<u>0</u>	<u>\$442,627</u>	<u>\$429,348</u>	<u>0</u>	<u>\$429,348</u>
Total State Funding	\$3,529,716	\$0	\$3,529,716	\$3,608,228	\$0	\$3,608,228	\$3,689,917	\$0	\$3,689,917
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	5,652	373	5,301	5,572	369	5,235	5,572	369	5,235

¹ The FY 2016 actual unique count of foreign inspections includes 12 OIP inspections (11 for China).² The State inspections that are funded by the FDA are now being obligated via formal contract funding vehicles and this number is expected to decrease in the future until there are no planned State Partnership inspections.³ The State cooperative agreement BSE inspections that are funded by the FDA are now being obligated via formal contract funding vehicles and this number along with the funding for these inspections are expected to decrease in the future until there are no planned State Cooperative Agreement BSE inspections.

DEVICES AND RADIOLOGICAL HEALTH

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
Devices and Radiological Health.....	450,221	447,605	440,988	489,696	48,708
<i>Budget Authority.....</i>	<i>323,170</i>	<i>323,157</i>	<i>322,555</i>	<i>140,069</i>	<i>-182,486</i>
<i>User Fees.....</i>	<i>127,051</i>	<i>124,448</i>	<i>118,433</i>	<i>349,627</i>	<i>231,194</i>
Center.....	351,990	354,457	342,819	396,261	53,442
Budget Authority.....	240,750	240,740	240,292	73,842	-166,450
User Fees.....	111,240	113,717	102,527	322,419	219,892
<i>Prescription Drug (PDUFA).....</i>				1,292	1,292
<i>Medical Device (MDUFA).....</i>	<i>104,991</i>	<i>108,007</i>	<i>96,150</i>	<i>314,750</i>	<i>218,600</i>
<i>Mammography Quality Standards Act (MQSA).....</i>	<i>6,249</i>	<i>5,710</i>	<i>6,377</i>	<i>6,377</i>	---
Field.....	98,231	93,148	98,169	93,435	-4,734
Budget Authority.....	82,420	82,417	82,263	66,227	-16,036
User Fees.....	15,811	10,731	15,906	27,208	11,302
<i>Medical Device (MDUFA).....</i>	<i>2,199</i>	<i>409</i>	<i>2,014</i>	<i>13,316</i>	<i>11,302</i>
<i>Mammography Quality Standards Act (MQSA).....</i>	<i>13,612</i>	<i>10,322</i>	<i>13,892</i>	<i>13,892</i>	---
<i>International Courier.....</i>	---	---	---	---	---
FTE.....	2,243	2,243	2,289	2,352	63

Authorizing Legislation: Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321-399); Radiation Control for Health & Safety Act (21 U.S.C. 360hh-360ss); Medical Device Amendments of 1976; Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 201); Safe Medical Devices Act of 1990; Mammography Quality Standards Act of 1992 (42 U.S.C. 263b); Medical Device Amendments of 1992; Food and Drug Administration Modernization Act; Medical Device User Fee and Modernization Act of 2002; Project Bioshield Act of 2004 (21 U.S.C. 360bbb-3); Medical Device User Fee Stabilization Act of 2005; Food and Drug Administration Amendments Act of 2007 (FDAAA); Patient Protection and Affordable Care Act, 2010; FDA Safety and Innovation Act (FDASIA), 2012

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The Devices and Radiological Health Program (the Devices Program) began in 1976, when President Gerald Ford signed the law that amended the Federal Food, Drug, and Cosmetic Act of 1938 to define medical devices and outline a risk-based classification system. The Devices Program operates with appropriations and user fees and is composed of the Center for Devices and Radiological Health and the Office of Regulatory Affairs.

The Devices Program is responsible for the national regulation of all medical devices, from simple articles such as tongue depressors to complex robotic equipment for surgery and cutting-edge products such as implantable defibrillators. To protect the public from unnecessary exposure to radiation, the Devices Program also regulates radiation-emitting products that include microwave ovens, X-ray equipment, and medical ultrasound and MRI

machines. In addition, the Devices Program monitors mammography facilities to make sure the equipment is safe and properly run.

FDA assures that patients and providers have timely and continued access to safe, effective, and high-quality medical devices and safe radiation-emitting products. FDA provides consumers, patients, their caregivers, and providers with understandable and accessible science-based information about the products it oversees. FDA facilitates medical device innovation by advancing regulatory science, providing industry with predictable, consistent, transparent, and efficient regulatory pathways, and by assuring consumer confidence in devices marketed in the U.S.

The vision of the Devices Program is to ensure that patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance – first in the world. The U.S. is the world’s leader in regulatory science, medical device innovation and manufacturing, and radiation-emitting product safety. Surveillance quickly identifies poorly performing devices, accurately characterizes real-world performance, and facilitates device approval or clearance. Devices are legally marketed in the U.S. and remain safe, effective, and of high-quality.



The following strategic priorities describe the most important areas that the Devices Program will focus on to reach this vision. These priorities are to:⁴⁴

- Establish a National Evaluation System for Medical Devices
- Incorporate Patient Input into Decision Making
- Promote a culture of quality and organizational excellence.

By addressing these priorities, the Devices Program aims to help medical device developers choose the U.S. as the country of first choice for their innovative new technologies – a key contributor to early patient access to high quality, safe and effective devices.

Recent accomplishments of the Devices Program include the following:⁴⁵

⁴⁴ For more information on guidance please visit

<http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/default.htm>

- Average of 217 days during 2016 to arrive at a decision for high-risk innovative devices; down from 278 days in 2015.
- Reduced the median time to approve an Investigational Device Exemption (IDE) study to just 30 days in FY 2016.
- On September 28, 2016, FDA approved a first of its kind device that is intended to automatically monitor glucose (sugar) and provide appropriate basal insulin doses. This technology can provide people with type 1 diabetes greater freedom to live their lives without having to consistently and manually monitor baseline glucose levels and administer insulin.

The following selected accomplishments demonstrate the Devices Program's delivery of its regulatory and public health responsibilities within the context of current FDA strategic goals and priorities.

Improve and Safeguard Access

The Devices Program is committed to flexible, smart regulation, and to working with industry and the clinical community to ensure that innovative new medical devices that demonstrate a reasonable assurance of safety and effectiveness are available for U.S. patients. Each year, the Devices Program evaluates the safety and effectiveness of new devices and approves or clears thousands of products for entry into the market. As a result, millions of U.S. patients benefit from innovative medical devices that reduce suffering, treat previously untreatable conditions, extend lives, and improve public health.

The Devices Program has evolved alongside changes in medical technology and the global marketplace. The Devices Program has implemented several new policies and programmatic improvements to ensure American patients have timely access to devices, without compromising standards of safety and effectiveness. Devices are introduced to the market more quickly, and more products that go through The Devices Program's premarket process are being approved and cleared for marketing.

Among the FDA strategic goals and priorities, the Devices Program supports FDA's Smart Regulation, Regulatory Science, and Safety and Quality priorities through efforts including the Clinical Trial Enterprise, Precision Medicine and Partner with Patients.

⁴⁵ For more information on guidance please visit

<http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/UCM481590.pdf>

Guidance Documents

Below are selected guidance documents issued by the Devices Program during calendar year 2016. These guidance documents help address various issues. This list does not represent any degree of importance or priority ranking among the published guidances.⁴⁶

Date	#	Title	Description
July 2016	FDA-2016-D-1270	Use of Standards in FDA Regulatory Oversight of Next Generation Sequencing (NGS)-Based In Vitro Diagnostics (IVDs) Used for Diagnosing Germline Diseases	This guidance provides recommendations for designing, developing, and validating NGS-based 119 tests for germline diseases.
Jun 2016	FDA-2015-D-137	Leveraging Existing Clinical Data for Extrapolation to Pediatric Uses of Medical Devices	This guidance explains the circumstances in which it may be appropriate to extrapolate existing medical device data to support pediatric device indications.
Feb 2016	FDA-2011-D-0469	Applying Human Factors and Usability Engineering to Medical Devices	This guidance will assist medical device developers in following appropriate human factors and usability engineering processes.
Jan 2016	FDA-2015-D-5105	Postmarket Management of Cybersecurity in Medical Devices	FDA is issuing this draft guidance to provide recommendations for managing postmarket cybersecurity vulnerabilities for marketed medical devices.

Regulatory Science Priorities

CDRH protects consumers by applying the best possible science to its regulatory activities, including premarket review of safety and effectiveness, postmarket product surveillance, and review of product quality. Rapid advances in innovative science have provided new technologies to discover, manufacture, and assess novel medical products and to improve device safety and quality. FDA must both keep pace with and utilize these new scientific advances in order to protect and promote public health.

One of CDRH's core functions is to advance regulatory science, which is the science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of medical devices and radiation-emitting products. This includes laboratory

⁴⁶ For more information on guidance please visit <http://www.fda.gov/RegulatoryInformation/Guidances/>.

research in the areas of physical, life, and engineering sciences as well as epidemiological research in postmarket device safety. CDRH conducts research in our own labs and through collaborations with academia, healthcare providers, other government agencies, and industry. CDRH relies upon this work to support innovation and regulatory decision-making in areas as varied as medical imaging, manufacturing, and clinical trials.

Regulatory Science Priorities include but are not limited to:

- Leverage “Big Data” for regulatory decision-making
- Modernize biocompatibility and biological risk evaluation of device materials
- Leverage real-world evidence and employ evidence synthesis across multiple domains in regulatory decision-making
- Advance tests and methods for predicting and monitoring medical device clinical performance.

These priorities help focus the Devices Program’s attention on the most important regulatory science research needed, as well as promote alignment with external scientists and potential scientific research partners. These priorities will be reassessed and updated periodically to reflect current regulatory science needs.⁴⁷ In addition, the Devices Program makes public information on 43 active research programs that advance Regulatory Science⁴⁸

Expanded Access for Medical Devices

When a patient has a serious or life-threatening condition that is not addressed by current approved treatments, options may exist to use an investigational medical device—one that has not been approved or cleared by FDA—to treat the patient. Normally, investigational devices with significant risks may only be used on human subjects through an FDA-approved clinical trial for which an investigational device exemption (IDE) was approved by FDA to allow the investigational device to be used in a clinical study.

However, there are circumstances under which a health care provider may use an investigational device outside of a clinical study to save the life of a patient or to help a patient suffering from a serious disease or condition for which no alternative treatment exists. The use of an investigational device outside of a clinical trial for treatment of a patient is called “expanded access.” If enrollment in an existing clinical trial protocol is not possible—either because a patient is not eligible for any ongoing clinical trials, or there are no ongoing clinical

⁴⁷ CDRH’s Regulatory Science Priorities are available at: <http://www.fda.gov/MedicalDevices/ScienceandResearch/ucm467550.htm>

⁴⁸ Available at <http://www.fda.gov/MedicalDevices/ScienceandResearch/ResearchPrograms/default.htm>

trials to address the patient's condition—patients and physicians may be able to use an investigational device using one of three mechanisms.⁴⁹

Early Feasibility Studies

Early Feasibility Studies (EFS) are small clinical studies designed to gain early insights into an innovative technology during the development process before starting a larger clinical trial. EFS often are a critical step in device innovation, but they are frequently conducted in other countries rather than in the United States. Device developers tend to conduct subsequent feasibility and pivotal clinical studies and then bring their products to market earlier in the countries where they conducted the EFS in order to leverage clinician experience with their technologies.

CDRH established a goal of increasing the number of EFS investigational applications (also known as investigational device exemption applications, or IDEs) submitted to each review division in the Center. Since 2013, the number of early feasibility studies approved has more than doubled—from 17 in FY 2013 to 40 in FY 2016. These results provide evidence that the EFS Program remains robust and permits efficient clinical trial progression in the U.S. while providing appropriate human subject protections.⁵⁰

Parallel Review of Medical Devices

On October 24, 2016, FDA and the Centers for Medicare & Medicaid Services (CMS) informed the public that the Parallel Review of medical devices pilot program will be fully implemented and extended indefinitely. FDA and CMS are soliciting nominations from manufacturers of innovative medical devices to participate in this program. The Parallel Review program is a collaborative effort between FDA, CMS, and the device manufacturer that is intended to reduce the time between FDA marketing authorization and Medicare coverage decisions through the CMS National Coverage Determination (NCD) process. This program is intended to ensure prompt and efficient patient access to safe, effective, and appropriate medical devices for the Medicare population.

Precision Medicine

CDRH has a unique role in advancing precision medicine due to the products under our jurisdiction. Precision medicine generally means tailoring treatments to specific characteristics, such as a patient's genetic makeup or the genetic profile of a tumor. Targeting treatments

⁴⁹ More information about the medical device expanded access program is available at this website:

<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm051345.htm>.

⁵⁰ More information about the EFS program is available in this guidance document:

<http://www.fda.gov/downloads/medicaldevices/deviceregulationand%20guidance/guidancedocuments/ucm279103.pdf>

based on genetic information can improve the success of the treatment and minimize exposure to adverse effects. To fully realize precision medicine, next generation sequencing (NGS) tests used for risk assessment, diagnosis, and treatment must be accurate and reliable. The Devices Program aims to ensure that NGS tests provide accurate, reproducible, and meaningful results relevant to a person's medical condition while continuing to foster innovation so that patients have access to the best available results possible.

The goal of the Precision Medicine Initiative (PMI) is to help translate scientific knowledge about genomics into clinical care. To help achieve that, FDA is drawing upon the latest computing and storage technologies to provide an open source, cloud-based environment where experts can share data, ideas, and methodologies. Today, the environment hosts more than 1,600 participants, including researchers, test developers, industry, academics, statisticians, and clinicians.

Partner with Patients

The Devices Program values patient perspectives and engagement with patients improves our understanding of the patient experience. By working directly with patients, rather than only on their behalf, we can better meet their needs and public health commitment to improve health and quality of life.

In FY 2016, the Device Program undertook efforts to promote a culture of meaningful patient engagement by facilitating interactions between patients and FDA staff, providing twenty on-site and offsite patient interaction opportunities. By November 30, 2016, 68 percent of Devices Program staff had at least one interaction with patients. These interactions enhance Devices Program staff understanding of the patient experience with medical devices.

The Devices Program is committed to working with partners to develop more patient-friendly information, promote more patient-centric clinical trials, advance benefit-risk assessments that are informed by patient perspectives, promote the use of patient-reported outcome data, and foster access to new devices that meet patients' needs.

Balancing Premarket & Postmarket Data Collection and the Expedited Access Pathway

When a device developer seeks U.S. marketing approval or clearance, the extent of premarket data that FDA requires—including data from clinical trials or engineering tests—impacts the amount of time needed to complete a premarket submission. Generally, the more data that is required, the longer it takes to acquire the data and make the submission. Consequently, FDA data requirements impact when U.S. patients have access to a device. Striking the right balance between premarket and postmarket data—including data from real-world use of a device that may be collected in an electronic health record or device registry—means balancing the potential benefits of earlier patient access to the device against the possible risks of patient

harm from exposure to an unsafe or ineffective device. Balancing premarket and postmarket data collection reflects a predictive and evaluative approach to understanding the benefit-risk profile of medical devices.

On April 15, 2015, the Devices Program launched the Expedited Access Pathway (EAP) Program to speed patient access to qualifying devices. EAP is a voluntary program for certain medical devices that demonstrate the potential to address unmet medical needs for life threatening or irreversibly debilitating diseases or conditions that are subject to PMA or are eligible for *de novo* requests.⁵¹

⁵¹ More information about the EAP program is available in this guidance document:

<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM393978.pdf>

Product Approvals

Below are examples of selected Devices Program product approvals during 2016. This list does not represent any degree of importance or priority ranking of products.⁵²

Date	Product Name	Description
Jun 2016	cobas EGFR Mutation Test v2 Approval	This is the first FDA-approved, blood-based genetic test that can detect epidermal growth factor receptor (EGFR) gene mutations in non-small cell lung cancer patients.
Jun 2016	AspireAssist	A new obesity treatment device that causes weight loss by removing about 30 percent of food from the stomach before the calories are absorbed into the body.
Apr 2016	Medtronic Micra Transcatheter Pacemaker System	A first-of-a-kind self-contained pacemaker implanted in the right ventricle via the femoral vein, provides bipolar sensing and pacing, similar to transvenous single chamber pacemaker systems.

Enhance Oversight

Ensuring manufacturer compliance with laws and regulations helps assure the safety and efficacy of devices and protects consumer confidence in U.S. medical products worldwide. The Devices Program quickly identifies major violations and takes prompt, clear, and appropriate actions to resolve issues before they have widespread negative impacts on public health. The Devices Program monitors postmarket performance including adverse events, responds quickly to identify and limit potential public health problems, and collaborates with industry to improve the quality of medical devices for U.S. patients.

Among FDA strategic goals and priorities, the Devices Program supports Smart Regulation through efforts including the National Medical Device Evaluation System and Unique Device Identification. At the same time, Globalization is supported by The Medical Device Single Audit Program and Safety and Quality by efforts including the Case for Quality Initiative and the Mammography Quality Standards Act Program.

⁵² For a complete list of product approvals, clearances, and designations, visit <http://www.fda.gov/NewsEvents/ProductsApprovals/>.

Guidance Documents

Below are other selected guidance documents issued by the FDA during calendar year 2016. These guidance documents help address various issues. This list does not represent any degree of importance or priority ranking among the published guidances.⁵³

Date	#	Title	Description
Jul 2016	FDA-2014-N-1039	General Wellness: Policy for Low Risk Devices	This final guidance provides clarity to industry and FDA staff on the CDRH compliance policy for low risk products that promote a healthy lifestyle (general wellness products).
May 2016	FDA-2011-D-0514	Postmarket Surveillance Under Section 522 of the Federal Food, Drug, and Cosmetic Act	This guidance will assist device manufacturers on how to fulfill the section's obligations, and recommendations on the format, content, and review of postmarket surveillance plan submissions.
Mar 2016	FDA-2016-D-06361	Assessment of Radiofrequency-Induced Heating in the Magnetic Resonance Environment	This guidance provides an approach to reduce the number of possible device configurations to a manageable number.

National Evaluation System for health Technology

CDRH is leading the establishment of the National Evaluation System for health Technology (NEST), which will quickly identify safety concerns, better characterize real-world performance of medical devices, and facilitate premarket clearance or approval of new devices and new uses of currently marketed devices. NEST will link and synthesize data being collected as part of routine clinical care from different sources across the medical device landscape, including clinical registries, electronic health records (EHRs) and medical billing claims. It will also help improve the quality of real-world evidence that health care providers and patients can use to make better informed treatment decisions and strike the right balance between assuring safety and fostering device innovation and patient access.

In April 2016, the Duke-Margolis Center for Health Policy published "Better Evidence on Medical Devices: A Coordinating Center for a 21st Century National Medical Device Evaluation System." This document outlines the expectations, roles, and responsibilities of the NEST Coordinating Center. In September 2016, the Duke-Margolis Center for Health Policy published

⁵³ For more information on guidance please visit <http://www.fda.gov/RegulatoryInformation/Guidances/>.

"The National Evaluation System for health Technology: Priorities for Effective Early Implementation", outlining the governance and oversight recommendations for the NEST Coordinating Center, as well as identifying priority areas and projects to support medical device evaluation and surveillance.⁵⁴

Also in September 2016, the Medical Device Innovation Consortium (MDIC) was selected by FDA to establish the NEST Coordinating Center, whose initial focus will be creating governance and operations for the system. Establishing the NEST is one of FDA's 2016-2017 strategic priorities and FDA established goals for increasing access to and use of real world evidence in our regulatory decisions.

Medical Device Innovation Consortium (MDIC)

Through the Medical Device Innovation Consortium (MDIC), FDA collaborates with patient organizations, nonprofit organizations, industry, and other federal agencies to find solutions for common medical device challenges. MDIC's focus is on advancing regulatory science to propel device development through the regulatory process, resulting in smarter regulation and earlier patient access to safe, effective, and high-quality devices. This includes providing a venue for leveraging resources, people, and intellectual capital to support the development of non-clinical device development tools that can reduce the need for or size of clinical studies to support market approval as well as steps to reduce the time and cost of clinical trials.

For example, in 2016, MDIC issued a blueprint on early feasibility studies as a best practices guide for sponsors looking to conduct U.S.-based EFS and "The Framework for Simplification of Clinical Trials in Regulated Medical Devices" outlining a vision and roadmap for simplification of medical device clinical trials. The ultimate goal is to improve the clinical trial ecosystem to lead to new treatments and diagnostics being available in the U.S. market earlier.⁵⁵

Cybersecurity

Many medical devices are "life critical systems," meaning they play a crucial role in monitoring and protecting human life. As more of these systems use technology to interconnect, we must take steps to secure them from hackers and cyber-attacks. The Devices Program works with hospitals, health care professionals, and patients to provide manufacturers with guidance for monitoring, identifying, and addressing cybersecurity vulnerabilities in their devices before and after they have entered the market.

⁵⁴ Available at <https://healthpolicy.duke.edu/files/2016/03/med-device-report-web.pdf>

⁵⁵ Available at <http://mdic.org/>

FDA entered into a partnership with the National Health Information Sharing and Analysis Center (NH-ISAC) and the Medical Device Innovation, Safety, and Security Consortium (MDISS) to foster rapid sharing of medical device vulnerabilities, threats, and mitigations within the health care ecosystem. Doing so will help to proactively address cybersecurity threats and vulnerabilities that may impact patient safety.

Digital connections provide great power to innovate and security must keep pace with that innovation. Safeguarding patients includes first identifying, and then addressing previously unforeseen medical device cybersecurity vulnerabilities. Through a joint approach encompassing the public and several government agencies, FDA is working toward the necessary changes in culture within the medical device ecosystem, accompanied by progress in the management of medical device cybersecurity.

Digital Health Program

The widespread adoption and use of digital health technologies like smartphone apps is creating innovative ways to improve health and health care delivery. These products can help people manage their own health and wellness, promote healthy living, and gain access to useful information when and where they need it. FDA encourages the development of digital health technologies, and has clarified that when technologies meet the definition of a medical device but pose low risk to patients, we do not intend to enforce certain regulatory requirements for such technologies.

FDA's Devices Program has clarified that we are focusing oversight on a small subset of technologies that present a greater risk to patients because those technologies perform the same functions as traditional medical devices or impact the functionality or performance of traditional medical devices. FDA is also working towards a framework that better aligns regulation with the rapid innovation cycles that occur with digital health products. The framework relies more on quality management systems and postmarket safety controls coupled with real world evidence than review of premarket data. Taking into account the global nature of these technologies, CDRH is working with other countries to create an internationally harmonized regulatory framework for digital health products.

Unique Device Identification

FDA is in the process of implementing a unique device identification (UDI) system that will improve the quality of information in medical device adverse event reports, help FDA identify product problems more quickly, and better target recalls and improve patient safety. Further, by providing a standard and clear way to document device use, incorporating UDI in EHRs, clinical information systems, billing systems, and registries will enable NEST to perform

enhanced analyses of devices on the market to better understand device performance in diverse populations.

When fully implemented, the label of most devices will include a unique device identifier (UDI) in human and machine readable form. Device labelers must also submit certain information about each device to the Global Unique Device Identification Database (GUDID). As of the end of the FY 2016, more than one million device identification records have been established in the GUDID.

The incorporation of UDI into electronic healthcare data sources, such as EHRs, will have many benefits for patients, the health care system, and the device industry. The UDI system improves the identification of medical devices by making it possible to rapidly and definitively identify a device through distribution and use.⁵⁶

Culture of Quality and Organizational Excellence

CDRH's 2016-2017 strategic priority "Promote a Culture of Quality and Organizational Excellence" focuses on improving quality internally and externally. We are working with stakeholders—industry, health care providers, patients, payers, and investors—to foster a culture of quality in the medical device ecosystem. The objective is to assure technologies perform consistency, reliably, and are available to those who will benefit from them when they are most needed. This is achieved by identifying and promoting practices that result in high-quality devices and adapting FDA regulatory approaches to align with those practices. Ultimately, this provides stakeholders with understandable and objective data and analysis on medical device quality; focuses stakeholder interactions on device quality; and facilitates medical device innovation.

FDA launched the Case for Quality in 2011 following an in-depth review of device quality data and feedback from both FDA and industry stakeholders. FDA's analysis flagged manufacturing quality risks and showed that firms that manage those risks by driving quality organization-wide are more productive, with fewer complaints and investigations and often with lower quality-related costs than their competitors. In other words: investing in quality pays. More recently, efforts under CDRH's "Culture of Quality" strategic priority include developing metrics, standards, and tools, and identifying successful industry practices—beyond what's required by law or regulation—that lead to high-quality devices and device use. CDRH intends to pilot voluntary use of those metrics and tools and to propose a voluntary program to recognize independent evaluation of product and manufacturing quality.

⁵⁶ Available at: <http://www.fda.gov/medicaldevices/deviceregulationandguidance/uniquedeviceidentification/default.htm>

CDRH is implementing a robust quality management program that includes many components and principles found in internationally recognized organizations, including the International Organization for Standardization (ISO) and the Baldrige Excellence Framework. The quality management program will facilitate consistency in plans, processes, measures, and actions, and will help us achieve our vision of patient access to medical devices through accountability to outcomes reflective of a quality-focused organization. Additionally, CDRH has an active customer service program to collect and act on feedback; we are implementing a more robust document control system; and we are developing an audit and performance evaluation program.

Next Generation Sequencing (NGS)

Next-Generation Sequencing (NGS) is a term used to describe a number of different modern sequencing technologies; sequencing means determining the order of the bases in a DNA segment. Sequencing can highlight changes in a gene that may be related to disease, creating opportunities for diagnostics and therapies. The Precision Medicine Initiative (PMI) directed FDA to develop a new regulatory approach for NGS that will advance precision medicine. FDA released white papers and draft guidances describing this new approach, which is based on the use of community-developed standards. FDA has also developed and released “precisionFDA,” an open-source platform inviting the NGS community to advance innovation and help lower regulatory barriers for NGS test developers. FDA continues to develop plans to implement this approach. While there is not a deadline, FDA is moving rapidly because of NGS’ rapid adoption in clinical settings.

Radiological Health Program

The Devices Program protects public safety by monitoring industry’s compliance with regulatory performance standards to reduce the incidence and severity of radiation injury. The Devices Program reviews initial and period reports as well as inspects establishments that manufacture radiation emitting electronic products to determine compliance with the law. The Devices Program has initiated multiple efforts to improve the efficiency and effectiveness of these programs through manufacturer engagement, reliance on international standards, and proposals to reduce or eliminate unnecessary reporting.

As a regulatory agency, FDA also shares in the responsibility for strengthening radiation protection of patients and health workers with other national and international agencies, institutions, and organizations. That is why FDA collaborated with stakeholders, including the International Atomic Energy Agency (IAEA) and the World Health Organization (WHO), to develop a list of priorities for radiation protection in medicine for the next decade called the

Bonn Call for Action. The Bonn Call for Action is divided into ten principal actions, each of which is considered essential for strengthening radiation protection over the next decade.⁵⁷

Mammography Quality Standards Act Program

The Mammography Quality Standards Act (MQSA) Program helps to ensure all women in the U.S. have access to quality mammography for the detection of breast cancer in its earliest, most treatable stages.

In FY 2016, FDA announced the approval of an alternative standard for using the Quality Assurance Program recommended by the American College of Radiology (ACR) Digital



Mammography Quality Control Manual for full-field digital mammography systems, for systems without advanced imaging capabilities. The alternative standard allows for use by mammography facilities of the ACR Digital Mammography Control Manual as an alternative to the quality assurance program recommended by the image receptor manufacturer.⁵⁸

As part of the MQSA Program, FDA and its state contract partners annually inspect more than 8,700 certified mammography facilities in the U.S. to ensure compliance with national quality standards for mammography. In FY 2016, more than 99 percent of mammography facilities had no serious violations of the law, and less than 1 percent of facilities were cited with the most serious violations. These MQSA-certified facilities provide nearly 39 million mammography procedures annually in the U.S.⁵⁹

Use of Symbols

In June 2016, FDA issued the “Use of Symbols in Labeling” final rule, which describes the circumstances in which manufacturers may use a standalone symbol in device labeling without any adjacent explanatory text. For example, if certain requirements are met under the final rule, manufacturers of sterile syringes could opt to use the symbol for “do not reuse” on a syringe package without adding the actual words “do not reuse” to the package.

The final rule, which went into effect on September 13, 2016, does not mandate the use of standalone symbols in device labeling. Under the final rule, device manufacturers have three options. They can choose to:

⁵⁷ Available at: <http://www.fda.gov/downloads/Radiation-EmittingProducts/RadiationSafety/RadiationDoseReduction/UCM439602.pdf>

⁵⁸ Available at: <http://www.fda.gov/Radiation-EmittingProducts/MammographyQualityStandardsActandProgram/Regulations/ucm489348.htm>

⁵⁹ More information about FDA’s mammography activities is available at: <http://www.fda.gov/mammography>

- not use symbols
- use symbols with adjacent explanatory text, or
- use standalone symbols that have been established in a standard if certain requirements are met, including providing an explanation of the symbols in a symbols glossary that is included in the labeling for the device.

Adding the option of standalone symbols is expected to reduce design costs for manufacturers because it is more consistent with how devices are currently labeled in Europe and other foreign markets. Replacing small and difficult-to-read text with a symbol will also help make some labeling more user-friendly and understandable, which is critical in medical device labeling, where space may be limited. The use of standalone symbols on a global scale may help promote better understanding to people who speak different languages through consistent labeling across products distributed in the U.S. and foreign markets.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2014 Actual	\$417,583,000	\$320,815,000	\$96,768,000
FY 2015 Actual	\$442,689,000	\$320,793,000	\$121,896,000
FY 2016 Actuals	\$447,605,000	\$323,157,000	\$124,448,000
FY 2017 Annualized CR	\$440,988,000	\$322,555,000	\$118,433,000
FY 2018 President's Budget	\$489,696,000	\$140,069,000	\$349,627,000

BUDGET REQUEST

The FY 2018 President's Budget is \$489,696,000, of which \$140,069,000 is budget authority and \$349,627,000 is user fees. This level provides a net increase of \$48,708,000. Budget authority decreases by \$182,486,000 compared to the FY 2017 Annualized CR level and user fees increase by \$231,194,000. The Center for Devices and Radiological Health (CDRH) amount in this request is \$ 396,261,000. The Office of Regulatory Affairs amount is \$93,435,000.

The FY 2018 budget allows the Devices Program to continue to ensure the safety and effectiveness of medical devices that U.S. patients rely on every day, while facilitating scientific innovations that extend and improve lives. Each year, millions of American patients benefit from innovative medical devices that reduce suffering, treat previously untreatable conditions, extend lives, and improve public health. The FY 2018 budget enables the Devices Program to continue to meet its core mission to protect and promote public health, including:

- assuring patients and providers have timely and continued access to safe, effective, and high-quality medical devices and safe radiation-emitting products

- providing consumers, patients, their caregivers, and providers with understandable and accessible science-based information about products
- facilitating medical device innovation by advancing regulatory science, providing industry with predictable, consistent, transparent, and efficient regulatory pathways
- assuring consumer confidence in devices marketed in the U.S.

Devices are coming to market more quickly, and more devices that go through the premarket program are being approved and cleared for marketing.

BUDGET AUTHORITY**Reductions (-\$10.9 million)****Center: -\$5.8 million (Medical Product Safety & Availability)**

Proposed budget reductions will require FDA to reprioritize and reevaluate CDRH activities related to post-market device surveillance and device adverse event reports. While some categories of adverse event reports will have longer review times, FDA will work to address the most serious and highest priority adverse event reports to mitigate potential negative impacts. The goal of FDA is to minimize the impact of these reductions on FDA's core mission activities.

Field: -\$5.1 million (Medical Product Safety & Availability)

ORA will apply strategic reductions to its programs in order to preserve the highest priority activities and operations in support of protecting public health. ORA will reduce existing workforce levels through attrition.

In order to continue operations under the FY 2018 request levels, ORA will apply the necessary program reductions to areas such as training, IT and lab equipment, and across all program office operating budgets while protecting resources for inspections and compliance activities.

Medical Product Budget Authority Recalibration (-\$171.6 million)**Center: -\$160.7 million / Field: -\$10.9 million (Medical Product Safety & Availability)**

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees.

USER FEES**Medical Product User Fee Recalibration and Regulatory Efficiencies (+\$231.2 million)****Center: +\$219.9 million / Field: +\$11.3 million (Medical Product Safety & Availability)**

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees. The budget also includes a package of administrative actions designed to achieve greater regulatory efficiency and speed the availability of innovative, safe, and effective medical products in the market. These actions include the improvements are described in the PDUFA VI and MDUFA IV commitment letters submitted to Congress in January 2017.

In FY 2018, CDRH will take actions to achieve regulatory efficiency and speed the development of safe and effective medical devices. CDRH will reaffirm its commitment to its least burdensome requirements by having all employees involved in the premarket review of devices receive training on the least burdensome approach, developing and applying decision support

tools to assure FDA data requests are least burdensome, and all 510(k) and PMA deficiency letters will provide a justification for every deficiency as well as supervisory review and concurrence. CDRH's premarket review processes will be standardized and more predictable; such as by eliminating unnecessary variance in communications with companies and reducing the number of unique document categories. CDRH will further reduce regulatory uncertainty in medical product development by implementing new performance goals for, and providing, earlier advice to inform pre-submission meetings. CDRH will reduce average total review times for PMA and 510(k) devices so that patients are able to more quickly benefit from FDA approved medical products.

PERFORMANCE

The Devices Program's performance measures focus on premarket device review, postmarket safety, compliance, regulatory science, and Mammography Quality Standards activities which assure the safety and effectiveness of medical devices and radiological products marketed in the United States, as detailed in the following table.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
<u>253203</u> : Percentage of received Original Premarket Approval (PMA), Panel-track PMA Supplement, and Premarket Report Submissions reviewed and decided upon. <i>(Outcome)</i>	FY 2015: 94% in 180 days Target: 80% in 180 days (Target Exceeded)	90% in 180 days	90% in 180 days	Maintain
<u>253204</u> : Percentage of 180 day PMA supplements reviewed and decided upon within 180 days. <i>(Outcome)</i>	FY 2015: 99% in 180 days Target: 90% in 180 days (Target Exceeded)	95% in 180 days	95% in 180 days	Maintain
<u>253205</u> : Percentage of 510(k)s (Premarket Notifications) reviewed and decided upon within 90 days. <i>(Outcome)</i>	FY 2015: 96% in 90 days Target: 95% in 90 days (Target Exceeded)	95% in 90 days	95% in 90 days	Maintain
<u>253208</u> : Percentage of De Novo requests (petitions to classify novel devices of low to moderate risk) reviewed and classified within 150 days. <i>(Output)</i>	FY 2015: 42% in 150 days (Historical Actual)	NA	50% in 150 days	New Goal
<u>253211</u> : Percentage of planned Medical Device Bioresearch Monitoring (BIMO) inspections (approximately 300 in total). <i>(Output)</i>	FY 2016: 309 Target: 300 (Target Exceeded)	91%	91%	Maintain
<u>252203</u> : Percent of total received Code Blue MDRs reviewed within 72 hours during the year. <i>(Output)</i>	FY 2015: 91% Target: 90% (Target Exceeded)	90%	90%	Maintain

<u>254202</u> : Percentage of time CDRH meets the targeted deadline of 60 working days to review GMP information and issue Device Warning Letters. <i>(Output)</i>	FY 2016: 45% Target: 50% (Target Not Met)	50%	50%	Maintain
<u>254203</u> : Percentage of time CDRH meets the targeted deadlines for on-time recall classification <i>(Output)</i>	FY 2016: 86% Target: 85% (Target Exceeded)	85%	85%	Maintain
<u>254211</u> : Percentage of planned domestic and foreign Class II and Class III device inspections (approximately 1,600 in total). <i>(Output)</i>	FY 2016: 2,075 Target: 1,600 (Target Exceeded)	57%	57%	Maintain
<u>252101</u> : Number of technical analyses of postmarket device problems and performance. <i>(Output)</i>	FY 2015: 51 Target: 50 (Target Exceeded)	50	50	Maintain
<u>253207</u> : Number of technical reviews of new applications and data supporting requests for premarket approvals. <i>(Output)</i>	FY 2015: 2,480 Target: 2,000 (Target Exceeded)	2,000	2,000	Maintain
<u>254101</u> : Percentage of an estimated 8,700 domestic mammography facilities that meet inspection standards, with less than 3% with Level I (serious) problems. <i>(Outcome)</i>	FY 2016: 99.2% Target: 97% (Target Exceeded)	97%	97%	Maintain

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

Premarket Device Review

FDA is committed to protecting and promoting public health by providing timely access to safe and effective medical devices. In FY 2015, FDA exceeded all of its MDUFA III performance goals.

De Novo Classification process

The De Novo classification process is an important new tool in the medical device review process. This process allows industry an alternate path to get novel devices of low to moderate risk to market without submitting a PMA.

Code Blue Medical Device Reports

Code Blue Medical Device Reports (MDRs) are defined as high priority MDR reports based on criteria including but not limited to: pediatric deaths, multiple deaths and serious injuries, device explosions, and electrocutions. Timely review of code blue MDRs can minimize widespread failure of the device, thereby limiting the loss of life due to similar events as the one submitted.

Warning Letters

Warning Letters are issued to achieve voluntary compliance and to establish prior notice. The use of Warning Letters and the prior notice policy are based on the expectation that most individuals and firms will voluntarily comply with the law. A Warning Letter is the agency's principal means for prompt voluntary compliance with the Federal Food, Drug, and Cosmetic Act (the Act) and is issued for violations of regulatory significance. Recent shifts in workload, organizational restructuring, and decreases in staff levels have resulted in the inability to meet internal targets for the timely review of GMP information and issuance of Device Warning Letters. Due to the staffing uncertainties, targets will decrease.

PROGRAM ACTIVITY DATA TABLES

Devices and Radiological Health Program Activity Data (PAD)

CDRH Workload and Outputs	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
Original PMAs and Panel-Track Supplements (without Advisory Committee input)			
Workload ¹	72	72	72
Total Decisions ²	69	69	69
Approved ³	55	55	55
Original PMAs and Panel-Track Supplements (with Advisory Committee input)			
Workload	1	1	1
Total Decisions ²	6	6	6
Approved	2	2	2
Modular PMAs			
Workload	72	72	72
Actions ⁴	106	106	106
180-day PMA Supplements			
Workload	210	210	210
Total Decisions ⁵	206	206	206
Approved	94	94	94
Real Time PMA Supplements			
Workload	329	329	329
Total Decisions ⁶	328	328	328
Approved	311	311	311
510(k) Premarket Notifications			
Workload	3,677	3,844	3,844
Total Decisions ⁷ (SE & NSE)	3,078	3,185	3,185
Cleared ⁹ (SE)	2,962	3,081	3,081
Humanitarian Device Exemptions (HDE)			
Workload	4	4	4
Total Decisions ²	4	4	4
Approved	3	3	3
Investigational Device Exemptions (IDE)			
Workload	284	290	290
Total Decisions ⁸	306	309	309
Approved	188	198	198
Investigational Device Exemption Supplements			
Workload	2,051	2,051	2,051
Closures ¹⁰	2,066	2,066	2,066
Pre-Submissions			
Workload	2,368	2,405	2,405
Closures ¹¹	2,324	2,335	2,335
De Novo			
Workload	54	70	70
Total Decisions ¹⁴	49	64	64
Granted	25	32	32
Standards			
Total Standards Recognized for Application Review	1,209	1,250	1275
Medical Device Reports (MDRs) ¹²			
Reports Received	1,335,278	2,672,800	2,672,800
Analysis Consults ¹³	737	1,678	1,678

¹ Workload' includes applications received and filed. (Receipt Cohort)

² Total Decisions' include approval, approvable, approvable pending GMP inspection, not approvable, withdrawal, and denial - regardless of the fiscal year received. (Decision Cohort)

³ Approved' includes applications approved regardless of the fiscal year received. (Decision Cohort)

⁴ Actions' include accepting the module, request for additional information, receipt of the PMA, and withdrawal of the module. (Decision Cohort)

⁵ Total Decisions' include approval, approvable, approvable pending GMP inspection, and not approvable. (Decision Cohort)

⁶ Total Decisions' include approval, approvable, and not approvable. (Decision Cohort)

⁷ Total Decisions' include substantially equivalent (SE) or not substantially equivalent (NSE). (Decision Cohort)

⁸ Total Decisions' include approval, approval with conditions, disapproved, acknowledge, incomplete, withdrawal, or other. (Decision Cohort)

⁹ Cleared' includes substantially equivalent decisions (SE). (Decision Cohort)

¹⁰ Closures' include approval, approval with conditions, disapproved, acknowledge, incomplete, no response necessary, withdrawal, or other. (Decision Cohort)

¹¹ Closures' include a meeting with Industry, deficiency, or other. (Decision Cohort)

¹² MDRs' include individual and summary Medical Device Reports.

¹³ Analysis Consults' include analysis of individual and summary Medical Device Reports (analyzing trends and signals in MDR data).

¹⁴ Total Decisions include granted, declined, and withdrawal – regardless of the fiscal year received. (Decision Cohort)

Field Devices and Radiological Health Program Activity Data (PAD)

Field Devices and Radiological Health Program Workload and Outputs	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
<i>FDA WORK</i>			
DOMESTIC INSPECTIONS			
<i>UNIQUE COUNT OF FDA DOMESTIC DEVICES</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>2,499</i>	<i>2,492</i>	<i>2,492</i>
Bioresearch Monitoring Program Inspections	272	300	300
Pre-Market Inspections	61	60	60
Post-Market Audit Inspections	69	60	60
GMP Inspections	1,420	1,400	1,400
Inspections (MQSA) FDA Domestic (non-VHA)	704	700	700
Inspections (MQSA) FDA Domestic (VHA)	54	50	50
Domestic Radiological Health Inspections	47	50	50
Domestic Field Exams/Tests	15	100	100
Domestic Laboratory Samples Analyzed	255	170	170
FOREIGN INSPECTIONS			
<i>UNIQUE COUNT OF FDA FOREIGN DEVICES</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>603</i>	<i>595</i>	<i>595</i>
Foreign Bioresearch Monitoring Inspections	15	14	14
Foreign Pre-Market Inspections	26	30	30
Foreign Post-Market Audit Inspections	30	20	20
Foreign GMP Inspections	728	550	550
Foreign MQSA Inspections	13	14	14
Foreign Radiological Health Inspections	78	50	50
<i>TOTAL UNIQUE COUNT OF FDA DEVICE</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>3,102</i>	<i>3,087</i>	<i>3,087</i>
IMPORTS			
Import Field Exams/Tests	29,992	19,800	19,800
Import Laboratory Samples Analyzed	<u>577</u>	<u>670</u>	<u>670</u>
Import Physical Exam Subtotal	30,569	20,470	20,470
Import Line Decisions	18,757,725	20,070,766	21,475,719
Percent of Import Lines Physically Examined	0.16%	0.10%	0.10%
STATE WORK			
<i>UNIQUE COUNT OF STATE CONTRACT DEVICES</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>7,803</i>	<i>7,880</i>	<i>7,880</i>
<i>UNIQUE COUNT OF STATE PARTNERSHIPS</i>			
<i>DEVICE ESTABLISHMENT INSPECTIONS¹</i>	<i>0</i>	<i>0</i>	<i>0</i>
Inspections (MQSA) by State Contract	6,716	6,800	6,800
Inspections (MQSA) by State non-Contract	1,044	1,060	1,060
GMP Inspections by State Contract	43	20	20
State Partnership GMP Inspections	0	0	0
State Contract Devices Funding	\$267,249	\$275,266	\$283,524
State Contract Mammography Funding	<u>\$9,720,997</u>	<u>\$9,957,944</u>	<u>\$10,157,103</u>
Total State Funding	\$9,988,246	\$10,233,210	\$10,440,627
<i>GRAND TOTAL DEVICES ESTABLISHMENT</i>			
<i>INSPECTIONS</i>	<i>10,905</i>	<i>10,967</i>	<i>10,967</i>

¹ The FY 2016 actual unique count of foreign inspections includes 12 OIP inspections (8 for China and 4 for India).² The State inspections that are funded by the FDA are now being obligated via formal contract funding vehicles.

NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
National Center for Toxicological Research (BA Only).....	63,331	63,329	63,211	60,211	-3,000
FTE.....	299	299	304	304	---

Authorizing Legislation: Federal Food, Drug, and Cosmetic Act (21 U.S.C. 393(b) (1)); Food and Drug Administration Modernization Act; Food and Drug Administration Amendments Act of 2007; FDA Food Safety Modernization Act (P.L. 111-353)

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The National Center for Toxicological Research (NCTR) was established in 1971. As a national scientific resource, NCTR conducts peer-reviewed research to support FDA's strategic priorities to advance regulatory science and engage globally to encourage the implementation of science-based standards. Further, in support of FDA's strategic goals to Enhance Oversight and Improve Access to FDA-regulated products, NCTR enhances FDA's basis for science-based regulatory decisions by conducting collaborative research to:

- identify adverse effects earlier in product development and understand the risks and benefits of nanomaterials used in FDA-regulated products
- provide strategies to reduce and rapidly detect contaminants in FDA-regulated products
- use biomarkers – biological indicators of disease – to foster precision medicine
- accelerate FDA's capability to manage and analyze research data using bioinformatics
- reduce costly and dangerous surgeries by expanding minimally-invasive imaging capabilities
- expedite the translation of laboratory findings to the clinic and to regulatory application.

The following selected accomplishments⁶⁰ demonstrate NCTR's delivery of its regulatory science and public-health responsibilities within the context of current priorities⁶¹.

Enhance Oversight

⁶⁰ More information on NCTR Research Accomplishments can be found at:

<http://www.fda.gov/AboutFDA/CentersOffices/OC/OfficeofScientificandMedicalPrograms/NCTR/ResearchAccomplishmentsPlans/default.htm>.

⁶¹ Please visit www.fda.gov for additional program information and detailed news items.

NCTR's research allows FDA to use regulatory science to inform standards development, analysis, and decision-making for the safety of FDA-regulated products. NCTR conducts a full range of studies in support of FDA's product portfolio as seen in the illustrations below. Within the Goal of Enhancing Oversight, NCTR conducts research focused on Pediatric Medicine, Cancer, Biomarker Development, and Antimicrobial Resistance that also address the FDA Strategic Priority on Regulatory Science.

Pediatric Medicine

Advancements at NCTR's bio-imaging facility allow FDA to gather information not previously obtainable to help the medical community understand pediatric-anesthetic use and its potentially adverse effects on children. These effects are assessed using minimally invasive imaging technology, allowing visualization of biological processes in "real time," with as little interference as possible with life processes. This research is aimed at the translation of these imaging technologies from the laboratory animal to the clinical setting to reduce adverse effects to children.

NCTR scientists, collaborating with CDER, found that longer durations of exposure to the pediatric anesthetics ketamine, isoflurane, nitrous oxide, propofol, and sevoflurane had adverse effects. Additionally, the scientists found that the chemical acetyl-L-carnitine provides neuroprotective or therapeutic properties when given before and during administration of the pediatric anesthetics. Information about this study can be viewed in the May 2016 issue of [*Anesthesiology*](#).⁶²

FY 2016 data from an NCTR study also show that prolonged exposure to anesthetics, such as sevoflurane, is capable of inducing and maintaining an effective surgical level of anesthesia in the developing nonhuman primate. Prolonged exposure also resulted in profound genetic changes, cytokine – molecules that aid in immune response – levels, breakdown of fats, and subsequently, nerve-cell damage. These data show that anesthetic-induced damage was also associated with changes in fat content. Therefore, theoretically fat content could be used as a biomarker for damage. In general, these data provide the scientific framework critical to updating the best practices for minimally-invasive pediatric anesthetic-assessment methods.

The effects of pediatric anesthesia are also being studied in collaboration with colleagues at the Mayo Clinic using an NCTR-developed method for assessing brain function in children. This

⁶² For more information visit: https://www.researchgate.net/publication/303180769_In_Vivo_Monitoring_of_Sevoflurane-induced_Adverse_Effects_in_Neonatal_Nonhuman_Primates_Using_Small-animal_Positron_Emission_Tomography.

method has been used extensively in nonhuman primate studies conducted at NCTR. The Mayo study plans to finish study subject enrollment in early FY17, after which data analyses and interpretation will begin. This study aims to determine if there are significant adverse effects of general anesthesia on subsequent brain function when given in the important period of rapid brain development after birth. This information may inform agency decisions about labeling and/or best practices for pediatric general anesthesia.

Research to understand the effects of drugs on children continued that specifically identified potential biomarkers of acetaminophen (APAP) injury in children. The pilot study compared the overdose group with healthy children and children receiving therapeutic doses of APAP. Researchers found markers in urine and blood that may be used as biological indicators, also called biomarkers, of liver injury. A manuscript written in FY 2016 verifies hemoxygenase 1 (HMOX1) as a biomarker of APAP liver injury in blood plasma and can be found in [Proteomics Clinical Application](#).⁶³ Additional research analyzing urine and blood is now being completed in adults who suffered acute liver failure and will continue through FY 2017. Identifying liver-injury biomarkers are critical to improving the delivery of precision medicine by allowing for earlier and targeted treatment in children and adults.

Rapid Detection of Bacterial Contamination in Foods

In FY 2016, NCTR scientists developed a method for rapidly detecting low levels of harmful bacteria such as *E-coli* O157:H7 and *Shigella* in foods. This method measures single bacterial cells without requiring a time-consuming period of growth on a Petri dish. Information about this research may be found online at the [International Journal of Food Microbiology](#).⁶⁴

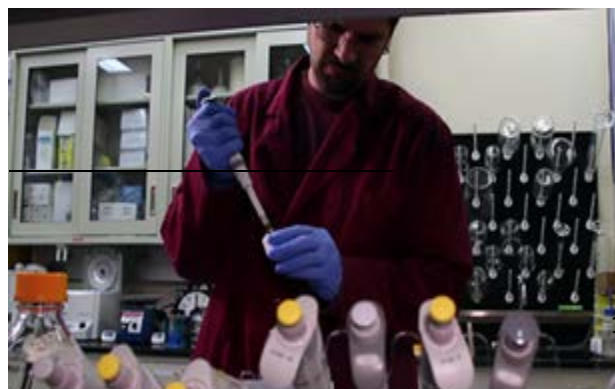
In FY 2017, collaborative research efforts by NCTR and CFSAN scientists include looking for ways to detect:

- *Listeria monocytogenes* faster,
- lower numbers of the *Listeria* cells in foods, and
- test large numbers of samples as to the likelihood that they came from a particular source.

Antimicrobial Resistance

CDC estimates that each year roughly one in six Americans get sick from eating contaminated

food. NCTR scientists continue to conduct projects to limit the emergence and spread of drug resistance in bacterial pathogens that



NCTR scientist conducting bacterial detection analysis.

[02/prca.201600123/epdf.](#)
[rticle/pii/S0168160515300970.](#)

compromise our ability to treat foodborne illnesses. These projects support FDA's regulatory needs related to the pool of antimicrobial-resistance genes and bacterial pathogens in feed, foods, clinical and environmental samples; and the potential effects of transmission of resistant bacteria on human health.

In FY 2016, NCTR scientists used techniques to better understand the diversity of the organisms and studied the presence of plasmids – independent DNA molecules commonly found in cells – that can contribute to antimicrobial resistance and enhanced disease-causing ability.

Understanding what contributes to antimicrobial resistance in these organisms will help develop ways to better address foodborne illness.

Also in FY 2016, NCTR scientists compared the relative impact of antimicrobial exposure on the dissemination of plasmids that can transfer antimicrobial resistance to a cell. This vastly understudied area of research evaluated the transfer of resistance in *Salmonella enterica* strains exposed to different concentrations of commonly used antimicrobial drugs. A manuscript describing this research can be found at [Genome Announcements](#)⁶⁵.

NCTR scientists are investigating other emerging public health concerns such as the genetic diversity of shiga-toxin producing *Escherichia coli* (STEC). The bacteria in the study were gathered from humans, cattle, and some food samples. In FY 2016, scientists completed detailed analyses that show these bacteria fall into distinct groupings based on their gene profiles. These data may help FDA to better understand which genetic factors influence the ability of STEC to persist in the food supply and potentially cause human disease.

Cell Mutations for Prediction

Genes are found in the DNA of every human cell and control how the cell functions – including how quickly it grows, how often it divides, and how long it lives. Despite all that is known about genes and their relationship to disease, more research is needed to better understand how genetic changes affect cells and disease, such as cancer. This knowledge may lead to improvements in the ability to develop personalized treatment plans.

In FY 2016, NCTR researchers used new technology (MARDI) – Mutation Analysis with Random DNA Identifiers– called DNA tagging that applies identification markers to DNA to improve detection of mutation not observed by existing methods. This less expensive technique identifies mutations faster and more accurately. Therefore, it can confirm mutations and

⁶⁵ For more information visit: <http://genomea.asm.org/content/4/5/e01122-16.abstract>.

exclude false positives – two critical aspects for drug evaluation. A manuscript describing the results is available online at [Environmental and Molecular Mutagenesis](#)⁶⁶.

Also in FY 2016, NCTR scientists identified unique rat and human microRNAs capable of discerning drug-induced fatty liver from non-alcoholic fatty liver disease (NAFLD), one of the most common reasons for liver transplants. This identification may allow for early detection, monitoring of disease progression, and improved drug selection in preclinical development programs. A manuscript reporting the study is available online at [Scientific Reports](#)⁶⁷.

In FY 2016, NCTR in collaboration with the National Taiwan University developed new algorithms to improve classification of liver disease patients into two subgroups – treatment sensitive and treatment non-sensitive patients – and an accompanying method to evaluate treatment effectiveness in each subgroup. This new procedure effectively identifies how a subgroup would respond so that a treatment, such as a cancer treatment, can be approved and administered only to those patients who are likely to benefit – improving precision medicine. A manuscript describing this study can be found at [BMC Medical Research Methodology](#)⁶⁸.

Improve and Safeguard Access

NCTR conducts research to evaluate FDA-regulated products in a more predictable, consistent, and efficient way and is often sought out as a collaborator and advisor due to its exemplary reputation in the research community. Within this Goal area, research in Bioinformatics, Precision Medicine, Nanotechnology, and Bio-Imaging addresses the FDA Strategic Priority on Regulatory Science. The Global Summit on Regulatory Science, Bioinformatics Collaborations, and Nanotechnology Collaborations address the FDA Strategic Priority on Globalization.

Bioinformatics Technologies and Resources

Bioinformatics uses software tools to develop and improve methods for storing, managing, and analyzing large quantities of biological data. NCTR develops, provides training for, and makes available bioinformatics tools to FDA and the global research community. FDA must have the software and database tools to manage the large amount of scientific data generated by new technologies required to improve product development, safety assessments, and risk analysis. Below are examples of NCTR's bioinformatics program.

⁶⁶ For more information visit:

<http://onlinelibrary.wiley.com/doi/10.1002/em.21992/abstract;jsessionid=97C51EA272D3BC16468426299C358AB0.f02t03>

⁶⁷ For more information visit: <http://www.nature.com/articles/srep23709>

⁶⁸ For more information visit: <http://www.ncbi.nlm.nih.gov/pubmed/26646831>

Publically Available Dataset/Database Name	Description
DILIRank	<p>Dataset listing 1,036 FDA-approved drugs ranked by potential to cause drug-induced liver injury (DILI); the largest publically available annotated DILI dataset. The 1,036 drugs listed were defined and verified as shown below:</p> <ul style="list-style-type: none"> • 192 “Most-DILI” concern • 278 “Less-DILI” concern • 312 “No-DILI” concern • 254 “Ambiguous-DILI” concern <p>DILIRank may be used by FDA reviewers, industry for drug development, and researchers for adverse drug reaction studies. It can be used to build scientific models that predict the likelihood of a drug to cause liver injury. A manuscript describing this study can be found online at Drug Discovery Today⁶⁹.</p>
Endocrine Disruptor Knowledge Base (EDKB) ⁷⁰	<p>Database of roughly 3,000 chemicals that interfere with the endocrine system; used to develop computer-based predictive models that are quicker and less expensive than traditional experiments. Incorporated into larger government-initiated toxicological projects, such as EPA’s Tox21.</p>

⁶⁹ For more information visit: <http://www.sciencedirect.com/science/article/pii/S1359644616300411>

⁷⁰ For more information visit: <http://www.fda.gov/ScienceResearch/BioinformaticsTools/EndocrineDisruptorKnowledgebase/default.htm>

Estrogenic Activity Database (EADB) ⁷¹	<p>Part of EDKB that assembles data from a variety of data sources and contains 18,114 data points collected for 8,212 chemicals tested in 11 different species. Incorporated into larger government-initiated toxicological projects, such as EPA's Tox21.</p>
FDALabel Database – Drug Labelings ⁷²	<p>Hundreds of new or updated drug labels with information about product indications, target populations, and adverse drug reactions are added weekly. FDALabel makes previously unavailable information easy for researchers and FDA staff who review labelings for the safety and effectiveness of drugs to access. FDALabel is regularly used by:</p> <ul style="list-style-type: none"> • researchers for adverse drug-reaction studies • FDA medical officers for drug review • pharmaceutical companies for drug development and repositioning • physicians and consumers for drug-safety information. <p>In FY 2016, NCTR customized FDALabel for use by CDER and CBER reviewers to perform customizable searches of about 90,000 labeling documents.</p>

Text Mining

NCTR, in collaboration with National Institutes of Health, applied a text-mining method to integrate two different types of research data resulting in identification of meaningful data associations. Text-mining methods apply computation approaches onto text for word recognition, frequency of use, and association – identifying similarities between documents based on such aspects as the words used. A simple example of text mining is the filtering or identification of e-mail messages containing certain words.

⁷¹ For more information visit: <http://www.fda.gov/ScienceResearch/BioinformaticsTools/EstrogenicActivityDatabaseEADB/default.htm>

⁷² For more information visit: <http://www.fda.gov/ScienceResearch/BioinformaticsTools/ucm289739.htm>

The NCTR study demonstrated that text-mining methodologies is an effective approach to integrate diverse data sources from different technologies. This allows FDA and the research community to better understand the mechanisms of disease and toxicity. A manuscript published in FY 2016 detailing the study is available online at [Toxicological Sciences](#)⁷³.

Precision Medicine

Biomarker development is a method for predicting FDA-regulated product toxicity and providing precision medicine solutions such as individually-tailored therapeutic drug regimens. A biomarker is a biological indicator of a biological state or condition. NCTR scientists continue research to identify new biomarkers that can be used to:

- identify populations susceptible to drug side-effects
- predict harmful effects of drugs during safety evaluations
- reduce or reverse cardiac injury
- improve therapeutic patient treatments as shown in the following research.

In FY 2016, NCTR scientists, with researchers from Beijing Pediatric Research Institute and the Arkansas Department of Health, determined that the levels of a key enzyme are controlled by microRNAs – small nucleic acids. This enzyme is involved in the metabolism of 6-10 percent of drugs in current clinical use. It is already known that an individual's genetics affect the activity of this enzyme, which can change the effectiveness and toxicity of certain drugs. However, the researchers identified a specific microRNA that suppresses this enzyme activity, bringing up new questions about the genetic and environmental factors that may affect drug metabolism. A manuscript describing this study is available online at [Biochemical Pharmacology](#)⁷⁴.

Doxorubicin (DOX) is an effective chemotherapy treatment that is limited by its chronic cardiotoxicity – toxicity of the heart – which is dose-dependent, cumulative, and irreversible. Because early biomarkers of drug-induced cardiotoxicity could enable a precision medicine-based approach to chemotherapy treatment, NCTR scientists are actively researching DOX.

In FY 2016, scientists from NCTR, National Cancer Institute, Korea University, and UltraPath Imaging identified a panel of 61 genes from DOX-treated mice that may be early indicators of drug cardiotoxicity. These genes were expressed differentially in heart mitochondria before and after drug-induced cardiac injury. Researchers found that a high dose of the heart-protecting drug dexrazoxane significantly reduced genetic changes and eliminated evidence of

⁷³ For more information visit: <http://toxsci.oxfordjournals.org/content/150/1/64>

⁷⁴ For more information visit: <http://www.sciencedirect.com/science/article/pii/S0006295215005390>

cardiac disease. Information about the study is available at [Toxicology and Applied Pharmacology](#)⁷⁵.

In another DOX study, NCTR scientists measured significant early changes in the levels of multiple metabolites – products of metabolism – in blood and heart tissue from mice treated with DOX. Early metabolic changes observed in plasma during the initial stages of DOX-induced cardiac injury could indicate biomarkers of cardiotoxicity. A manuscript describing the study is now available at [Journal of Applied Toxicology](#).⁷⁶

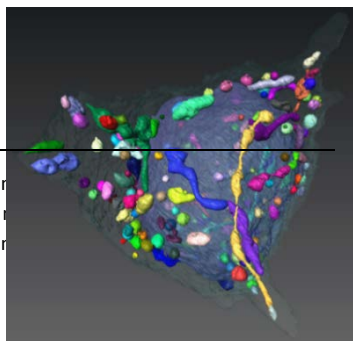
Also within precision medicine, researchers at NCTR and CDER, Wright Patterson Air Force Base, Wright State University, and CDC constructed a model to predict adverse outcomes from exposure to thyroid-acting chemicals, drugs, radioactive materials, or iodine deficiency. This model takes into account the lactating mother and the rapid-developing endocrine system of the nursing infant from delivery to 90 days postpartum. This model may help to establish national and international guidelines for breast milk iodine concentrations, an important area with little existing data. Information about the study is available online at [PLOS One](#)⁷⁷.

Nanotechnology

The NCTR and Office of Regulatory Affairs (ORA) Nanotechnology Core Facility (NanoCore) support collaborative efforts within FDA, U.S. government agencies, and university researchers by providing analytical project support. This work informs FDA and other government agencies on the toxicity and safety of nanotechnology-based materials.

There has been a global increase of nanotechnology-enabled products regulated by FDA. The NanoCore conducts research to foster development of FDA-regulated products containing nanoparticles and the standards to assess the safety of these products. The NanoCore is conducting collaborative studies with CDER and CVM to understand how nanomaterials travel through the blood and distribute in different parts of the body.

In one FY 2016 project, NCTR scientists initiated research involving nanocrystals and their interaction with intestinal microbiota. Nanocrystals are promising drug molecules that increase a drug's solubility, in turn increasing the effectiveness of that drug. Results from these studies will help to establish science-based minimum standards for conducting hazard analysis of



This NanoCore image shows a 3D reconstruction of a rat neuron, an example of the two- and three-dimensional electron microscopy techniques to quantify mitochondria defects.



NanoCore scientist conducting electron microscopy.

⁷⁵ For more information, visit <https://doi.org/10.1016/j.taap.2016.05.001>
⁷⁶ For more information, visit <https://doi.org/10.1016/j.japto.2016.05.001>
⁷⁷ For more information, visit <https://doi.org/10.1371/journal.plosone.0161111>

regulated products containing nanomaterials.

The biological impacts of nanomaterials are virtually unknown, especially if the material has the potential to be migrated to food and ingested. In collaboration with the [Arkansas Research Alliance](#)⁷⁸, NCTR developed a model to test the effects of graphene on intestinal microbiota living in the human gut, also called the human microbiome. The study, which continues in FY 2017, is evaluating graphene-induced toxicity to the intestinal microbiota and the gut-associated immune response. Early results suggest no major effects to growth of gut bacteria belonging to human microbiome and no major effects to intestinal permeability. Having access to science-based information like this is critical for FDA to regulate nanomaterial-containing products to ensure that they are safe for humans.

Magnetic Resonance Imaging (MRI)

Full-brain MRI imaging offers the potential to dramatically improve detection of neurotoxicity produced by new drugs, and to spur new drug development and evaluations. Additionally, NCTR continues the development of minimally-invasive diagnostic methods for identifying nervous system tissue anomalies. The technology, derived from FDA-regulated MRI instruments, is called magnetic resonance spectroscopy (MRS).

NCTR, in collaboration with Huntington Medical Research Institute, has developed a method to improve the use of MRS scans to predict or diagnose medical abnormalities without the need for biopsies. The method is being used to identify Alzheimer's, dementia, and mild cognitive impairment.



Preclinical MRI machine - one of the pieces of equipment used in the NCTR Bio-Imaging Facility.

In FY 2016, NCTR developed a method using MRI and image analysis of MRI files to screen brain samples for evidence of neuro-irregularities (presumed toxicities). The method could potentially qualify brain-toxicity biomarkers while also locating the effected tissue within the brain. The method has been to monitor and assess hexachlorophene, a potent neurotoxicant

⁷⁸ For more information visit: <http://www.aralliance.org/>.

used to treat burns and prevent *Staphylococcus aureus* infections in infants. A publication about this method can be found in [Neurotoxicology](#)⁷⁹.

New and continuing imaging research at NCTR includes:

- studying the relationship of MRI findings with biological fluid biomarkers
- using an advanced sodium MRI approach to detect early signals of neurotoxicity
- correlating MRI results to current assessment methods to assess MRI sensitivity.

Collaborations

A critical component of NCTR's and FDA's science portfolio is collaborations with other entities to leverage knowledge and to establish partnerships where expertise from each entity can contribute to regulatory-science research projects. A strong in-house science base and a network of collaborations are necessary to support FDA's success in addressing public-health challenges.

Scientific advancements are enhanced by participation in meetings and conferences where experts present their current research. Collaborations and relationships built at these meetings provide FDA with access to cutting-edge science. Support of this important strategic priority is reflected in the following highlighted collaborations. Below are some of those important collaborations.

Global Summit on Regulatory Science

Because of the importance for international regulators, policy makers, and scientists to exchange views on how to develop and implement innovative methodologies into regulatory assessments, NCTR established an annual internationally renowned Global Summit on Regulatory Science.

Now in its seventh year, the Global Summit's goal is to engage the global community and harmonize research strategies via collaborations that aim to build knowledge of and promote regulatory science, define research needs, and seek to strengthen product safety worldwide by training regulatory scientists.

The Global Summit is led by the Global Coalition which is comprised of regulatory science leaders from around the world. NCTR's Director serves as the co-chair of the Coalition's executive committee and works with the Coalition to promote global interaction. The 2016 Global Summit provided a forum for scientists from government, industry, and academia from

⁷⁹ For more information visit: <http://www.sciencedirect.com/science/article/pii/S0161813X16301516>

19 countries. The 2017 Global Summit on Regulatory Science is planned to be held in Brasilia, Brazil on September 18-22, 2017.

Bioinformatics Collaborations

NCTR and the Arkansas state university system held the second annual [Arkansas Bioinformatics Consortium](#)⁸⁰ conference in April 2016 to leverage statewide bioinformatics capabilities. The conference – organized by NCTR and the Arkansas Research Alliance – focused on precision medicine and regulatory sciences applications.

In September 2016, in support of the Precision Medicine Initiative, the NCTR-led 1st Sequencing Quality Control Phase 2 public workshop was held at the NIH campus with over 150 participants and 20 presentations given. The workshop resulted in the establishment of a working group to tackle projects to assess the technical performance of next-generation sequencing technologies for precision medicine.

Nanotechnology Collaborations

The NCTR/Office of Regulatory Affairs Nanotechnology Core Facility (NanoCore) supports collaborative efforts within FDA, other U.S. government agencies, and with university researchers providing analytical project support. NCTR and the NanoCore provide analytical support for nanotechnology investigative projects with FDA Product Centers CDRH, CDER, CFSAN, CVM, and ORA. This work informs FDA and other U.S. government agencies on the toxicity and safety of nanotechnology-based materials.

Through a Memorandum of Understanding between the State of Arkansas and FDA, a consortium of five Arkansas research universities provided FDA with comprehensive data on the synthesis and detection of graphene. This study of graphene continues into FY 2017.

In FY 2016, the NanoCore co-organized the sixth “Nanotechnology for Healthcare Conference” with the University of AR for Medical Sciences, University of AR at Fayetteville, University of AR at Little Rock, and the Winthrop Rockefeller Institute. The Conference brought together international researchers and experts focused on human disease diagnostics, therapeutics, and prevention using nanotechnology. The Conference also covered approaches to develop international standards and methods for measuring nanomaterials and their impact. The keynote address was delivered by the 1996 Nobel Laureate in Chemistry, Sir Harold Kroto.

The 2016 Global Summit on Regulatory Science with the theme of “Nanotechnology Standards and Applications” was hosted by FDA, the Global Coalition, and the AR Research Alliance at the

⁸⁰ For more information visit: [http:// www.arkansasbioinformatics.org](http://www.arkansasbioinformatics.org)

NIH campus. Panel discussions and speaker presentations, including former FDA Commissioner Dr. Robert M. Califf, explored the most immediate research needs in nanotechnology science, measurement methods, and standards relevant to regulatory applications.

Cancer Research Collaborations

Through the same MOU between the State of Arkansas and FDA, a consortium of five Arkansas research universities with significant expertise and investment in bioinformatics, computational science, DNA research, animal research, and clinical research work closely with researchers at NCTR to improve liquid biopsies. Researchers are using DNA found in cell-free components of blood – such as plasma – to develop precision medicine treatments for lung cancer, and eventually lung-cancer screening to supplement conventional imaging.

This project will use data from the treatment of genetic mouse models of lung cancer along with clinical samples and data from lung-cancer patients to refine the liquid biopsy approach. This approach has lower risks to patients than standard cancer-based biopsies and is more rapid and convenient.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2014 Actual	\$62,488,000	\$62,488,000	\$0
FY 2015 Actual	\$63,312,000	\$63,312,000	\$0
FY 2016 Actuals	\$63,329,000	\$63,329,000	\$0
FY 2017 Annualized CR	\$63,211,000	\$63,211,000	\$0
FY 2018 President's Budget	\$60,211,000	\$60,211,000	\$0

BUDGET REQUEST

The FY 2018 Budget Request is \$60,211,000 and is all budget authority. Budget authority decreases by \$3,000,000 compared to the FY 2017 Annualized CR level. This reduction in budget authority will delay the progress or start of critical research projects on food safety issues such as food contamination, dietary supplements, and antimicrobial resistance – delaying advances in regulatory science.

However, the FY 2018 budget request allows NCTR to conduct ground-breaking research to support the FDA Strategic Goals to Enhance Oversight and Improve and Safeguard Access. These areas of research include emerging technologies and toxicology assessments required by FDA. Specifically, NCTR will continue to:

- expedite the translation of scientific advancements to regulatory application

- develop new tools and approaches to assess the safety and efficacy of regulated products
- integrate toxicology safety assessments maximizing existing and emerging technologies
- provide valuable research data on products using new technologies
- help FDA better understand data submissions that are generated using new technologies.

NCTR will conduct research to enhance oversight of FDA-regulated products by using funding to develop tools and methods that will be used to inform standards development, analysis, and decision-making for the safety of FDA-regulated products and to expedite the translation of basic science to regulatory application. This research allows FDA to capitalize on the global scientific advancements and expand FDA's regulatory-science capacity by increasing the speed at which *in vitro* and animal models are put to use in determining safety of FDA-regulated products.

NCTR will conduct research to improve and safeguard access to FDA-regulated products by increasing regulatory-science capacity to evaluate FDA-regulated products in a more predictable, consistent, and efficient way. NCTR will use base funding to conduct research to advance bioinformatics technologies, precision medicine, biomarkers, bio-imaging, human microbiome, and nanotechnology. This research will be done in collaboration with scientists from around the world in government, academia, and industry to exchange views on how to develop, apply, and implement innovative methodologies into regulatory assessments.

BUDGET AUTHORITY

Center: -\$3.120 million (Food Safety)

As part of the FY 2018 Budget, NCTR will reduce FTE through attrition and will scale back investments in IT and other administrative savings and lower priority research. NCTR will also prioritize to minimize impact on the most urgent applied research projects. It is the goal of FDA to minimize the impact of these reductions on FDA's core mission activities.

PERFORMANCE

NCTR's performance measures focus on research to advance the safety of FDA-regulated products, on developing a strong FDA science base for emerging technologies, and on providing personalized medicine solutions in order to protect and improve the health of the American public as detailed in the following table.

Measure	Most Recent Result / Target for Recent Result	FY 2017 Target	FY 2018 Target
<u>263103</u> : Conduct translational and regulatory research to advance the safety of products that FDA regulates (<i>Output</i>)	FY 2016: Developed a new <i>in vitro</i> FluoroJade-C cellular toxicity assay that is simple, fast, and appears to be applicable to different types of cells from a variety species. Validation of this approach is ongoing and a manuscript is under revision (<i>Target Met</i>)	1) Initiate super-high field 23Na-MRI feasibility experiments – establish novel neurotoxicity biomarker proof of concept 2) Report preliminary findings on the neurological effects of commonly used chemotherapy drugs doxorubicin and cyclophosphamide	Report initial findings concerning opioid exposure during prenatal development on neural precursor cells
<u>263201</u> : Develop science base for supporting FDA regulatory review of new and emerging technologies (<i>Output</i>)	FY 2016: Published data indicating the potentially harmful neurological effects of sevoflurane and identified neuroprotective effects of Acetyl-L-carnitine using minimally invasive imaging approaches (<i>Target Met</i>)	1) Provide data on the toxicity of graphene nanomaterials leading to guidance for FDA-regulation of nanomaterials 2) Identify and validate predictive biomarkers for nanomaterial-associated immunotoxicity	Conduct analysis and risk assessment of drug-nanocrystals on the human gastrointestinal tract
<u>262401</u> : Develop biomarkers to assist in characterizing an individual's genetic profile in order to minimize adverse events and maximize	FY 2016: Completed a study regarding the understanding and prediction of rare and unpredictable side effects. Four publications resulted from the study (<i>Target Met</i>)	Complete initial phase of research to identify drugs that have differential toxicological effects depending on age and/or sex of an	Complete a study that will promote women's health by facilitating the development of personalized approaches to treat breast cancer

Measure	Most Recent Result / Target for Recent Result	FY 2017 Target	FY 2018 Target
therapeutic care (Output)		individual in an effort to develop a bioinformatics-based safety assessment	
<u>264101</u> : Develop risk assessment methods and build biological dose-response models in support of food protection (Output)	FY 2016: Completed research concerning the molecular interactions that occur during simultaneous infection of <i>Salmonella</i> and norovirus. The research findings could constitute a mechanism to explain why some individuals would sustain norovirus infection for months versus the 2-3 days normally observed (Target Met)	Develop bioinformatics methods in support of microbial pathogen characterization and food protection	Provide data on how exposure of the human gastrointestinal tract to low concentrations of antimicrobial veterinary drug residues in food will affect intestinal bacteria and intestinal permeability of the consumer
<u>263104</u> : Use new omics technologies to develop approaches that assess risk and assure the safety of products that FDA regulates (Output)	FY 2016: Developed a method to detect biomarkers, in this case extracellular vesicles (EVs), in easily obtainable body fluids such as blood and urine. EVs are small membrane-bound bodies that are highly involved in cellular communication. The results of this study were published in <i>Biomarkers of Liver Disease</i> (Target Met)	Finalize research to identify translational biomarkers to aid in prevention and/or early detection of Drug Induced Liver Injury induced by FDA-regulated products	Using a multi-omics approach, identify an antimicrobial resistance marker of <i>Staphylococcus aureus</i> associated with antimicrobial-coated medical devices commonly used in a hospital setting
<u>263102</u> : Develop computer-based models and infrastructure to predict the health risk of biologically active products (Output)	FY 2016: A data mining approach was developed that clusters patients into biomarker subgroups. Each subgroup corresponds to an optimal liver cancer treatment regimen (Target Met)	Develop and refine FDA Label with new functionality based on feedback from FDA reviewers and scientists	Develop a novel data mining and data visualization method for safety surveillance of the FDA Adverse Event Reporting Systems (FAERS). FAERS contains adverse drug reaction reports submitted

Measure	Most Recent Result / Target for Recent Result	FY 2017 Target	FY 2018 Target
			mandatorily and voluntarily by patients, health care professionals, and manufacturers to support post-market drug safety surveillance

PROGRAM ACTIVITY DATA TABLE

Program Workload and Outputs	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
Research Outputs			
Research Publications	160	155	170
Research Presentations	148	148	135
Patents (Industry)	5	5	5
Leveraged Research			
Federal Agencies (Interagency Agreements)	3	3	3
Nongovernmental Organizations	19	19	19
Active Research Projects	165	160	154

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OFFICE OF REGULATORY AFFAIRS – FIELD ACTIVITIES

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
Office of Regulatory Affairs	1,139,170	1,092,819	1,121,641	1,051,206	-70,435
<i>Budget Authority</i>	1,022,793	1,022,759	1,005,877	876,782	-129,095
<i>User Fees</i>	116,377	70,060	115,764	174,424	58,660
<i>Prescription Drug (PDUFA)</i>	14,360	9,814	12,725	42,702	29,977
<i>Medical Device (MDUFA)</i>	2,416	412	2,213	14,639	12,426
<i>Generic Drug (GDUFA)</i>	55,167	38,403	55,973	71,717	15,744
<i>Biosimilars (BsUFA)</i>	1,382	400	1,416	2,485	1,069
<i>Animal Drug (ADUFA)</i>	411	378	427	1,665	1,238
<i>Animal Generic Drug (AGDUFA)</i>	259	188	302	570	268
<i>Family Smoking Prevention and Tobacco Control Act</i>	16,663	9,749	16,631	14,550	-2,081
<i>Mammography Quality Standards Act (MQSA)</i>	13,612	10,322	13,892	13,892	---
<i>Food and Feed Recall</i>	1,000	---	1,000	1,000	---
<i>Food Reinspection</i>	5,382	---	5,382	5,382	---
<i>Voluntary Qualified Importer Program</i>	4,320	---	4,320	4,320	---
<i>Third Party Auditor Program</i>	1,141	---	1,141	1,141	---
<i>Outsourcing Facility</i>	264	394	342	361	19
FTE.....	5,003	5,003	5,134	4,894	-240

Authorizing Legislation: Filled Milk Act (21 U.S.C. §§ 61-63); Federal Meat Inspection Act (21 U.S.C. § 679(b)); Federal Import Milk Act (21 U.S.C. § 141, et seq.); Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 301, et seq.); The Office of Criminal Investigations (OCI) of ORA conducts criminal investigations and executes search warrants as permitted by the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 372), the Public Health Service Act (42 U.S.C. 262) and the Federal Anti-Tampering Act (18 U.S.C. 1365); Poultry Products Inspection Act (21 U.S.C. § 467f(b)); Small Business Act (15 U.S.C. § 638); The Fair Packaging and Labeling Act (15 U.S.C. 1451, et seq.); Executive Order 11490, § 1103; Comprehensive Drug Abuse Prevention and Control Act of 1970 (84 Stat. 1241); Controlled Substances Act (21 U.S.C. § 801, et seq.); Lead-Based Paint Poisoning Prevention Act (42 U.S.C. § 4831(a)); Federal Advisory Committee Act (5 U.S.C. Appx. 2); Federal Caustic Poison Act (44 Stat. 1406); Egg Products Inspection Act (21 U.S.C. § 1031, et seq.); Stevenson-Wydler Technology Innovation Act of 1980 (15 U.S.C. § 3701, et seq.) and Executive Order 12591; Equal Access to Justice Act (5 U.S.C. § 504); Consumer-Patient Radiation Health and Safety Act of 1981 (42 U.S.C. §§ 10007 and 10008); Patent Term Extension (35 U.S.C. § 156); Pesticide Monitoring Improvements Act of 1988 (21 U.S.C. §§ 1401-1403); Food, Agriculture, Conservation, and Trade Act of 1990 (7 U.S.C. §138a); Effective Medication Guides of the Agriculture, Rural Development, Food and Drug Administration (FDA), and Related Agencies Appropriations Act of 1997 (Public Law 104-180); Best Pharmaceuticals for Children Act (Public Law 107-108), as amended by Pediatric Research Equity Act of 2003 (Section 3(b)(2) of Public Law 108-155); and Drug Quality and Security Act of 2013.

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The Office of Regulatory Affairs (ORA) advances FDA’s mission to protect public health by conducting field operational activities to ensure the safety, effectiveness, and quality of a wide range of products accounting for about 20 cents of every dollar consumers spend in the United States. These activities are conducted in support of each of the FDA Centers and help to provide awareness, surveillance, and enforcement of FDA regulations related to our nation’s food supply, human and veterinary drugs, vaccines, blood products, allergenics, cellular and gene therapy products, tissue and tissue products, medical devices, cosmetics, dietary supplements, tobacco products, and products that emit radiation.

ORA is responsible for a wide range of mission critical activities involving FDA-regulated products and manufacturing facilities, including:

- inspections and investigations (including criminal investigations)
- sample collection and analyses
- screening FDA-regulated products offered for import into the United States
- executing recalls and other enforcement activities, including responding to consumer complaints and emergencies
- developing and fostering state and local partnerships.

ORA has staff in 227 offices across 49 states, including the U.S. Virgin Islands and the Commonwealth of Puerto Rico and has staff both temporarily and permanently assigned to foreign posts. ORA manages 13 scientific laboratories that conduct applied research and perform highly specialized analyses of domestic and imported products. In addition, ORA also funds state, local, tribal, and territorial regulatory jurisdictions to conduct inspections, collect samples, perform analyses, advance conformance with national regulatory program standards, and enhance program capacity and infrastructure.

Recent Accomplishments

Three of ORA’s most significant accomplishments from the past year are as follows.

National Integrated Food Safety System (NIFSS)

FDA is committed to a fully integrated national food safety system, a hallmark component of the Food Safety and Modernization Act (FSMA). The NIFSS is accomplished through the development and implementation of standards, and the use of contracts, grants, and cooperative agreements with key federal, state, local, tribal, and territorial regulatory and public health partners, as well as with key industry and state associations. ORA continues its

involvement in developing and implementing the necessary rules, standards, outreach, and training to help ensure quality and consistency across the system.

Extending FDA's Global Presence

ORA maintains cadres of investigators to conduct foreign inspections in the food, drug, and device program areas. ORA collaborates with its international counterparts to unify international standards and leverage resources. FDA introduced several programs to involve international stakeholders in the regulation of the global supply chain.

Strategic Coordinated Oversight of Recall Execution (SCORE)

To facilitate FDA's response when regulated foods are associated with real and potential public health risks, the Agency recently established a new process to streamline and strengthen decisions about compliance and enforcement actions. The Strategic Coordinated Oversight of Recall Execution (SCORE) team, a decision-making body of key senior leaders, was established in April 2016 to specifically address challenging food safety situations.

Enhance Oversight

Risk-Related Preventive Focus

ORA has strengthened the surveillance and compliance programs used to monitor FDA regulated products by enhancing strategies that focus on high-risk products and by focusing on preventive approaches, as outlined in FSMA. In partnership with the Office of Food and Veterinary Medicine, ORA is building functional preventive measures across the food system platform. The measures create a comprehensive regulatory framework for prevention and strengthen FDA's inspection, compliance, imports review, sampling, and outbreak response tools.

Working with the Centers, ORA uses the risk-based approach to target firms to inspect, enabling ORA to focus on its on-site inspections of the highest risk facilities and industries both domestically and abroad. In addition, ORA actively advocate for enhanced partnerships with federal, state, local, tribal, and territorial public health regulatory partners. The strengthening of the domestic network of regulators permits ORA to apply its highly skilled staff of investigators to focus on the areas of regulation that pose the highest risk to the American public, including the growing supply of products introduced into the United States from the global marketplace.

Sampling approaches have also changed to help the Agency to better understand risks, assess the value of strategies to control those risks, and prevent contaminated products from reaching consumers. FDA has created a new sampling approach that is not only surveillance or compliance based, but also serves as a mechanism to actively identify risks, and when possible,

identify areas where preventive controls should be put into place to better protect public health.

To speed its response when there are foods on the market presenting a real or potential danger to consumers' health, FDA created the SCORE team. The team consists of key senior leaders who engage in the most challenging recall situations, those complicated by such issues as the nature of the product, the scope of available evidence, and the company's response. The team supports the FDA's field staff across the country by evaluating the whole range of options for the use of the FDA's compliance and enforcement authorities, and making swift decisions about the best course of action to take. In 2016, SCORE reviewed and directed operations in cases that include flour contaminated with peanut protein, (a major food allergen), facilities contaminated with *Listeria monocytogenes*, pistachios in which *Salmonella* was detected, suspension of registration of a ready to eat manufacturer, and baby food that was not manufactured in compliance with infant formula regulations. All of these cases resulted in recalls and announcements issued by the firms and FDA.

NIFSS and Program Standardization

FDA prioritizes its inspectional efforts in coverage of the highest risk products, facilities, and global marketplace. Therefore, it must rely on the strength and capability of federal, state, local, tribal, and territorial public health regulatory partners through contracts, grants, and cooperative agreements to contribute to domestic oversight by funding their performance of surveillance inspections, including verification of compliance with hazard-based preventative controls and other applicable standards. This domestic network of regulators is used to enhance FDA's own coverage of the domestic inventory and better protect the American food supply. However, there must be steps taken to ensure uniformity in the regulation and approach taken by each of the FDA partners. FDA works with the Partnership for Food Protection (PFP) in a collaborative effort with fellow public health regulatory partners to:

- create national standards for inspections
- improve coverage of domestic food facilities
- develop training and certification programs
- improve recall and response effectiveness
- increase collaborative efforts
- promote the National Integrated Food Safety System.

To meet the responsibilities specified by FSMA, FDA has made significant investments in the development of NIFSS. FDA has worked closely with its partners to develop guidance, rules, and standards which will help provide framework to the regulation these partners provide in

FDA's stead. This national curriculum standard framework will continue to grow and will be evaluated and enhanced through training and continual improvement.

In FY 2016, FDA continued its strong partnerships with State manufactured food regulatory programs and promoted widespread participation in the national regulatory program standards. FDA currently has food safety inspection contracts with 47 regulatory agencies in 43 States and Puerto Rico. Manufactured Food Regulatory Program Standards (MFRPS) are implemented nationally with the goal of creating an integrated, risk-based, food safety system focused on protecting public health. The vast majority (91 percent) of States with food safety inspection contracts are enrolled in the MFRPS. In partnership with the Association of Food and Drug Officials, a Manufactured Food Regulatory Program Alliance (MFRPA) has been implemented to provide recommendations for improving and maintaining the MFRPS and manufactured food regulatory programs within an integrated food safety system. The MFRPA also hosts annual meetings, workgroups, and other forums to promote conformance with MFRPS.

Additionally, similar cooperative agreement programs are conducted to promote implementation of the Animal Feed Regulatory Program Standards and Voluntary National Retail Food Regulatory Program Standards. FDA also administered a cooperative agreement with a national agricultural association to facilitate long-term improvements to the national food safety system by providing states with information to aid in the research and identification of resources and changes needed to enforce the requirements of state laws and regulations related to Food for Animals that are modeled after FDA's Current Good Manufacturing Practices (cGMP), Hazard Analysis, and Risk-Based Preventive Controls for Food for Animals rule.

FDA is enhancing produce safety through advancing and implementing the Produce Safety Rule by awarding \$21.8 million in cooperative agreements to 42 states to enhance their capacity, coordination, and training efforts; and by administering a \$1 million cooperative agreement with the National Association of State Departments of Agriculture to assist with national collaborative produce efforts and the development and dissemination of best produce practices.

Further, ORA advanced efforts to improve the national egg safety programs through a cooperative agreement with two state agencies designed to conduct egg regulatory program self-assessments of state egg laws and regulations in comparison to the current federal egg safety laws and regulations; develop and implement an agreement and protocol for sharing egg regulatory inspections and information between states and the FDA; and identify gaps and areas of improvement between Federal and State egg programs.

Import Operations

IMPORT LINES BY PROGRAM AREA
FY 2012 - FY 2018 (Est.)

Program Area	2012	2013	2014	2015	2016	2016 Percent Growth*	2016 Percent of Total Lines	Estimate 2017	Estimate 2018
Foods	10,805,094	11,502,065	12,180,223	13,080,429	13,952,537	5%	37.70%	14,643,462	15,368,602
Cosmetics	2,349,615	2,433,747	2,596,057	2,930,682	2,939,034	4%	7.94%	3,064,891	3,196,137
Human Drugs	592,591	590,079	641,908	688,208	739,309	4%	2.00%	770,786	803,603
Animal Drugs & Feeds	331,505	368,447	391,388	416,860	434,384	5%	1.17%	457,000	480,794
Biologics	65,469	74,402	82,710	150,673	151,911	14%	0.41%	172,563	196,021
Medical Devices & Rad Health	13,651,985	14,320,961	16,668,422	17,252,283	18,757,725	6%	50.69%	19,889,362	21,089,270
Tobacco Products	17,757	19,316	20,161	16,680	32,972	8%	0.09%	35,663	38,573
Total	27,814,016	29,309,017	32,580,869	34,535,815	37,007,872	5%	100.00%	39,033,727	41,173,000

*Percentage growth based off a 5 year average (FY 2012 - FY 2016)

Over the last decade, there has been a very significant increase in FDA-regulated products introduced for import into the U.S. market. While such vast growth has been difficult to match with available resources, FDA has made several advancements in how imported products are targeted and processed for entry.

ORA works in partnership with the U.S. Customs and Border Protection (CBP) and the Commercial Operations Advisory Committee (COAC) in an effort to improve and streamline the import process to expedite the release of compliant products. COAC is a 20 member council that meets quarterly and is chartered to provide advice to the Secretaries of the Department of the Treasury and the Department of Homeland Security on the commercial operations of CBP and related functions, taking into consideration issues such as:

- global supply chain security and facilitation
- CBP modernization and automation

- customs broker regulations
- trade enforcement
- U.S. government approach to trade and safety of imports
- protection of intellectual property rights.

FDA has collaborated with CBP and the International Trade Data System (ITDS) Board of Directors to transition to the Automated Commercial Environment (ACE) as the “single-window portal” through which to import goods into the United States. To facilitate entry via ACE, FDA developed “FDA Supplemental Guidance for the Automated Commercial Environment/ International Trade Data System” which identifies commodity-specific data elements needed to submit FDA-regulated products for import into the United States. Import entries submitted through ACE continue to increase along with filers, products, and expansion of ports.

FDA is also implementing a rule for FDA Safety and Innovation Act Section 708 in International Mail Facilities nationwide which will institute the “Administrative Destruction of Certain Drugs Refused Admission to the United States.” The authority under this rule allows FDA to destroy, without the opportunity for export, drugs refused for admission that are valued at \$2,500 or less with due process prior to the destruction. ORA is developing the necessary operational and information technology system changes to fully implement this authority. In FY 2016, ORA successfully piloted new processes for our Administrative Destruction authority in two international mail facilities. Regulatory procedures have been developed and finalized, training for field staff has been developed and is scheduled. Full national implementation is planned for FY 2017.

ORA continues to work to implement the Foreign Supplier Verification Program (FSVP) and the Voluntary Qualified Importer Program (VQIP). The FSVP regulation specifically requires U.S. food importers to develop, maintain, and follow a program that verifies that their foreign suppliers have established adequate preventive controls and that the human and/or animal food(s) produced within the foreign supplier’s facility are in compliance with the Federal Food, Drug, and Cosmetic Act (FD&C Act). VQIP is a formal voluntary program under which importers of food may submit evidence of regulatory compliance and safety controls in return for the facilitated entry of import entries into the United States. During FY 2016 ORA established a team dedicated entirely to the stand-up of FSVP. Team members are currently working with other components of FDA in various activities, including development of a list of FSVP firms and identifying investigators who will attend training, such as Alliance Training, Train the Trainer, and Regulator Training during FY 2017.

Under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, FDA is responsible to receive and review food defense risks prior notice for all food and animal feed

imported or offered for import. ORA's Division of Food Defense Targeting (DFDT) was established to meet the Agency's responsibilities under this Act. In an effort to enhance operations, the DFDT developed and implemented a new IT system, the Prior Notice (PN) Manager. The PN Manager has fundamentally changed and improved how ORA targets, processes and responds to prior notice submissions, enhancing operations and providing more efficient work processes. It has allowed for enhanced prior notice targeting rules including a rules based food defense targeting platform with automated review status transmission to CBP via the ACE/ITDS portal.

Cultivating a Global Regulatory Network

FDA continues to increase its regulatory presence globally to ensure that the food, feed, and medical products available in the United States meet U.S. regulatory requirements. FDA fosters this global product safety net by leveraging and collaborating with domestic and foreign partners. Through enhancing existing partnerships and encouraging new partnerships and cross-Agency coalitions, ORA improves and increases information sharing, joint work planning and compliance collaborations with federal, international, and state public health regulatory partners.

ORA is actively involved in the Office of Global Regulatory Operations and Policy's efforts to establish a Mutual Reliance agreement with members of the European Union (EU). To date, ORA participated in 14 European assessments organized by the European Medicines Agency in support of Mutual Reliance efforts. The Mutual Reliance efforts enable sharing of inspection data and outcomes so that inspectional resources of all parties can be shifted to higher-risk work.

ORA is continuing to participate in the Medical Device Single Audit Program Pilot with four foreign regulatory authorities. This program includes the use of third party auditors to provide FDA with additional information related to the status of manufacturers, thus expanding FDA's knowledge of regulated industry. ORA also conducted a Secure Supply Chain Pilot Program (SSCPP) designed to enhance the security of imported drugs. The SSCPP allows pre-qualified companies who have been designated to take part in this two-year program to have expedited entry for the importation of up to five selected drug products into the United States.

ORA is actively engaged in the Center for Food Safety and Applied Nutrition's (CFSAN) efforts to expand the Agency's international arrangements under the Systems Recognition program. Under this program, the Agency works with more developed countries on a process by which FDA will assess if the country's food and feed safety system provides protections comparable to those in the United States. This approach allows FDA to focus import screening efforts on areas

of higher risk. To date, FDA has entered into System Recognition arrangements with New Zealand and Canada and is exploring additional opportunities.

ORA is participating in the Codex Committee on Food Import and Export Inspection and Certification Systems (CCFICS). CCFICS develops principles and guidelines related to food import and export inspection and certification systems with a view to harmonizing methods and procedures which protect the health of consumers, ensure fair trading practices, and contribute to facilitating international trade in food stuffs. Covering 99 percent of the world's population, the committee has seen several standards endorsed and adopted into the international food code including standards on guidelines for food import control systems, guidelines for national food control systems, and principles for food import and export inspection and certification.

To ensure continued global trade of domestically produced food commodities, ORA participated in audit activities throughout the year, hosting several foreign regulatory delegations to ensure appropriate regulatory oversight and safe manufacturing practices. In one audit, focused on U.S. facilities that export seafood to Europe, FDA hosted the European Union's Directorate General for Health and Food Safety (DG Sante). Visits were made to several domestic fishery facilities and ORA played a key role providing information, oversight, and guidance to FDA's EU counterparts. Other key audits included dairy and gelatin audits by the Taiwanese government.

Leveraging Laboratory Capabilities

ORA provides oversight of regulatory science standards in laboratories through the use of programs, systems, and cooperative agreements. FDA works collaboratively with external partners, including states, foreign government regulatory authorities, and industry, to allow these stakeholders to provide input on laboratory standards and on the identification of sampling assignments. This strategy has strengthened the surveillance of FDA-regulated food products by gaining cooperation up front and allowing stakeholders to participate in developing assignments.

ORA funds and manages FERN cooperative agreement programs designed to assist state laboratories with building their capability and capacity and demonstrating competency in FDA regulatory testing methodologies and reporting requirements. FDA currently funds 34 FERN network laboratories, including 15 microbiological, 14 chemical, and five radiological laboratories. Throughout FY 2016, the FERN Microbiological Cooperative Agreement Program (mCAP) labs were involved in testing avocados for *Salmonella* and *Listeria monocytogenes* as part of a large-scale assignment. Positive results from FERN laboratories were shared with

industry and as a result, recalls were conducted as appropriate. This ongoing work has found several contaminated samples collected at the retail level.

ORA's Winchester Engineering and Analytical Center (WEAC) and FERN National Program Office (NPO) have successfully started a FERN Radiological Proficiency Test (PT) program. Laboratory comparison studies have allowed FERN NPO and WEAC to gain information regarding the proficiencies of the five FERN Radiological Cooperative Agreement Program (CAP) laboratories, as well as other non-CAP network Radiological laboratories. PT studies have helped identify analytical gaps or needs to be addressed to be prepared to respond in a coordinated fashion to any radiological emergencies. As of November 2016, WEAC and FERN NPO have successfully completed five PTs with a total of 23 labs participating. This Radiological PT program will continue to prepare an average of two studies a year.



A separation lab at ORA Forensic Chemistry Center in Cincinnati, OH. Here analysts prepare samples and subject them to chromatographic analysis to detect contaminants, impurities, or to perform identity testing.

Currently, specialized ORA labs are standing up advanced pharmaceutical testing research programs to develop regulatory methods to evaluate new biotech drugs dominating the cancer and auto-immune therapy sectors. ORA is standing up two groups at Pacific Regional Lab Southwest and New York Regional Labs specialized in pharmaceutical testing. Advanced instrument platforms such as Nuclear Magnetic Resonance Spectroscopy and Mass Spectrometry systems are being acquired for these laboratories to be able to effectively probe the critical quality attributes of protein-based or nanoparticle-based drugs. Following the advent of innovator drugs incorporating protein/nanoparticle moieties, biosimilars are gaining market share especially in the areas of oncology and rheumatoid arthritis. As of April 20, 2017, FDA has approved four biosimilar drugs to be used in the United States.

In addition to equipment investment, personnel with specific skill sets have been identified to spearhead the research projects. ORA strategic research plan in this area includes first bringing

online heparin testing using the nuclear magnetic resonance (NMR) platform. Heparin, an injectable blood thinner used to treat and prevent deep vein thrombosis and pulmonary embolism, is prone to adulteration with other compounds. In 2008, a case of heparin being adulterated with oversulfated chondroitin caused a large number of serious injuries. Therefore, heparin lots are now tested by the FDA Center for Drug Evaluation and Research (CDER) lab for purity and this testing will be turned over to ORA to be performed on its new NMR platform. On the mass spectrometry (MS) platform, ORA strategic research will focus on developing characterization methods on a spectrum of drug compounds spanning from small (simple compound as the active pharmaceutical ingredient) to large formulations (active compounds encapsulated within antibodies, nanoparticles as the active pharmaceutical ingredient).

On the regulatory pharmaceutical testing front, ORA laboratories have provided analytical support to a large-scale assignment issued by CDER involving products manufactured in India. The Domestic-Import India-Origin Solid Oral Generic Dosage Forms and Control Samples (Tier 1) Survey Assignment was issued April 2015 and targeted domestic-import samples manufactured in India. Samples targeted for this assignment were identified by CDER as high-risk (Tier 1) based on factors such as historical quality data, increased sales volume, and recently reported cGMP violations by India manufacturers. ORA pharmaceutical labs collected and analyzed comparable drug products manufactured outside of India (control samples). Along with assessing product quality, results obtained from the India drug products and control drug products will serve as effective benchmarks for quality and surveillance purposes. In FY 2015, approximately 250 samples were collected and ORA labs completed testing for approximately 131 drug products. The assignment was extended through FY 2016 with additional sampling and testing (Tier 2).

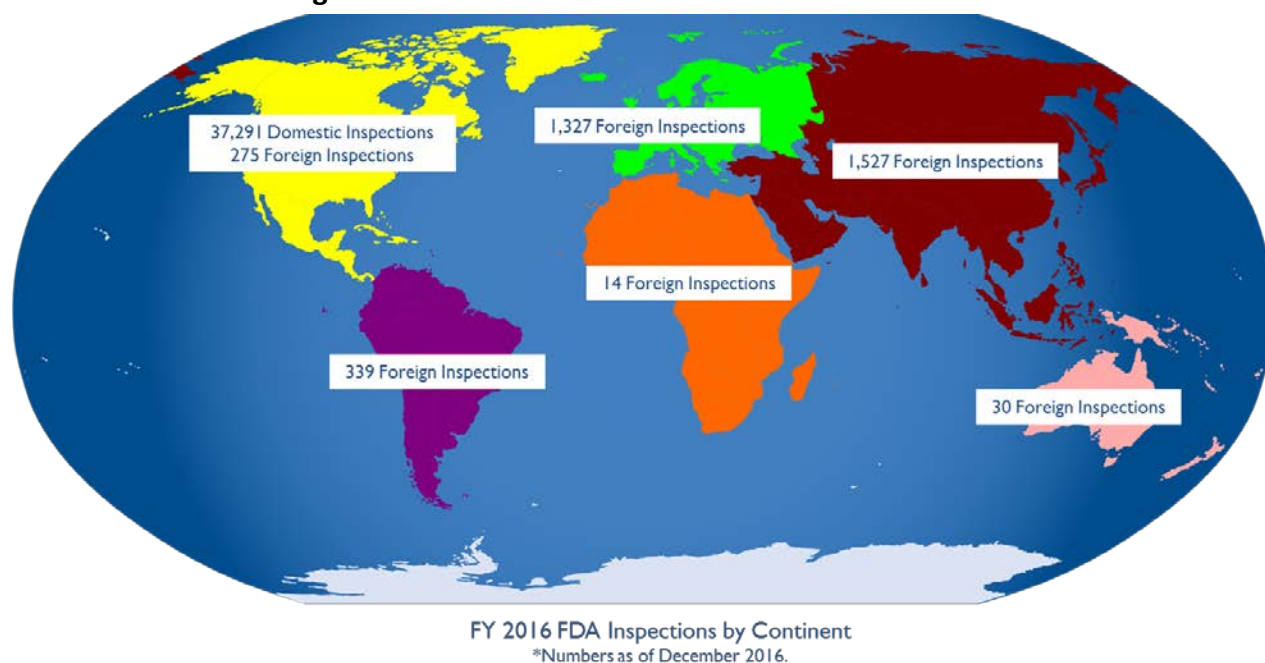
ORA continues to expand its analytical repertoire by developing and utilizing methods using cutting-edge technology to respond to public health needs. Utilizing a newly integrated technology called Whole Genome Sequencing (WGS) to perform sub-species level microbial identification of the organisms found in the samples, an ORA lab contributed to the first recall in FDA history that was primarily based on WGS results. Working with State partners and exchanging genetic information, the cause of the infections was traced to inks used at the tattoo parlor. The regulatory outcome was built on a solid scientific case that represented effective federal-state collaboration, communication, and utilization of new technology. In order to promote this technology further, ORA continues to work with State regulatory partners to initiate and utilize WGS in state laboratories on a national level.

To increase capabilities to screen imported commodities for chemical and biological contaminants, FDA implemented the first Analytical Screening Station at the Port of Everglades. These capabilities enhance FDA's presence at U.S. Ports of Entry with real-time analytical tools

to stop adulterated products from coming into the U.S. market. These screening stations serve to increase product surveillance and promote FSMA with a proactive approach to providing analytical support for imported products.

ORA provides ISO/IEC 17025:2005 cooperative agreements to assist human and animal food testing laboratories in obtaining and maintaining accreditation to the ISO standard, and currently funds 36 state laboratories in furtherance of this goal. The intended outcome of this program is for microbiological and chemical food analyses performed on behalf of State manufactured human and animal food regulatory programs to be conducted within the scope of an ISO/IEC 17025:2005 laboratory, thus advancing the NIFSS.

Surveillance of FDA-Regulated Products



ORA works with each Center to develop and implement a work plan that outlines assignments in more than 500 activity areas that span all of FDA's regulated commodities while maintaining flexibility to respond to unplanned activities, such as new product recalls, emergencies, and outbreaks that may arise, to ensure quick containment and mitigation. ORA accomplishes the FDA mission through a highly skilled professional and administrative staff including consumer safety officers (CSOs) or field investigators, compliance officers, laboratory analysts, recall staff, consumer complaint coordinators, criminal investigators, state cooperative program specialists, and many other critical staff functions nationwide.

Under the Generic Drug User Fee Act (GDUFA), FDA committed to conducting risk-adjusted biennial current cGMP surveillance inspections of human generic Active Pharmaceutical Ingredients and finished dose form manufacturers, with the goal of achieving risk adjusted parity in domestic and foreign inspections by 2017. The Food and Drug Administration Safety and Innovation Act (FDASIA) Section 705 requires FDA to replace the previous two-year drug inspectional frequency requirement with a risk-based inspection schedule for domestic and foreign drug facilities. To accomplish this goal, FDA has employed a site selection surveillance inspection model that runs annually on all facilities in the FDA's inventory.

FDA's foreign inspections are a critical component of protecting the health and safety of U.S. citizens. These inspections help to ensure that products produced in foreign countries intended for the U.S. market meet the same standards of quality, purity, potency, safety, and efficacy as those manufactured domestically.

ORA made significant advancements to its foreign workplanning process through the development and implementation of a new IT system. The Workplanning, Inspection, and Tracking System (WITS) captures and tracks the entire foreign food inspection planning and scheduling process in real-time and includes GIS mapping technology that identifies facilities specific locations. WITS has allowed ORA to streamline the foreign food inspection program, automating the creation of documents, removing duplicative steps in the process and capturing the facility verification process through use of an intelligent questionnaire. This system has greatly improved ORA-Center coordination, collaboration, communication, and data integrity. ORA is currently working to deploy WITS beyond food commodities to include all foreign inspections and is evaluating its potential use for domestic inspections as well.

The Agency continues to leverage the work of its dedicated foreign inspections cadre, inspection staff located at FDA's foreign offices, and its domestic-based investigators to continue to enhance the overall coverage of the foreign establishment inventory. Through improvements to technology systems, FDA also continues to increase transparency and access to importers and other government agencies, helping to improve the efficiency of import entry reviews.

Protecting the U.S. food supply requires an integrated approach for identifying, investigating, and responding to foodborne illnesses and food-related incidents. This approach has improved responses to mitigate the number of illnesses associated with incidents related to food products. ORA's investment in developing training and mobilization of joint ORA and state Rapid Response Teams reduces exposure times, increases consumer protection, and minimizes the loss of consumer confidence, while lessening potential detrimental economic impact on industry.

ORA has expanded its assistance to state agencies regarding the capacity of inspection of medical devices with the addition of the California Department of Public Health to the FDA's Medical Device Contractual Inspection Program.

ORA is heavily involved in many critical aspects of FDA's human drug compounding program, including inspections and enforcement, policy development and implementation, state collaboration and coordination, and stakeholder outreach. In FY 2016 alone, ORA conducted 135 inspections of compounders, many of which belong to the category of compounders called outsourcing facilities that was created by the Drug Quality and Security Act of 2013.

Enforcement of FDA Authorities

In 2016, the criminal investigative work of ORA's Office of Criminal Investigations (OCI) resulted in 257 arrests, 274 convictions, and over \$374.5 million in forfeiture, fines, and restitution.

Many of these cases involved the distribution and sale of substandard and falsified products manufactured outside of the United States.

In continuing efforts to combat transnational criminal networks threatening public health, OCI increased its international presence through the assignment of Special Agents overseas. Since FY 2014, an OCI Special Agent has been stationed at Europol, in the Netherlands, and in FY 2016, OCI assigned a Special Agent at the Interpol Global Complex for Innovation (IGCI) in Singapore to work with Interpol's Global Health and Safety Sub-directorate. The IGCI is a cutting-edge research and development facility used for the international identification of crimes and criminals, innovative training, and operational support and partnerships.

Each year, OCI participates in Operation Opson, an Europol - Interpol joint operation targeting counterfeit and substandard food and beverages. Run from November 2015 through February 2016 and across 57 countries, Operation Opson V resulted in the seizure of 11,131.18 tons, 1,449,056.40 liters, and 5,549,328 units of counterfeit or substandard food and beverages.

OCI's Cybercrime Investigations Unit (CciU) is on the leading edge of combating the global trafficking of substandard and falsified FDA-regulated products on the internet. Each year, CciU agents team-up with internal and external partners as part of Interpol's annual Operation Pangea. FDA's collaborative efforts under Operation Pangea have resulted in more than 2,400 illegal online pharmacy websites being taken offline and the seizure of over \$81 million worth of potential dangerous illegal medicines and medical devices worldwide.

Through FY 2016, OCI has conducted training sessions on cybercrime, counterfeit drugs, and drug diversion for foreign criminal law enforcement agencies in Mexico, Canada, Central and South America, Africa, Asia, Australia, the Middle East, and Europe.

In 2014, OCI entered into a Letter of Intent Agreement with the French National Gendarmerie to combat counterfeit drugs and other transnational crimes affecting public health. In 2016, as part of the agreement, an officer of the National Gendarmerie attended OCI's Special Agent Training Program at the Federal Law Enforcement Training Center in Charleston, South Carolina.

FDASIA Section 706 allows FDA to obtain certain records from a drug manufacturer in lieu of or in advance of an inspection. In FY 2016, ORA initiated a time-limited six-month use of this authority in advance of already-planned cGMP surveillance inspections of foreign drug establishments. This program allowed ORA to garner data and qualitative feedback from ORA investigators and establishments regarding the appropriate scope and volume of records to request, the burden of producing and reviewing those records, and the process for requesting and confirming receipt of records. Investigators provided input on the usefulness of particular records for planning and targeting their on-site inspection time. In FY 2017, ORA will complete

and analyze the results of this initial use of the authority, and accordingly plan to expand its use.

In FY 2016, ORA's Florida District Office used the authority under 706 for the first time to obtain records in advance of an inspection at a firm involved with the manufacturing and processing of prescription drugs after reports of an associated *Burkholderia cepacia* outbreak.

In FY 2016, FDA successfully enjoined 16 firms and executed four seizures of goods at facilities for violations to the FD&C Act and promulgated regulations.

FDA also utilized administrative authorities under FSMA. Specifically, FDA hand-delivered a Suspension of Registration order to a seafood manufacturer in New York. The firm was a processor and manufacturer of ready-to-eat (RTE) seafood products found to contain *Listeria monocytogenes*. Some of the strains had a pattern combination that was seen previously; some coming from clinical samples.

Improve and Safeguard Access

ORA has taken steps to improve the consistency, transparency, and efficiency of its processes to benefit the health and wellness of the American public with a focus on Safety and Quality.

Premarket Activities

Implementation of GDUFA commits FDA to prioritizing inspections of establishments not previously inspected and those that are associated with Abbreviated New Drug Applications (ANDAs) that are otherwise approvable or eligible for tentative approval except for an outstanding inspection. ORA collaborates with CDER in prioritizing ANDA inspections, targeting inspectional resources, and creating efficiency by identifying generic drug manufacturing facilities for inspection to coincide with Center reviews of applications. ORA continues to conduct pre-approval and Bioresearch Monitoring (BIMO) inspections to support original and prior approval supplements to meet the GDUFA commitment goals.

Strengthen Organizational Excellence

ORA enhances program integrity through its commitment to operational, workforce, and organizational excellence. This investment includes recruiting, training, developing, and retaining a diverse, world class workforce, and the creation of leadership roadmaps to support professional development. To that end, ORA has launched several efforts intended to

strengthen the core underpinnings of the organization: grade parity and career ladders, workforce development, and organizational culture and values.

Workforce Development

FDA employees must be highly skilled and meet professional standards to carry out their responsibilities. ORA and key training partners will continue to develop, design, and deliver training to FDA's workforce, as well as to state and local partners, to ensure that regulators at every-level possess the scientific and technical competence and skills to oversee the diverse commodities over which FDA has jurisdiction.

Throughout the implementation of FSMA, the Agency has looked for various new and innovative ways to train ORA and Center staff for these new rules. For the seven new FSMA rules, FDA has worked closely with industry, academia, and other stakeholders to develop training which will be comprehensive and helpful to all concerned. For some programs, the training curriculum for the rules involved two different parts: training that regulators and other stakeholders attend together, allowing for an open exchange of ideas and flow of information; and training specifically for regulators to learn how to implement the new rules. The training has been developed as a cooperative effort between FDA, industry and academia.

Throughout the year, ORA served as expert participants with the CFSAN and Center for Veterinary Medicine (CVM) counterparts to develop and complete several information webinars dubbed "FSMA Chats." During these chats, which started in FY 2016, FDA experts provide updated information regarding particular FSMA programs and answer questions from FDA staff, key stakeholders and regulated industry. This has allowed interaction between stakeholders in a new and innovative manner that allows for an open exchange of ideas outside of the normal regulatory pathways.

ORA has developed plans for continuous improvement of training in alignment with Job Task Analysis results. Outcomes of these reviews include a major curriculum revamp for each program area, incorporating a blended learning approach and providing quality training in an efficient, timely, and cost-effective manner. This training includes increased incorporation of web modules, webinars, and on-the-job training at the student's locality.

FDA is exploring additional investigator and analyst certification programs to institute professional standards for regulatory employees who execute the authority of FDA as defined in the FD&C Act and related acts. Programs already exist for Seafood, Low Acid Canned Foods/Acidified Foods (LACF/AF), Drug, Import, Medical Device, Clinical BIMO, Blood Bank, and Plasma Center certifications. These certification programs provide a foundation to ensure highly skilled individuals are available to carry out FDA's mission.

The Management and Leadership Development Program (MLDP) offers training and development opportunities for all ORA staff, with an emphasis on those seeking a future management position or wanting to develop into a candidate better qualified for career advancement. ORA's MLDP launched several new FY 2016 initiatives that provided further opportunity to enhance ORA's leadership culture including partnering and collaborating with the FDA Alumni Association to create a mentoring program partnering current ORA managers with rehired annuitants to expand leadership competencies. The FDA Alumni Advisory Program is the recipient of the 2016 FDA Honors Innovator Award. Continuing ORA's Resilient Leadership Training Program helps leaders to lead with calm, clarity, and conviction.

Values Initiative

ORA recently launched an initiative that sought to capture stakeholder's thoughts about ORA's core values and the values that best reflect today's environment. This initiative included surveys and stakeholder engagement at every level of the organization, and resulted in a new set of values for ORA including: Accountability, Commitment to Public Health, Communication, Diversity and Inclusion, Integrity and Respect, and Quality.

Commitment to Quality

ORA is committed to quality and continual improvement. ORA's Quality Management System (QMS) responsibilities include providing centralized QMS guidance, leadership, communications, training, and collaboration with internal and external stakeholders. These efforts help to ensure that QMS is an effective, efficient, practical, and long-term system that provides feedback to ORA on the quality of its work and results in continual improvement for all of ORA's processes, products, and services.

In order to keep pace with the acceleration of scientific innovation, globalization, and recent legislative authorities, pending approval, FDA will be implementing a Program Alignment initiative that will result in organizational and operational changes to ensure that FDA achieves its mission-critical objectives and optimizes the coordination of the work performed among the Centers and ORA. A key part of this process is to enhance the specialization of ORA investigators which will allow FDA to have more commodity-based and vertically-integrated regulatory programs with well-defined leads, coherent policy and strategy development, well-designed and coordinated implementation, and a de-layered management structure. Full implementation of program alignment is expected in FY 2017.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
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FY 2014 Actual	\$962,111,000	\$917,317,000	\$44,794,000
FY 2015 Actual	\$998,913,000	\$934,393,000	\$64,520,000
FY 2016 Actual	\$1,092,819,000	\$1,022,759,000	\$70,060,000
FY 2017 Annualized CR	\$1,121,641,000	\$1,005,877,000	\$115,764,000
FY 2018 President's Budget	\$1,051,206,000	\$876,782,000	\$174,424,000

BUDGET REQUEST

The FY 2018 budget request is \$1,051,206,000, of which \$876,782,000 is budget authority and \$174,424,000 is user fees. Budget authority decreases by \$129,095,000 compared to the FY 2017 Annualized CR budget and user fees increase by \$58,660,000.

The FY 2018 President's Budget allows FDA to continue to ensure that food, feed, and medical products are available to the American public are safe and effective.

BUDGET AUTHORITY

Reductions (-\$68.1 million)

Food Safety: -\$53.7 million

In order to continue operations under the FY 2018 request level, ORA will apply the necessary program reductions to areas such as partnerships, training, IT and lab equipment, and across all program office operating budgets. While every effort will be made to protect resources for priorities including inspections and compliance activities, some reductions may occur due solely to reduced staff. ORA will reduce existing workforce levels through attrition, and will work to minimize the impact related to field exams, import entry review, investigations, sample analysis, and inspections for surveillance, compliance, and follow up activities, both domestically and abroad. It is FDA's goal to minimize the impact of these reductions on FDA's core mission activities.

ORA will reduce several state cooperative agreements. This impact includes reductions to the cooperative agreements supporting:

- the Food Emergency Response Network (FERN), a network able to respond to biological, chemical, or radiological food contamination emergencies
- the International Standards Organization (ISO) accreditation which supports non-FDA laboratories in achieving and maintaining this accreditation
- the Manufactured Food Regulatory Program Standards (MFRPS), which help develop and implement standards for federal and state programs to better direct regulatory activities toward reducing foodborne illness

- the Animal Feed Regulatory Program Standards (AFRPS), which help ensure a uniform and consistent approach to feed regulation
- the retail food protection standardization program, which helps prevent foodborne illness associated with the preparation, service, and sale of foods in food service and retail establishments.

Medical Product Safety & Availability: -\$14.4 million

ORA will apply strategic reductions to its programs in order to preserve the highest priority activities and operations in support of protecting public health. ORA will reduce existing workforce levels through attrition.

In order to continue operations under the FY 2018 request levels, ORA will apply the necessary program reductions to areas such as training, IT and lab equipment, and across all program office operating budgets, while protecting resources for inspections and compliance activities.

Medical Product User Fee Recalibration (+\$60.7 million)

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees.

USER FEES

Medical Product User Fee Recalibration (+\$60.7 million)

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees.

PERFORMANCE

ORA's performance measures focus on import screening activities, laboratory capacity, and domestic and foreign inspections in order to ensure that food, feed and medical products available to the American public are safe and effective, as detailed in the following table.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
<u>214212</u> : Percentage of planned import food field	FY 2016: 172,449 Target: 160,158	99%	99%	Maintain

OFFICE OF REGULATORY AFFAIRS – FIELD ACTIVITIES

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
exams (approximately 160,000 in total). <i>(Output)</i>	(Target Exceeded)			
<u>214206</u> : Maintain accreditation for ORA labs. <i>(Outcome)</i>	FY 2016: 13 labs Target: 13 labs (Target Met)	13 labs	13 labs	Maintain
<u>214209</u> : As required by the FSMA Legislation, cover all of the High Risk domestic inventory (approximately 19,000 firms) every three years. <i>(Output)</i>	FY 2016: 99.8% Target: 100% (Target Not Met)	33%	66%	Maintain
<u>214305</u> : Increase laboratory surge capacity in the event of terrorist attack on the food supply. (Radiological and chemical samples/week). <i>(Outcome)</i>	FY 2016: 2,500 rad & 2,100 chem Target: 2,500 rad & 2,100 chem (Target Met)	2,500 rad & 2,100 chem	2,500 rad & 2,100 chem	Maintain
<u>224211</u> : Percentage of planned foreign and domestic high-risk human drug inspections (approximately 560 in total). <i>(Output)</i>	FY 2016: 698 Target: 560 (Target Exceeded)	64%	64%	Maintain
<u>234212</u> : Percentage of registered domestic blood bank and biologics manufacturing inventory inspected (approximately 900 in total). <i>(Output)</i>	FY 2016: 992 Target: 900 (Target Exceeded)	99%	99%	Maintain
<u>234213</u> : Percentage of planned human foreign and domestic tissue establishment inspections (approximately 570 in total). <i>(Output)</i>	FY 2016: 703 Target: 570 (Target Exceeded)	82%	82%	Maintain
<u>244212</u> : Percentage of domestic and foreign high-risk animal drug and feed inventory inspected	FY 2016: 248 Target: 225 (Target Exceeded)	99%	99%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
(approximately 225 in total). (Output)				
<u>244203</u> : Percentage of planned targeted prohibited material BSE inspections (approximately 477 in total). (Output)	FY 2016: 100% Target: 100% (Target Met)	99%	99%	Maintain
<u>253211</u> : Percentage of planned Medical Device Bioresearch Monitoring (BIMO) inspections (approximately 300 in total). (Output)	FY 2016: 309 Target: 300 (Target Exceeded)	91%	91%	Maintain
<u>254211</u> : Percentage of planned domestic and foreign Class II and Class III device inspections (approximately 1,600 in total). (Output)	FY 2016: 2,075 Target: 1,600 (Target Exceeded)	57%	57%	Maintain

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

FSMA High Risk Domestic Inspection Coverage

FDA is committed to ensuring that the U.S. food supply continues to be among the safest in the world. ORA plays a critical role in the implementation of FSMA, and recognizes the importance of complying with high-risk domestic inspections mandated by FSMA legislation. FSMA legislation requires inspecting the entire high-risk domestic inventory every three years. This goal serves to cumulatively track the progress over the three-year period as the coverage of the high-risk domestic inventory approaches the FSMA-driven goal of 100 percent. FY 2016 marked the final year of a three-year cycle.

The identified inventory to be inspected at the beginning of the FY 2014 to F 2016 cycle was approximately 19,000 firms; however this inventory number does not remain static over the course of the inspection cycle. Therefore as the inventory changes over the three-year period, FDA must make adjustments to work plans to meet the 100 percent target. Upon completion of FY 2016, the cumulative percentage reached 99.8 percent, very nearly achieving the 100 percent target. This high level of accomplishment was achieved despite the dynamic and

uncertain conditions facing FDA. For example, given that this goal tracks the inspections of the high-risk inventory there are more likely to be issues uncovered during these inspections. This requires ORA to redirect resources to conduct follow-up actions and reinspections, which use resources that otherwise would be deployed for inspecting the rest of the required inventory. The near-miss of the 100 percent target in FY 2016 resulted from a combination of changes in the inventory and utilization of resources for follow up or reinspections conducted within the domestic foods high-risk inventory that count as inspections but do not count toward additional coverage of the inventory, as these are inspections conducted at the same firm more than once.

FY 2017 marks the beginning of a new cycle and the target returns to 33 percent to signify that FDA is targeting the first third of the inventory for the new three-year cycle. FDA came very close to meeting our FY 2016 goal of 100 percent, and most of the remaining FSMA high risk firm inspections were completed in early FY 2017.

Moving from Numbers to Percentages for Field Targets

ORA is in the process of improving the field performance measures to make the measures more outcome oriented and better aligned with ORA's Program Alignment initiative. Several ORA performance goals will now be targeting either a percentage of the number specified in the work plan or a percentage of total inventories. Reporting a percentage rather than a number will clarify that these goals are intended to align with the public health priorities reflected in the work planning and inventory coverage. This also allows FDA the flexibility to respond dynamically to changing circumstances during the year, as work plans are revised to reflect emerging risks and evolving public health priorities. While the reporting format will change from numbers to percentages, the underlying level of activities for inspections and import field exams will be maintained from FY 2016 through FY 2017 and FY 2018.

PROGRAM ACTIVITY DATA TABLES**Field Foods Program Activity Data (PAD)**

Field Foods Program Workload and Outputs	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	7,933	8,000	8,000
Domestic Food Safety Program Inspections	5,783	Activities no longer planned to this level due to enactment of FSMA and alignment of resources into only high and low risk categories.	Activities no longer planned to this level due to enactment of FSMA and alignment of resources into only high and low risk categories.
Imported and Domestic Cheese Program Inspections	182		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	249		
Domestic Fish & Fishery Products (HACCP) Inspections	716		
Import (Seafood Program Including HACCP) Inspections	321		
Juice HACCP Inspection Program (HACCP)	161		
Interstate Travel Sanitation (ITS) Inspections	922		
Domestic Field Exams/Tests	2,398	2,500	2,500
Domestic Laboratory Samples Analyzed	16,927	13,000	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS	1,269	1,400	1,400
All Foreign Inspections	1,269	1,400	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	9,202	9,400	9,400
IMPORTS			
Import Field Exams/Tests	252,766	168,200	168,200
Import Laboratory Samples Analyzed	<u>23,736</u>	<u>35,300</u>	<u>35,300</u>
Import Physical Exam Subtotal	276,502	203,500	203,500
Import Line Decisions	13,952,537	14,650,164	15,382,672
Percent of Import Lines Physically Examined	1.98%	1.39%	1.32%
Prior Notice Security Import Reviews (Bioterrorism Act Mandate)	87,817	80,000	80,000
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	8,952	9,088	9,088
UNIQUE COUNT OF STATE PARTNERSHIPS FOOD ESTABLISHMENT INSPECTIONS	676	100	100
State Contract Food Safety (Non HACCP) Inspections	7,897	8,000	8,000
State Contract Domestic Seafood HACCP Inspections	964	1,000	1,000
State Contract Juice HACCP	91	100	100
State Contract LACF	110	100	100
State Partnership Inspections	676	100	100
State Contract Foods Funding	\$13,283,752	\$13,682,265	\$14,092,732
Number of FERN State Laboratories	19	19	19
Number of Food Safety State Laboratories	15	15	15
Annual FERN State Cooperative Agreements/Operations Funding	\$19,038,534	\$17,705,837	\$16,466,428
Total State & Annual FERN Funding	\$32,322,286	\$31,388,101	\$30,559,161
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	18,830	18,588	18,588

Field Cosmetics Program Activity Data (PAD)

Field Cosmetics Program Workload and Outputs	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget
<i>FDA WORK</i>			
DOMESTIC INSPECTIONS			
<i>UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS</i>	<i>133</i>	<i>100</i>	<i>100</i>
Domestic Inspections	133	100	100
FOREIGN INSPECTIONS			
<i>UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS</i>	<i>3</i>	<i>0</i>	<i>0</i>
Foreign Inspections	3	0	0
IMPORTS			
Import Field Exams/Tests	12,036	1,600	1,600
Import Laboratory Samples Analyzed	393	400	400
Import Physical Exam Subtotal	12,429	2,000	2,000
Import Line Decisions	2,939,034	3,085,986	3,240,285
Percent of Import Lines Physically Examined	0.42%	0.06%	0.06%
<i>GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS</i>	<i>136</i>	<i>100</i>	<i>100</i>

¹ The FY 2016 actual unique count of foreign inspections includes 178 OIP inspections (147 for China, 9 for India, & 22 for Latin America).

Field Human Drugs Program Activity Data (PAD)

Field Human Drugs Program Workload and Outputs	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget
<i>FDA WORK</i>			
DOMESTIC INSPECTIONS			
<i>UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS</i>	<i>1,846</i>	<i>1,767</i>	<i>1,767</i>
Pre-Approval Inspections (NDA)	88	135	135
Pre-Approval Inspections (ANDA)	92	215	215
Bioresearch Monitoring Program Inspections	616	550	550
Drug Processing (GMP) Program Inspections	805	650	650
Compressed Medical Gas Manufacturers Inspections	97	50	50
Adverse Drug Events Project Inspections	88	88	88
OTC Monograph Project and Health Fraud Project Inspections	51	70	70
Compounding Inspections ¹	135	130	130
Domestic Laboratory Samples Analyzed	1,301	1,300	1,300
FOREIGN INSPECTIONS			
<i>UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS</i>	<i>1231</i>	<i>1275</i>	<i>1275</i>
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	100	98	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	173	190	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	214	255	255
Foreign Drug Processing (GMP) Program Inspections	909	900	900
Foreign Adverse Drug Events Project Inspections	7	10	10
<i>TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS</i>	<i>3,077</i>	<i>3,042</i>	<i>3,042</i>
IMPORTS			
Import Field Exams/Tests	10,053	10,000	10,000
Import Laboratory Samples Analyzed	<u>1,009</u>	<u>620</u>	<u>620</u>
Import Physical Exam Subtotal	11,062	10,620	10,620
Import Line Decisions	739,309	776,274	815,088
Percent of Import Lines Physically Examined	1.50%	1.37%	1.30%
<i>STATE WORK</i>			
<i>UNIQUE COUNT OF STATE PARTNERSHIP HUMAN DRUG ESTABLISHMENT INSPECTIONS</i>²	<i>0</i>	<i>0</i>	<i>0</i>
State Partnership Inspections: Compressed Medical Gas Manufacturers Inspections	0	0	0
State Partnership Inspections: GMP Inspections	0	0	0
<i>GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS</i>	<i>3,077</i>	<i>3,042</i>	<i>3,042</i>

¹ The number of compounding inspections includes inspections of compounders that are and are not registered with FDA as outsourcing facilities.

² The FY 2016 actual unique count of foreign inspections includes 82 OIP inspections (41 for China, 35 for India, & 6 for Latin America).

³ The State inspections that are funded by the FDA are now being obligated via formal contract funding vehicles.

Field Biologics Program Activity Data (PAD)

Field Biologics Program Workload and Outputs	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget
<i>FDA WORK</i>			
DOMESTIC INSPECTIONS			
<i>UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>1,875</i>	<i>1,909</i>	<i>1,909</i>
Bioresearch Monitoring Program Inspections	80	100	100
Blood Bank Inspections	895	900	900
Source Plasma Inspections	180	190	190
Pre-License, Pre-Market Inspections	61	55	55
GMP Inspections	38	28	28
GMP (Device) Inspections	4	7	7
Human Tissue Inspections	638	650	650
FOREIGN INSPECTIONS			
<i>UNIQUE COUNT OF FDA FOREIGN BIOLOGICS</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>68</i>	<i>47</i>	<i>47</i>
Bioresearch Monitoring Program Inspections	17	11	11
Foreign Human Tissue Inspections	2	0	0
Blood Bank Inspections	7	7	7
Pre-License, Pre-market Inspections	7	7	7
GMP Inspections (Biologics & Device)	34	20	20
<i>TOTAL UNIQUE COUNT OF FDA BIOLOGIC</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>1,943</i>	<i>1,956</i>	<i>1,956</i>
IMPORTS			
Import Field Exams/Tests	155	45	45
Import Line Decisions	151,911	162,545	173,923
Percent of Import Lines Physically Examined	0.10%	0.03%	0.03%
<i>GRAND TOTAL BIOLOGICS ESTABLISHMENT</i>			
<i>INSPECTIONS</i>	<i>1,943</i>	<i>1,956</i>	<i>1,956</i>

OFFICE OF REGULATORY AFFAIRS – FIELD ACTIVITIES

Field Animal Drugs & Feeds Program Activity Data (PAD)

Field Animal Drugs and Feeds Program Workload and Outputs	FY 2016 Actuals			FY 2017 Annualized CR			FY 2018 President's Budget		
	Total	Animal Drugs	Feeds	Total	Animal Drugs	Feeds	Total	Animal Drugs	Feeds
FDA WORK									
DOMESTIC INSPECTIONS									
<i>UNIQUE COUNT OF FDA DOMESTIC ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS</i>	<i>1,822</i>	<i>255</i>	<i>1,589</i>	<i>1,664</i>	<i>298</i>	<i>1,398</i>	<i>1,664</i>	<i>298</i>	<i>1,398</i>
Pre-Approval /BIMO Inspections	39	39	0	79	79	0	79	79	0
Drug Process and New ADF Program Inspections	221	221	0	175	175	0	175	175	0
BSE Inspections	1,341	0	1,341	1,205	0	1,205	1,205	0	1,205
Feed Contaminant Inspections	13	0	13	25	0	25	25	0	25
Illegal Residue Program Inspections	397	0	397	450	0	450	450	0	450
Feed Manufacturing Program Inspections	250	0	250	200	0	200	200	0	200
Domestic Laboratory Samples Analyzed	1,555	8	1,547	1,560	20	1,540	1,560	20	1,540
FOREIGN INSPECTIONS									
<i>UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS</i>	<i>126</i>	<i>118</i>	<i>8</i>	<i>76</i>	<i>71</i>	<i>5</i>	<i>76</i>	<i>71</i>	<i>5</i>
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	13	13	0	40	40	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	109	109	0	33	33	0	33	33	0
Foreign Feed Inspections	7	0	7	5	0	5	5	0	5
BSE Inspections	5	0	5	0	0	0	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	1,948	373	1,597	1,740	369	1,403	1,740	369	1,403
IMPORTS									
Import Field Exams/Tests	7,935	796	7,139	3,795	495	3,300	3,300	495	3,300
Import Laboratory Samples Analyzed	894	4	890	867	2	865	867	2	865
Import Physical Exam Subtotal	8,829	800	8,029	4,662	497	4,165	4,167	497	4,165
Import Line Decisions	446,903	48,661	385,723	469,248			492,711		
Percent of Import Lines Physically Examined	1.98%	1.64%	2.08%	0.99%			0.85%		
STATE WORK									
<i>UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS</i>	<i>3,702</i>	<i>0</i>	<i>3,702</i>	<i>3,832</i>	<i>0</i>	<i>3,832</i>	<i>3,832</i>	<i>0</i>	<i>3,832</i>
<i>UNIQUE COUNT OF STATE PARTNERSHIPS ANIMAL FEEDS ESTABLISHMENT INSPECTIONS ¹</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>
<i>UNIQUE COUNT OF STATE COOPERATIVE AGREEMENT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS ²</i>	<i>2</i>	<i>0</i>	<i>2</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>	<i>0</i>
State Contract Inspections: BSE	3,694	0	3,694	3,500	0	3,500	3,500	0	3,500
State Contract Inspections: Feed Manufacturers	623	0	623	620	0	620	620	0	620
State Contract Inspections: Illegal Tissue Residue	134	0	134	130	0	130	130	0	130
State Partnership Inspections: BSE and Other	0	0	0	0	0	0	0	0	0
State Cooperative Agreement BSE Inspections	2	0	2	0	0	0	0	0	0
State Contract Animal Drugs/Feeds Funding	\$3,073,399	0	\$3,073,399	\$3,165,601	0	\$3,165,601	\$3,260,569	0	\$3,260,569
BSE Cooperative Agreement Funding	\$0	0	\$0	\$0	0	\$0	\$0	0	\$0
State Contract Tissue Residue Funding	<u>\$456,317</u>	<u>0</u>	<u>\$456,317</u>	<u>\$442,627</u>	<u>0</u>	<u>\$442,627</u>	<u>\$429,348</u>	<u>0</u>	<u>\$429,348</u>
Total State Funding	\$3,529,716	\$0	\$3,529,716	\$3,608,228	\$0	\$3,608,228	\$3,689,917	\$0	\$3,689,917
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	5,652	373	5,301	5,572	369	5,235	5,572	369	5,235

¹ The FY 2016 actual unique count of foreign inspections includes 12 OIP inspections (11 for China).² The State inspections that are funded by the FDA are now being obligated via formal contract funding vehicles and this number is expected to decrease in the future until there are no planned State Partnership inspections.³ The State cooperative agreement BSE inspections that are funded by the FDA are now being obligated via formal contract funding vehicles and this number along with the funding for these inspections are expected to decrease in the future until there are no planned State Cooperative Agreement BSE inspections.

OFFICE OF REGULATORY AFFAIRS – FIELD ACTIVITIES

Field Devices and Radiological Health Program Activity Data (PAD)

Field Devices and Radiological Health Program Workload and Outputs	FY 2016 Actual	FY 2017 Annualized CR	FY 2018 President's Budget
<i>FDA WORK</i>			
DOMESTIC INSPECTIONS			
<i>UNIQUE COUNT OF FDA DOMESTIC DEVICES</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>2,499</i>	<i>2,492</i>	<i>2,492</i>
Bioresearch Monitoring Program Inspections	272	300	300
Pre-Market Inspections	61	60	60
Post-Market Audit Inspections	69	60	60
GMP Inspections	1,420	1,400	1,400
Inspections (MQSA) FDA Domestic (non-VHA)	704	700	700
Inspections (MQSA) FDA Domestic (VHA)	54	50	50
Domestic Radiological Health Inspections	47	50	50
Domestic Field Exams/Tests	15	100	100
Domestic Laboratory Samples Analyzed	255	170	170
FOREIGN INSPECTIONS			
<i>UNIQUE COUNT OF FDA FOREIGN DEVICES</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>603</i>	<i>595</i>	<i>595</i>
Foreign Bioresearch Monitoring Inspections	15	14	14
Foreign Pre-Market Inspections	26	30	30
Foreign Post-Market Audit Inspections	30	20	20
Foreign GMP Inspections	728	550	550
Foreign MQSA Inspections	13	14	14
Foreign Radiological Health Inspections	78	50	50
<i>TOTAL UNIQUE COUNT OF FDA DEVICE</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>3,102</i>	<i>3,087</i>	<i>3,087</i>
IMPORTS			
Import Field Exams/Tests	29,992	19,800	19,800
Import Laboratory Samples Analyzed	<u>577</u>	<u>670</u>	<u>670</u>
Import Physical Exam Subtotal	30,569	20,470	20,470
Import Line Decisions	18,757,725	20,070,766	21,475,719
Percent of Import Lines Physically Examined	0.16%	0.10%	0.10%
<i>STATE WORK</i>			
<i>UNIQUE COUNT OF STATE CONTRACT DEVICES</i>			
<i>ESTABLISHMENT INSPECTIONS</i>	<i>7,803</i>	<i>7,880</i>	<i>7,880</i>
<i>UNIQUE COUNT OF STATE PARTNERSHIPS</i>			
<i>DEVICE ESTABLISHMENT INSPECTIONS¹</i>	<i>0</i>	<i>0</i>	<i>0</i>
Inspections (MQSA) by State Contract	6,716	6,800	6,800
Inspections (MQSA) by State non-Contract	1,044	1,060	1,060
GMP Inspections by State Contract	43	20	20
State Partnership GMP Inspections	0	0	0
State Contract Devices Funding	\$267,249	\$275,266	\$283,524
State Contract Mammography Funding	<u>\$9,720,997</u>	<u>\$9,957,944</u>	<u>\$10,157,103</u>
Total State Funding	\$9,988,246	\$10,233,210	\$10,440,627
<i>GRAND TOTAL DEVICES ESTABLISHMENT</i>			
<i>INSPECTIONS</i>	<i>10,905</i>	<i>10,967</i>	<i>10,967</i>

¹ The FY 2016 actual unique count of foreign inspections includes 12 OIP inspections (8 for China and 4 for India).² The State inspections that are funded by the FDA are now being obligated via formal contract funding vehicles.

TOBACCO CONTROL ACT

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
Family Smoking Prevention and Tobacco Control Act.....	564,117	476,525	563,045	625,646	62,601
Center (UF Only).....	547,454	466,776	546,413	611,096	64,683
Field (UF Only).....	16,663	9,749	16,631	14,550	-2,081
FTE.....	780	780	910	930	20

Authorizing Legislation: Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321-399); The Family Smoking Prevention and Tobacco Control Act of 2009 (P.L. 111-31); The Federal Cigarette Labeling and Advertising Act (15 U.S.C. 1333); Public Health Service Act of 1944 (42 U.S.C. 201); Federal Advisory Committee Act of 1972, as amended.

Allocation Methods: Competitive Grants; Contracts; Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The Center for Tobacco Products (CTP) oversees the implementation of the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act). FDA works to protect Americans from tobacco-related death and disease by regulating the manufacture, distribution, and marketing of tobacco products, and by educating the public about tobacco products and the dangers their use poses.

FDA executes its regulatory and public health responsibilities in program areas that support the following objectives:

- reducing initiation of tobacco product use
- decreasing the harms of tobacco products
- encouraging cessation among tobacco product users.

To achieve its goals, FDA relies on statutory authorities to regulate the manufacturing, marketing, and distribution of tobacco products. FDA requires domestic tobacco product manufacturers to register and provide a list of tobacco products they manufacture, and tobacco product manufacturers and importers are required to submit a listing of ingredients in their products. Industry must report harmful and potentially harmful constituents and FDA prohibits inaccurate, false, or misleading tobacco product labeling and marketing.

Some of FDA's authorized activities include:

- inspecting tobacco product manufacturing establishments and tobacco retailers to ensure compliance with laws and regulations

- establishing tobacco product standards to protect public health
- issuing regulations on the marketing and advertising of tobacco products
- strengthening health warnings for tobacco products
- taking enforcement action, for violations of the Tobacco Control Act and implementing regulations.

The following selected accomplishments demonstrate FDA's delivery of its regulatory and public health responsibilities.

Compliance

As of March 31, 2017, FDA had contracts for tobacco retailer compliance check inspections in 55 states, territories, and tribal jurisdictions. Compliance check inspections pertain to tobacco marketing, sales, and distribution of tobacco products at retail locations and include ensuring compliance with age and ID verification requirements. Since the program's inception in October 2010 through March 31, 2016, FDA conducted more than 758,000 compliance check inspections at tobacco retail establishments and has commissioned more than 2,500 officers and employees from the states, territories, and their political subdivisions.

Regulation

The Tobacco Control Act gave FDA immediate authority to regulate cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco. The Tobacco Control Act also gave FDA the authority to regulate additional tobacco products through the issuance of regulation. On May 10, 2016, FDA finalized a rule – Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act – which extends FDA's authority to all tobacco products, including the regulation of electronic nicotine delivery systems (such as e-cigarettes and vape pens), cigars, hookah (waterpipe) tobacco, pipe tobacco and nicotine gels, among others.

This rule helps implement the bipartisan Tobacco Control Act and allows FDA to improve public health and protect future generations from the dangers of tobacco use through a variety of steps, including restricting the sale of these tobacco products to minors nationwide.



Under the final deeming rule, manufacturers of newly deemed tobacco products are required to:

- register establishments with FDA
- report product and ingredient listings
- report harmful and potentially harmful constituents
- market new tobacco products only after receiving authorization from FDA
- make direct and implied claims of reduced risk only after receiving a risk or exposure modification order from FDA
- not distribute free samples.

Also under the final deeming rule, the following provisions, which already applied to the originally regulated tobacco products, now apply to newly “deemed” tobacco products:

- minimum age and identification restrictions to prevent sales to underage youth
- requirements to include health warnings
- prohibition of vending machine sales, unless in a facility that never admits youth.

This final rule went into effect on August 8, 2016.

FDA also understands that newly regulated entities will need assistance in complying with the FD&C Act and FDA regulations. As a result, FDA is working to educate newly regulated industry through multiple means, including:

- Issuing several guidances on the deeming rule to help industry and the public understand FDA’s current thinking on provisions in the rule
- Publishing the Small Entity Compliance Guide for Deeming to help small businesses understand and comply with the final deeming rule
- Hosting a two day public seminar in October 2016 to help industry understand the requirements for a new tobacco product application and the submission process
- Publishing 15 deeming related compliance webinars on the CTP website
- Redesigning the tobacco regulation portion of the FDA website and creating specific sections dedicated to assisting manufacturers and retailers
- Setting up a call center to answer questions from consumers, retailers, manufacturers, and importers. As of March 31, 2017, CTP has responded to more than 5,000 inquiries.

Substantial Equivalence

Manufacturers may submit Substantial Equivalence (SE) Reports to seek FDA authorization to legally market a new tobacco product. FDA has made significant progress in this important area and has built a science-based process to review these SE Reports to determine whether the new product is substantially equivalent to a valid predicate.

A substantially equivalent tobacco product is a product FDA has determined has the same characteristics as a predicate tobacco product or has different characteristics than the predicate tobacco product but the information submitted demonstrates that the new product does not raise different questions of public health. A predicate tobacco⁸¹ product is one that was commercially marketed in the United States – other than in a test market – as of February 15, 2007, or a product previously found to be substantially equivalent by FDA.

FDA reviews these SE reports to determine if the new tobacco product is substantially equivalent and is in compliance with the requirements of the law. If both of these criteria are met, FDA issues a written order permitting the product to be legally marketed in the United States. A manufacturer cannot legally market a new tobacco product if they have not received marketing authorization from FDA⁸².

FDA has prioritized the review of regular⁸³ SE submissions and has made progress in each of the three phases in the SE review process:

- acceptance review phase – FDA makes a decision to either accept or refuse the application based on requirements in the statute
- notification and predicate eligibility phase – the applicant is notified that scientific review will begin, and a date for the start of review is provided
- substantive scientific review phase and issuance of a decision.

All regular SE reports received are immediately entered into review. As of March 31, 2017:

- 76 percent of all full⁸⁴ regular SE reports received to date have been resolved by a final decision⁸⁵.

⁸¹ <http://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/SubstantialEquivalence/ucm304517.htm#3>

⁸² If a new tobacco product was commercially marketed after February 15, 2007 but before March 22, 2011; and a Substantial Equivalence Report was submitted by March 22, 2011, then this new tobacco product may continue to be marketed unless FDA issues an order that the new product is not substantially equivalent to an appropriate predicate product.

⁸³ SE reports received after March 22, 2011 are “regular” reports and products covered by those reports cannot be marketed unless FDA first issues a finding of substantial equivalence.

⁸⁴ In March 2015, FDA issued guidance permitting companies to submit “streamlined” SE reports under certain conditions. Review of these streamlined reports is ongoing and is not counted here.

⁸⁵ Final decisions include refuse-to-accept, withdrawn, substantially equivalent (SE), not substantially equivalent (NSE)

- FDA completed acceptance reviews of 5,757 of the 5,870 SE submissions received to date.
- FDA issued a Scientific Advice and Information Request Letter or a Preliminary Finding Letter for 88 percent of the pending full regular SE reports.

These letters communicate to the manufacturer the deficiencies in a SE Report that preclude either further scientific review or issuance of an SE Order.

In FY 2015, FDA implemented performance measures, including timeframes for review of regular SE reports and review of Exemption from SE requests.⁸⁶ FDA has been able to develop these goals because of the increased knowledge of scientific evidence and data gathering needed to adequately review these SE reports.

FDA is also continuing scientific review of provisional SE reports.⁸⁷

As of March 31, 2017:

- FDA has begun scientific review of 1,270 provisional SE Reports.
- 23 percent of full provisional SE reports have been resolved by a final decision.⁸⁸

FDA expects the time required for review of SE submissions to decrease as CTP continues to improve the efficiency of its review process and companies continue to improve the completeness and quality of their applications.

Public Education

FDA's first ever national public education campaign to help prevent youth tobacco use – "The Real Cost" – continues to exceed paid media reach and frequency goals by reaching at least 86 percent of the target audience every quarter since launching February 11, 2014.



The campaign is designed to reduce the number of youth aged 12 to 17 who smoke, and results announced in January, 2017 from a two-year outcome evaluation indicate the campaign is succeeding in meeting this goal. So far, "The Real Cost" campaign prevented over 345,000 U.S.

⁸⁶ Exemption from SE is an alternative to substantial equivalence in which the only change is to an additive, the product change is minor and a full substantial equivalence report is not necessary to ensure that permitting the tobacco products to be marketed is appropriate for the protection of public health.

⁸⁷ SE reports received before March 23, 2011 for products introduced to market or changed between February 16, 2007, and March 22, 2011 are "provisional" reports and products covered by those reports can continue to be marketed until FDA issues a finding of not-substantial equivalence.

⁸⁸ Final decisions include refuse-to-accept, withdrawn, substantially equivalent (SE), not substantially equivalent (NSE).

youth from smoking from 2014 to 2016, exceeding our goals for the campaign. Considering most tobacco dependence begins during adolescence, youth-focused tobacco prevention campaigns like “The Real Cost” can have long-term effects on future rates of tobacco-related morbidity and mortality.

To keep the target audience engaged with its messaging, FDA refreshed the campaign with a third wave of advertising in October 2016. This strategy is based on target audience research that suggests the personality trait of sensation-seeking, which is closely linked with risk taking behavior, is associated with a preference for novel messaging. As such, FDA has launched new advertising every year to keep these high sensation-seeking youth engaged with the campaign. Additional advertising is planned for launch in 2017.

Additionally, the campaign won a 2016 Shorty Award for Best Overall Tumblr Presence. The Shorty Awards honor the best of social media by recognizing the top influencers, brands and organizations on Facebook, Twitter, Tumblr, YouTube, Instagram and Snapchat.

FDA also expanded “The Real Cost” brand in April 2016 by launching advertising designed to prevent and reduce smokeless tobacco use among youth aged 12 to 17 who live in rural areas and are at risk for smokeless tobacco initiation. This campaign messaging aims to deliver facts about the dangers of smokeless tobacco use to drive shifts in the beliefs of rural teens to ultimately create attitude and behavior change.

On May 12, 2015, FDA launched the first phase of its “Fresh Empire” campaign in four Southeast markets in the United States: Atlanta, GA; Birmingham, AL; Charlotte, NC; and Raleigh, NC. The campaign is designed to prevent and reduce tobacco use among at-risk multicultural youth aged 12 to 17 including African American, Hispanic, and Asian American/Pacific Islander youth.



The campaign targets youth who identify with the Hip Hop peer crowd – an innovative and promising segmentation approach that focuses on youth who share the same core ideals, have similar life experiences and common interests, and may be at higher risk for tobacco use. FDA expanded the “Fresh Empire” campaign to markets throughout the U.S. in October 2015 and plans to launch new advertising in market in 2017.

On May 3, 2016, FDA launched a public education campaign aimed at preventing and reducing tobacco use among lesbian, gay, bisexual, and transgender (LGBT) young adults aged 18 to 24. LGBT young adults are nearly twice as likely to use tobacco as other young adults, ultimately resulting in the loss of tens of thousands of LGBT lives to tobacco use each year. Of the more



than 2 million young adults who identify as LGBT, more than 800,000 smoke occasionally and are at risk of progressing to regular tobacco use. The “This Free Life” campaign is designed to reach the occasional or “social” smokers to help prevent tobacco-related death and disease in the LGBT community.

The campaign won a significant multicultural award of excellence at the 18th Annual Association of National Advertisers (ANA) Multicultural Marketing & Diversity Conference in October 2016. The awards seek to raise awareness of the outstanding work in African-American, Asian, Audio, B-to-B, Digital, Experiential, Hispanic, LGBT, People with Disabilities, Print, and Total Market advertising. “This Free Life” won an ANA Multicultural Excellence Award in the LGBT category.

Enhance Oversight

FDA is committed to regulating the manufacture, marketing, and distribution of tobacco products to protect public health and to reduce tobacco use, especially among youth. FDA’s implementation of the Tobacco Program is carried out with the use of regulations and guidance that explain FDA’s expectations to the regulated industry and the public.

FDA has established a framework for industry registration, product listing, and submission of information concerning ingredients and harmful and potentially harmful constituents (HPHCs) in tobacco products and tobacco smoke. Furthermore, FDA ensures industry compliance by enforcing warning label and advertising requirements, and by restricting access and marketing of cigarettes and smokeless tobacco products to youth through the use of compliance inspections, warning letters, civil money penalties, and no-tobacco-sale-orders.

Maintaining a Strong Science Base for Oversight Actions

FDA invests in priority tobacco regulatory research areas to address gaps and add to the evidence base in order to inform FDA’s tobacco regulatory activities and help assess the impact of regulatory actions. In FY 2016, FDA invested more than \$193 million in scientific research. Through research, FDA better understands patterns of tobacco use, the harms caused by tobacco use, and where regulatory intervention consistent with FDA’s statutory authority is most needed.

FDA research supports regulatory and public education efforts to improve public health. In addition to conducting independent research to support regulatory science, the Center for Tobacco Products partners with FDA’s National Center for Toxicological Research (NCTR), Center for Devices and Radiological Health (CDRH), and Southeast Regional Lab, as well as other governmental agencies, including the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC). By leveraging the resources of other Federal agencies,

FDA brings science-based regulation to the manufacturing, marketing, and distribution of tobacco products.

NIH Partnerships

FDA avoids duplication of resources and enhances scientific research capability by collaborating with NIH and tapping into its well-established infrastructure. In FY 2016, FDA funded 106 research projects via NIH. These research projects include grants, intramural projects, and contracts which will address important FDA research priorities. Below are some of CTP's areas of research.

FDA funds NIH's Tobacco Regulatory Science Program (TRSP) and works with TRSP to stimulate tobacco regulatory research and fund projects to study:

- the impact of marketing and communications on tobacco use behavior
- perceptions, knowledge, attitudes, and beliefs regarding tobacco products
- toxicity, carcinogenicity, and health risks of tobacco products
- varying nicotine levels and other constituents' effects on initiation, dependence, and quitting.

FDA also funds research via NIH that includes studying the impact of flavor and sweetness of different tobacco products on use behaviors such as experimentation and initiation among youth and young adults.

In FY 2016, FDA funded new grants to research toxicity and addictiveness of waterpipes, abuse liability of reduced nicotine content cigarettes, and tobacco regulatory science projects for new investigators.

FDA continues to fund the Center for Evaluation and Coordination of Training and Research (CECTR) in Tobacco Regulatory Science via NIH to support evaluation of the CTP-funded research projects and facilitate coordination and communications of research and scientific training among those projects.

FDA collaborates with NIH to fund the 14 Tobacco Centers of Regulatory Science (TCORS). The objective of the Centers is to conduct multidisciplinary research that will inform FDA's regulatory actions related to the manufacture, distribution, and marketing of tobacco products.

FDA funds the Population Assessment of Tobacco and Health (PATH) Study via NIH's National Institute on Drug Abuse (NIDA) and works collaboratively with them on the scientific aspects of the study. The PATH Study is a longitudinal cohort study launched in 2013 with a nationally representative sample of U.S. civilian, non-institutionalized persons ages 12 and older. The

study follows approximately 46,000 never, current, and former users of tobacco products. It is intended to yield data to inform CTP's regulatory activities including:

- comprehensive data on tobacco product use, attitudes, associated health outcomes
- biomarkers of tobacco exposure and related disease.



Data collection for Wave 2 of the PATH Study was completed October 2015, and Wave 3 began October 2015 and was completed October 2016. Wave 4 launched in December 2016. Starting in FY 2017, FDA will collect data on the full cohort every two years instead of every year to allow for sub-studies in the off years to address high priority areas.

CDC Partnerships

FDA is partnering with the Division of Laboratory Sciences at CDC on research projects which use laboratory-based approaches to expand knowledge to inform regulation of tobacco products. These research projects include:

- analyses of tobacco products and mainstream smoke
- method development for biomarkers
- exposure assessments under actual use conditions
- further method development for HPHCs.

CDC is also providing the analyses of tobacco exposure biomarkers from research data collected in the PATH Study. In order to provide critical data on youth use and perceptions of tobacco products, FDA collaborates with the Office of Smoking and Health, CDC to conduct the National Youth Tobacco Survey (NYTS) on an annual basis.

FDA funding has expanded the scope and increased the frequency of data collection for the NYTS. The NYTS is a large annual survey of a nationally representative sample of middle and high school students that focuses exclusively on tobacco. Data from this survey will allow FDA to monitor awareness of, susceptibility to, and experimentation with and use of, a wide range of tobacco products.

FDA National Center for Toxicological Research (NCTR) Partnership

NCTR will continue research on:

- the toxicology of compounds and cigarette smoke
- biomarker discovery

- the toxic and addictive potential of tobacco products via cell culture and animal models
- developmental bioinformatics projects.

FDA Center for Devices and Radiological Health (CDRH) Partnership

In FY 2016, CDRH began research on effects of atomizer temperature on electronic cigarette aerosol.

Other Research Collaborations

FDA conducts research via research contract organizations, and includes research studies focused on studying chemistry and engineering, addiction, toxicity and carcinogenicity, health consequences, behavior, communications, and marketing. For example, there are studies that help inform the development of surveys and questionnaires, evaluate the impact of various tobacco product constituents on exposure, physiological responses, use behavior, and the assessment of user and non-user beliefs about emerging tobacco products.

In FY 2016, CTP contracted with the Institute of Medicine – now called the National Academy of Medicine – to conduct an evaluation of health effects from e-cigarettes and identify gap areas for future federally funded research in this area.

Enforcement of the Tobacco Control Act

FDA has a comprehensive compliance and enforcement program to monitor industry compliance with regulatory requirements, and to restrict access and marketing of tobacco products to youth.

Tobacco Retailer Inspections

As of March 31, 2017, FDA had contracts for tobacco retailer compliance check inspections in 55 states, territories, and Tribal jurisdictions. Compliance check inspections pertain to tobacco marketing, sales, and distribution of tobacco products at retail locations and include ensuring compliance with age and ID verification requirements.

In August 2016, FDA began including newly deemed products in the scope of its retail inspections. As of March 31, 2017, FDA had issued more than 4,600 warning letters to tobacco retailers for selling newly-regulated tobacco products such as e-cigarettes, e-liquids, and cigars to minors in retail stores and online.⁸⁹

Since the Tobacco Retailer Inspection Program's inception in October 2010 through March 31, 2017, FDA has commissioned more than 2,500 officers and employees from the states,

⁸⁹ These warning letters are included in the total number of warning letters reported in the "CTP Tobacco Retailer Inspection Program" table.

territories, and their political subdivisions, and provides a training program for those that perform inspections. FDA currently utilizes more than 700 commissioned inspectors.

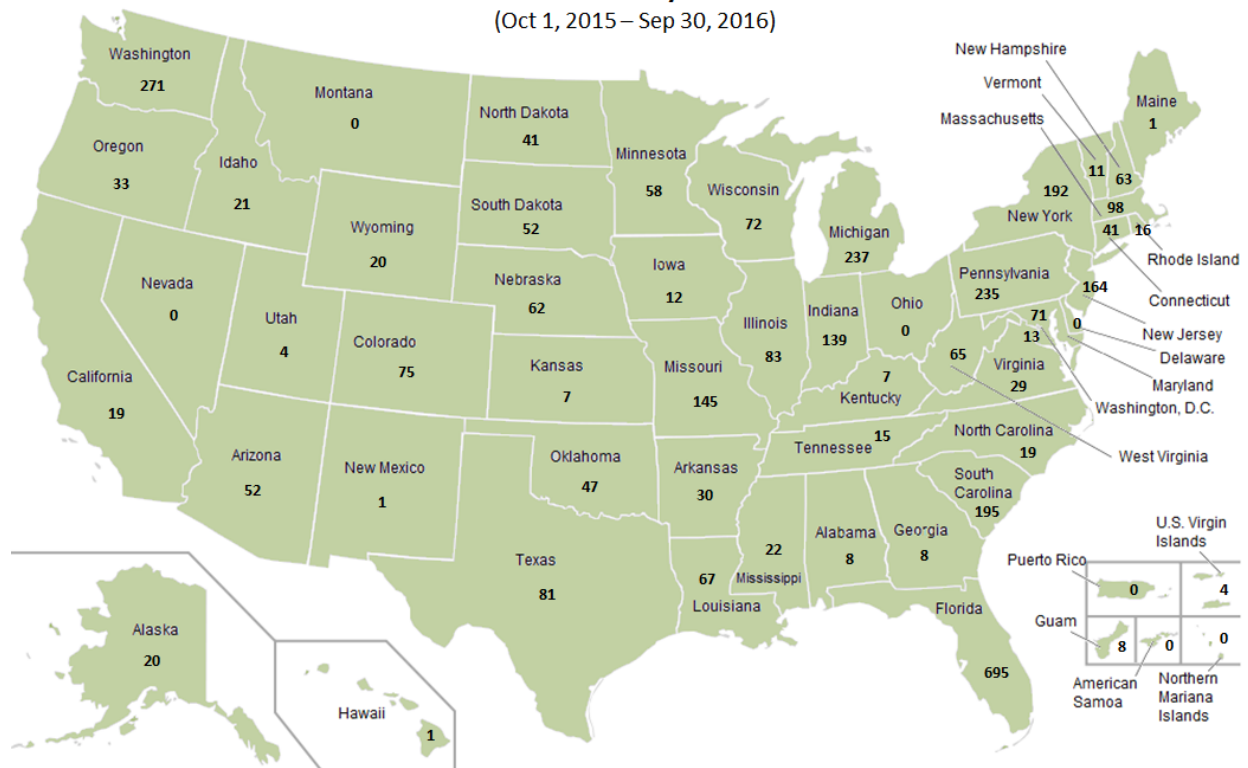
Although most tobacco retailers comply with FDA's tobacco laws and regulations, FDA conducts compliance check inspections and issues advisory and enforcement actions such as Warning Letters, Civil Money Penalties, and No-Tobacco-Sale-Order, when violations are found. The following table lists the different enforcement actions that have resulted from these inspections.

CTP Tobacco Retailer Inspection Program

Enforcement Action	FY 2015 Actuals	FY 2016 Actuals	Total Since the Program's Inception on 10/1/2010 (as of 3/31/2017)
Retailer Inspections	162,865	165,098	758,871
Warning Letters	16,521	13,921	56,901
Civil Money Penalties	3,290	3,630	11,877
No-Tobacco-Sale-Orders ⁹⁰	0	31	47

⁹⁰ Under the law, the FDA may pursue an NTSO against retailers that have a total of five or more repeated violations of those restrictions during compliance inspections within 36 months.

FY16 Civil Money Penalties
(Oct 1, 2015 – Sep 30, 2016)



Although most retailers comply after receiving a warning letter, FDA issued 3,630 civil money penalties in FY 2016 (Oct 1, 2015 – Sep 30, 2016).

Tobacco Manufacturer Inspections

FDA regularly inspects registered establishments that manufacture or process tobacco products to determine compliance with existing laws and regulations. FDA conducted approximately 55 tobacco manufacturing inspections in FY 2016. Tobacco Manufacturers of newly deemed tobacco products are required to register in FY 2017 and FDA expects the number of registered establishments will significantly increase.

Promotion, Advertising, and Labeling Activities

FDA conducts surveillance of websites, social media, and magazines and other publications that promote and sell regulated tobacco products in the U.S. market. In FY 2016, FDA began surveillance of websites that sell newly deemed tobacco products, including regulated electronic nicotine delivery systems (ENDS) products and took enforcement actions when violations were found. Since the program's inception in October 2010 through March 31, 2017, FDA has issued over 500 warning letters as a result of these surveillance activities. In 2016, 110 warning letters were issued.

FDA also conducts investigations of events where free samples of tobacco are distributed and events sponsored by the tobacco industry to ensure compliance with the Tobacco Control Act.

Improve and Safeguard Access to FDA-Regulated Products to Benefit Health

FDA's authority to regulate tobacco products includes premarket review of new tobacco products to determine if their marketing is appropriate for the protection of the public health, or if they are substantially equivalent to existing products. Tobacco products are inherently dangerous. FDA's responsibility is to review new tobacco products in accordance with FDA's authorities.

New products and product changes are reviewed following three marketing pathways:

- premarket tobacco product application (PMTA)
- reports demonstrating substantial equivalence (SE) to commercially marketed products
- exemption from demonstrating substantial equivalence.

On November 10, 2015, FDA announced that for the first time it has authorized the marketing of new tobacco products through the premarket tobacco product application (PMTA) pathway. As of November 30, 2016, FDA has issued marketing orders for eight PMTA applications and refused to file four PMTAs for statutorily regulated products.

In addition, two other PMTAs for statutorily regulated products have been submitted and are being reviewed to determine whether they meet the requirements for filing. FDA has also

refused to accept 362 of the 364 PMTAs received for newly deemed products because they did not meet statutory requirements.

Currently, CTP reviews for acceptance determine if the application falls under our jurisdiction and addresses environmental considerations, both required by statute. If these two factors are not met, CTP must issue a Refuse to Accept (RTA) letter.

The RTA decision closes all activity for the application. However, an applicant may always resubmit a new application with the missing items. By providing timely responses to applications that cannot be accepted, FDA provides manufacturers with more time to resubmit with the information that is required. FDA uses a scientific review to determine if new tobacco products should come to market under this pathway.

Furthermore, before making marketing claims that imply modified risk, manufacturers must submit a Modified Risk Tobacco Product (MRTP) application, and receive an FDA order authorizing a claim that the product reduces harm or the risk of tobacco-related disease.

FDA continued substantive reviews on ten MRTP applications received in June 2014. These MRTP applications were made available to the public and a docket was opened for public comment. A meeting of FDA's Tobacco Product Scientific Advisory Committee was held on April 9-10, 2015, to review these applications and provide recommendations to FDA. The docket was reopened in July 2015, to solicit comments on amendments that were submitted. There are complex scientific and legal questions related to issuing letters since these are the first MRTP applications to reach this stage in review. On December 14, 2016, following science-based review, FDA took action on the first applications reviewed through the MRTP pathway, denying one claim and deferring final action for the remaining claims.

CTP's OSBA informs small businesses of existing guidances, regulations, and submission pathways through publications and online webinars. In FY 2016, OSBA published 15 tobacco compliance webinars on its website, with topics ranging from imported product regulations to health warning statement requirements. OSBA also answers questions from regulated industry, including small tobacco product manufacturers and retailers, consumers of regulated tobacco products, and the general public. OSBA responds to thousands of calls, emails, and correspondence every year to assist in answering specific questions about requirements of small businesses and how to comply with the law.

Promote Informed Decisions

Public Education Campaigns

FDA is using sustained, comprehensive public education campaigns to work in concert with regulatory action to reduce use of tobacco products and improve public health. As authorized by the Tobacco Control Act, these activities involve planning, developing, producing, and delivering national multimedia public education campaigns.

Multimedia campaigns enable FDA to educate the public about the harms and risks of regulated tobacco products. Specifically, the campaigns will equip the public with important facts about:

- health risks of regulated tobacco products
- addictiveness of regulated tobacco products
- harmful and potentially harmful constituents in regulated tobacco products.

A critical factor in reducing youth tobacco use is to produce and maintain effective levels of campaign awareness within the target population. Studies have specifically confirmed the effectiveness of media campaigns in reducing youth tobacco use. The NIH National Cancer Institute and Community Preventive Services Task Force has conducted comprehensive scientific reviews of studies on the effectiveness of media campaigns to reduce tobacco use. The reviews concluded that media campaigns to prevent and control tobacco use are effective.

FDA is implementing multi-year outcome evaluation studies of its public education campaigns. The study designs are longitudinal, meaning the studies will attempt to follow the same individuals over time to track changes in targeted tobacco-related knowledge, attitudes, beliefs, intentions, and behaviors. In FY 2015, published outcome evaluation findings for “The Real Cost” showed that over 90 percent of the target audience is aware of the campaign and its messaging - a key precursor to behavior change.⁹¹

Additional findings published in FY 2017 show that increasing levels of campaign exposure are associated with positive changes in campaign-related beliefs – for example, if I smoke I will get wrinkles – and that “The Real Cost” advertising exceeded its ultimate goal of reducing the number of youth aged 12 to 17 who smoke by preventing over 345,000 U.S. youth from smoking from 2014 to 2016.

FDA is also conducting separate outcome evaluations of “The Real Cost” smokeless campaign messaging, the “Fresh Empire” campaign, and the “This Free Life” campaign to measure whether exposure to campaign messaging creates positive changes in knowledge, attitudes, beliefs, and intentions among the target audiences.

Strengthen Organizational Excellence

⁹¹ <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0144827>

FDA provides the infrastructure necessary to support the Agency's responsibilities and authorities of the Tobacco Control Act. Examples include:

- strategic IT systems which support industry applications
- compliance inspections
- scientific data analysis
- collection of tobacco user fees.

In addition, FDA is hiring additional staff to:

- conduct reviews of product applications, including SE, PMTA, and MRTTP
- expand research capabilities
- support inspection efforts
- enforce the deeming regulation
- draft regulations and guidances.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User
FY 2014 Actual	\$570,536,000	\$0	\$570,536,000
FY 2015 Actual	\$554,469,000	\$0	\$554,469,000
FY 2016 Actuals	\$476,525,000	\$0	\$476,525,000
FY 2017 Annualized CR	\$563,045,000	\$0	\$563,045,000
FY 2018 President's Budget	\$625,646,000	\$0	\$625,646,000

BUDGET REQUEST

The FY 2018 Budget Request is \$625,646,000, all from user fees. This amount is the FY 2018 level authorized in the Tobacco Control Act less the amounts for GSA Rent and FDA Headquarters, which are shown in their own sections of the budget request. This amount is an increase of \$29,308,000 above the FY 2017 President's Budget.

The Center for Tobacco Products amount in this request is \$611,096,000.

In FY 2018, CTP plans to continue its efforts on six current strategic priorities:

- Product Standards
- FDA-wide Comprehensive Nicotine Regulatory Policy
- Premarket and Postmarket Controls: Regulations and Product Reviews
- Compliance and Enforcement
- Public Education

- Investing in Human Capital.

Specifics on CTP's FY 2018 strategic priorities and its many other efforts are provided below.

Strategic Priorities

Product Standards

Section 907 of the Federal Food, Drug, and Cosmetic Act gives FDA the authority to issue, via notice-and-comment rulemaking, tobacco product standards that are appropriate for the protection of the public health. This authority is one of the most powerful tools that FDA has to regulate tobacco. CTP is advancing a product standard strategy to yield strong standards to improve public health, by exploring potential standards for addictiveness, toxicity, and appeal.

FDA-wide Comprehensive Nicotine Regulatory Policy

FDA regulates a broad range of nicotine-delivering products, from cigarettes to medicinal nicotine gum and patch. FDA is exploring an integrated, agency-wide policy on nicotine-containing products that is public health based and recognizes the reality that people use tobacco for the nicotine but die from the toxins in the tobacco and in tobacco smoke. Beyond finalizing the "deeming rule," related activities include:

- developing jurisdiction policy on nicotine-containing products across FDA
- working with CDER and CDRH to determine how regulation of therapeutic nicotine products – Rx, OTC, drugs, devices – should evolve
- considering regulatory guidance on premarket review policy based on the principle of relative toxicity and risk.

Premarket and Postmarket Controls: Regulations and Product Reviews

FDA's reviews act as a gatekeeper between tobacco products and consumers. FDA ensures that new products cannot be commercially sold without review by requiring manufacturers to seek FDA authorization before:

- marketing new tobacco products
- marketing new tobacco products demonstrating substantial equivalence⁹² to certain commercially marketed products
- modifying existing tobacco products.

⁹² An alternative to new product applications where the characteristics are the same as predicate products (which is a product that was commercially marketed in the United States as of February 15, 2007, or a product previously found to be substantially equivalent) or the characteristics are different, but the product does not raise different questions of public health.

To help industry better understand expectations and aid them in preparing complete applications, CTP is exploring developing additional rules and guidances for product review pathways, tobacco product manufacturing practices, and registration and product listing. This will improve transparency and provide consistent submission guidelines which will speed application review by FDA staff. In addition to developing rules and guidances, CTP will continue to establish performance measures for product reviews.

Compliance and Enforcement

FDA focuses on the utilization of a national program of inspections, investigations, monitoring, and review of covered tobacco products, sales, manufacturing, and advertising. FDA's compliance programs focus on appropriate enforcement actions that are supported by evidence of violations of the law.

Public Education

FDA maximizes its impact on public health by focusing public education efforts on at-risk audiences such as general market youth who are already experimenting with cigarettes or open to it, multicultural including African American, Hispanic, Asian/Pacific Islander, and American Indian/Alaska Native youth, rural youth, and lesbian, gay, bisexual, and transgender (LGBT) young adults.

Investing in Human Capital

FDA invests in its workforce by continually assessing workloads and identifying strategies to help manage work/life balance, strengthening retention and anticipating future staffing needs, and engaging employees via the annual Employee Viewpoint Survey. FDA also promotes employee diversity and inclusion to cultivate an engaged workforce that reflects the country it serves.

Additional FY 2018 Support Activities

FDA will continue to:

- partner with other agencies, including NIH, CDC, and FDA's National Center for Toxicological Research to expand the tobacco regulatory science base
- provide priority research support to CDC and NCTR
- fund new TCORS and other research grants via NIH
- fund research projects via NIH to address FDA time-sensitive research.

In FY 2018, FDA will continue to fund PATH Study analyses and sub-studies via NIH. These sub-studies will enable FDA to gain more in depth insight into a rapidly evolving tobacco market and

provide the PATH Study with a way to more comprehensively examine new and emerging issues related to tobacco use behavior and health.

Enforcement of the Tobacco Control Act and implementation of regulations are a priority for FY 2018. Continued planned activities include:

- conducting compliance check inspections via the Tobacco Retailer Inspection Program⁹³
- coordinating with ORA to conduct inspections of tobacco manufacturing facilities
- providing outreach, education, and assistance to small tobacco manufacturers and retailers via CTP's Office of Small Business Assistance
- enforcing promotional, advertising, and labeling requirements
- conducting surveillance, investigations, and sample collections
- identifying criminal violations in tobacco-related cases.

In addition to research and enforcement, FDA is committed to communicating to the public the risks associated with the use of tobacco products, which result in more than 480,000 deaths each year. In FY 2018, FDA will further develop and continue public health education efforts to reach at-risk populations, particularly youth, with messages about the dangers of tobacco use.

FDA will:

- continue outcome evaluation for "The Real Cost" smokeless campaign, the "Fresh Empire" campaign, and the "This Free Life" campaign
- continue its tobacco education campaigns targeting discrete at-risk and underserved audiences
- continue to develop interactive digital communication technologies and products such as CTP's content sharing platform, the Exchange Lab.

⁹³ The results of the Tobacco Retailer Inspection Program can be found on FDA's website at http://www.accessdata.fda.gov/scripts/oc/inspections/oc_insp_searching.cfm

PERFORMANCE

The Tobacco Control Act Program's performance measures focus on activities in order to achieve public health goals, as detailed in the following table.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
<u>280005</u> : Total number of compliance check inspections of retail establishments in States under contract. <i>(Outcome)</i>	FY 2016: 165,098 Target: 110,000 (Target Exceeded)	125,000	140,000	+15,000
280006: Review and act on original Regular SE Reports within 90 days of FDA receipt (applies to cigarettes, cigarette tobacco, smokeless tobacco, and roll-your-own tobacco products). <i>(Output)</i>	FY 2016: 63% Target: 60% (Target Exceeded)	70%	80%	+10%
<u>280007</u> : Educate at-risk general market 12-17 year olds about the harmful effects of tobacco use. <i>(Output)</i>	FY 2016: Reached 86% of general market at risk 12-17 year olds with campaign messaging. (Target Exceeded)	Reach 75% of 12-17 year olds with campaign messaging within 1 year.	Reach 75% of 12-17 year olds with campaign messaging within 1 year.	Maintain

Compliance Check Inspections

Highlighted from the above table, a key element in enforcing the Tobacco Control Act involves contracts with U.S. state, territory, and tribal agencies, as well as private entities, to conduct retailer compliance checks. Under these contracts, FDA conducted more than 165,000 compliance check inspections of retail establishments in FY 2016. Although this number was much higher than the expected FY 2016 full year target of 110,000, it reflects the high level of variability inherent in this goal that requires estimating the number of compliance checks that each jurisdiction will be able to conduct.

FDA is on target to meet or exceed the FY 2017 full year goal of 125,000 compliance checks. It is important to note however, that some contracts are expiring and will need to be renewed in FY 2017 in order for these efforts to continue. Although most states, territories, tribes, and private entities are expected to renew their contracts, there are always outside factors that may prohibit them from doing so. The FY 2017 and 2018 targets consider these challenges, but have still been increased.

PROGRAM ACTIVITY DATA TABLE

CTP Workload and Outputs	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget
Tobacco Retailer Inspections			
Number of Inspections	165,098	125,000	140,000
Tobacco Manufacture Inspections			
Number of Inspections ¹	52	52	200
Substantial Equivalence Reviews			
Number of Regular Full SE Reports ²	122	100	100

¹ Outyear estimates are based on the number of firms registered with FDA. FDA inspects each registered firm biennially.

² Limited to Regular Full SE Reports received for currently regulated products.

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FDA HEADQUARTERS

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
FDA Headquarters.....	299,524	301,574	293,259	322,486	29,227
Budget Authority.....	191,549	191,374	191,201	125,432	-65,769
User Fees.....	107,975	110,200	102,058	197,054	94,996
<i>Prescription Drug (PDUFA).....</i>	<i>52,139</i>	<i>54,405</i>	<i>46,202</i>	<i>82,622</i>	<i>36,420</i>
<i>Medical Device (MDUFA).....</i>	<i>6,259</i>	<i>8,293</i>	<i>5,732</i>	<i>29,260</i>	<i>23,528</i>
<i>Generic Drug (GDUFA).....</i>	<i>24,690</i>	<i>26,680</i>	<i>25,050</i>	<i>47,270</i>	<i>22,220</i>
<i>Biosimilars (BsUFA).....</i>	<i>1,354</i>	<i>190</i>	<i>1,388</i>	<i>4,602</i>	<i>3,214</i>
<i>Animal Drug (ADUFA).....</i>	<i>913</i>	<i>813</i>	<i>947</i>	<i>5,475</i>	<i>4,528</i>
<i>Animal Generic Drug (AGDUFA).....</i>	<i>388</i>	<i>209</i>	<i>453</i>	<i>1,452</i>	<i>999</i>
<i>Family Smoking Prevention and Tobacco Control Act</i>	<i>20,789</i>	<i>19,119</i>	<i>20,749</i>	<i>24,815</i>	<i>4,066</i>
<i>Mammography Quality Standards Act (MQSA).....</i>	<i>248</i>	<i>491</i>	<i>253</i>	<i>253</i>	<i>---</i>
<i>Food and Feed Recall.....</i>	<i>75</i>	<i>---</i>	<i>75</i>	<i>75</i>	<i>---</i>
<i>Food Reinspection.....</i>	<i>480</i>	<i>---</i>	<i>480</i>	<i>480</i>	<i>---</i>
<i>Voluntary Qualified Importer Program.....</i>	<i>277</i>	<i>---</i>	<i>277</i>	<i>277</i>	<i>---</i>
<i>Third Party Auditor Program.....</i>	<i>73</i>	<i>---</i>	<i>73</i>	<i>73</i>	<i>---</i>
<i>Outsourcing Facility.....</i>	<i>290</i>	<i>---</i>	<i>379</i>	<i>400</i>	<i>21</i>
FTE.....	1,209	1,209	1,273	1,332	59

*FY 2016 and FY 2017 do not reflect the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2018, FDA proposes to discontinue the transfer.

Authorizing Legislation: The Federal Food Drug and Cosmetic Act (21 U.S.C. 321-399); Radiation Control for Health and Safety Act (21 U.S.C. 360hh-360ss); The Federal Import Milk Act (21 U.S.C. 142-149); Public Health Service Act (42 U.S.C. 201, et seq.); Foods Additives Amendments of 1958; Color Additives Amendments of 1960; Animal Drug Amendments (21 U.S.C. 360b); Controlled Substances Act (21 U.S.C. 801-830); The Fair Packaging and Labeling Act (15 U.S.C. 1451-1461); Safe Drinking Water Act (21 U.S.C. 349); Saccharin Study and Labeling Act; Federal Anti-Tampering Act (18 U.S.C. 1365); Medical Device Amendments of 1976; Infant Formula Act of 1980; Drug Enforcement, Education, and Control Act of 1986; Generic Animal Drug and Patent Term Restoration Act; Prescription Drug Marketing Act of 1987; Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 201); Prescription Drug Amendments of 1992; Safe Medical Device Amendments of 1992; Nutrition Labeling and Education Act of 1990; Dietary Supplement Health and Education Act of 1994; Animal Medicinal Drug Use Clarification Act of 1994; Animal Drug Availability Act of 1996; Food Quality Protection Act of 1996; Federal Tea Tasters Repeal Act (42 U.S.C. 41); Safe Drinking Water Act Amendments of 1996 (21 U.S.C. 349); Food and Drug Administration Modernization Act of 1997; Antimicrobial Regulation Technical Corrections Act of 1998; Medical Device User Fee and Modernization Act of 2002; Public Health Security and Bioterrorism Preparedness and Response Act of 2002; Best Pharmaceuticals for Children Act of 2002 (21 USC 355a Sec. 505A); Animal Drug User Fee Act of 2003 (21 U.S.C. 379j-11 - 379j-12); Pediatric Research Equity Act of 2003 (21 USC 351 Sec. 505B); Project Bioshield Act of 2004 (21 U.S.C.360bbb-3); Minor Use and Minor Species Animal Health Act of 2004; Food Allergy Labeling and Consumer Protection Act of 2004 Medical Device User Fee Stabilization Act of 2005; Sanitary Food Transportation Act of 2005 Dietary Supplement and Nonprescription Drug and Consumer Protection Act (21 U.S.C. 379aa-1); Pandemic and All-Hazards Preparedness Act, Food and Drug Administration Amendments Act of 2007; Protecting Patients and Affordable Care Act of 2010; The Family Smoking

Prevention and Tobacco Control Act of 2009 (P.L. 111-31); The Federal Cigarette Labeling and Advertising Act (15 U.S.C. 1333); FDA Food Safety Modernization Act, Public Law 111-353 (January 4, 2011); The Food and Drug Administration Safety and Innovation Act (P.L. 112-144); Pandemic and All-Hazards Preparedness Reauthorization Act of 2013, the Drug Quality and Security Act (2013), and the 21st Century Cures Act (P.L. 114-255).

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

FDA Headquarters (HQ) provides strategic direction and a wide array of services, including cross-agency special medical, scientific, and regulatory programs, legal advice and counsel, and litigation services across FDA's programs. The following narrative describes FDA HQ activities within the FDA Strategic Goal framework.

Enhance Oversight

FDA HQ provides strategic leadership and coordination to enhance FDA's oversight of production, manufacturing, the global supply chain, and post market product use. FDA HQ provides policy direction and expertise to establish standards and guidance to protect patient and consumer safety. FDA HQ develops and standardizes policies and best practices across FDA consistent with statutes and regulations.

FDA's Oversight includes:

- inspecting manufacturing and production facilities
- providing surveillance of adverse events
- preventing unsafe products from harming consumers.

Within the area of Oversight, FDA provides Smart Regulation, Safety and Quality, Regulatory Science and Globalization. The following, selected accomplishments demonstrate FDA HQ's delivery of its regulatory and public health responsibilities within the context of current priorities.⁹⁴

Food Safety Modernization Act (FSMA) Rules Published

The FDA Food Safety Modernization Act was signed into law in 2011, creating a blueprint for sweeping changes to the nation's food protection system.

⁹⁴ Please visit <http://www.fda.gov/> for additional program information and detailed news items.

The seven foundational FSMA food safety rules support and strengthen the nation's food safety system by establishing requirements for farmers, food companies and importers to prevent foodborne illness.

2016 FSMA Rules

In 2016 FDA issued the sixth and seventh final rules known as the Sanitary Transportation and Intentional Adulteration rules. The Sanitary Transportation final rule (published in April 2016) creates a modern risk-based framework for food safety by preventing practices during transportation that create food safety risks, such as:

- failure to properly refrigerate food
- inadequate cleaning of vehicles between loads
- failure to properly protect food.

This rule also establishes requirements for shippers, loaders, carriers by motor or rail vehicle, and receivers involved in transporting human and animal food to use sanitary practices to ensure the safety of that food.

The Mitigation Strategies to Protect Food Against Intentional Adulteration rule, (published in May 2016) directs domestic and foreign food facilities (required to register under the Federal Food, Drug, and Cosmetic Act) to address hazards that may be intentionally introduced by terrorist acts. These food facilities must develop strategies to minimize or prevent vulnerabilities identified at actionable steps in a food operation.

As part of FSMA implementation, FDA published final guidance in November 2016 to establish a voluntary, fee-based program to expedite review and import of foods into the United States from importers with a proven food safety track record. This program, the Voluntary Qualified Importer Program (VQIP), will benefit both importers and consumers. VQIP allows FDA to focus its resources on the potentially dangerous food imports that are most likely to harm the public.

Emergency Preparedness and Response

FDA HQ coordinates Agency emergency response to adverse events with FDA-regulated products, foodborne illnesses, product tampering issues, man-made and natural disasters, and emergencies affecting FDA staff, systems, and facilities. The Office of Crisis Management (OCM) will continue to enhance agency preparedness and response capabilities through intra- and inter-agency exercises, plan development and execution, standard operating procedures, and enhanced incident management systems in order to improve the overall operation and effectiveness of FDA's emergency response.

FDA HQ provides nationwide, 24-hour, seven-day-a-week emergency response system, including Late Duty Officers coverage after-hours, weekends, and holidays through the Office of Emergency Operations (OEO). OCM also provide surveillance and signal monitoring, including FDA's Emergency Operations Network Incident Management System, and Consumer Complaint reporting and monitoring functions

In FY 2016, FDA HQ coordinated the emergency response to 64 significant incidents including:

- 18 serious adverse or injury event incidents
- 30 natural disasters
- 11 man-made disasters
- 5 National Special Security Events.

FDA HQ evaluated 4,149 consumer complaints including 61 reports of suspected product tampering in FY 2016 to ensure FDA's timely identification of and response to emergency safety concerns related to FDA-regulated products. FDA HQ worked diligently to develop, maintain, and coordinate an effective emergency response capability for public health emergencies by developing guidance detailing FDA's operational approach for responding to emergencies.

In FY 2016 FDA HQ coordinated eleven Agency responses to World Health Organization (WHO) International Food Safety Authorities Network (INFOSAN) inquiries involving food products (strawberries, pistachios, oysters, milled flour, scallops, etc.). FDA HQ also addressed eleven draft notices of Public Health Emergency of International Concern (PHEIC) in FY 2016, including multiple Zika notices, chikungunya, novel influenza variants, salmonella associated with an FDA regulated commodity, etc.

In FY 2016, FDA HQ conducted, evaluated and reported Table Top and Full Scale Exercises that included a medically downed patient in a High Containment Laboratory with Federal, State and Local resource participation. The resulting after action report emphasized the need for additional training in basic patient assessment and patient transport to a "clean area" for further triage. In addition, FDA HQ created and presented 7 training opportunities for over 70 laboratory researchers.

In addition, FDA HQ supported HHS/ASPR/OEM with the following Incident Annex updates; Food, Agriculture Incident Annex, including Plant, Animal and Food Agriculture Input, the Federal Evacuation Annex, and the Chemical Incident Annex development, review and publication.

FDA HQ also provided training for key emergency response staff on how to better respond to complex incidents and make informed decisions during an event. FDA HQ supports ready

access to classified information transmitted through secure government networks to ensure complete risk assessments during actual events.

The FDA Coordinated Outbreak Response and Evaluation (CORE) team rapidly detects and responds to major foodborne illness outbreaks in coordination with local, state, and federal agencies and laboratories. For example, in the fall of 2016, FDA, CDC, and state and local officials investigated a multi-state outbreak of hepatitis A. FDA's investigation linked the outbreak to frozen strawberries imported from Egypt. FDA then facilitated the recall of the International Company for Agricultural Production and Processing (ICAPP) frozen strawberry products.

Geographic Information System Mapping

In FY 2016, FDA HQ expanded the use of the Geographic Information System (GIS) to build risk-based models to assess the impact of global events to the U.S. supply chain. FDA HQ completed maps for more than 85 project requests involving FDA regulated firms.

Global Health Security and Counterterrorism

FDA HQ provides leadership, coordination, and oversight for FDA's work to support national and global health security, prevent counterterrorism, and address emerging threats. The portfolios include serving as point of entry on policy and planning matters; serving as a focal point for the HHS [Public Health Emergency Medical Countermeasures Enterprise](#) (PHEMCE) and the Department of Defense (DoD) medical countermeasure (MCM) programs to support the warfighter; and coordinating the [Medical Countermeasures Initiative](#) (MCMi) to facilitate the development of safe and effective MCMs against chemical, biological, radiological, and nuclear (CBRN) agents and emerging threats, such as pandemic influenza, Ebola virus, and Zika virus.

As part of the MCMi, FDA HQ funds research to improve FDA's ability to perform science-based review of MCMs designed to lessen the effects of CBRN and emerging infectious disease threats.

Notable accomplishments in FY 2016 and FY 2017:

- developing a lung model based on 'organs-on-a-chip' technology to use to develop drugs for acute radiation syndrome
- [mapping immune responses](#) to biothreats and MCMs in humans and developing animal models to support MCM development
- studying disease progression and effects of Zika Virus in non-human primate animal models as part of an FDA-established interagency collaboration.

FDA scientists continued activities to support the development of MCMs for Ebola, including:

- development of improved small animal models
- identification of potential markers of Ebola virus disease progression
- development and validation of analytical procedures for evaluating Ebola to use outside of specialized, high-containment laboratories.
- FDA regulatory science initiatives to respond to the Zika virus outbreak included:
 - understanding the effectiveness of technologies that reduce pathogens in blood
 - evaluating the impact of red blood cell storage on Zika virus infection
 - expanding the database of Zika virus-infected samples essential to the development of diagnostic devices
- developing mouse model to study the long-term effects of Zika virus infection and to support MCM development.

FDA HQ develops and coordinates the implementation policies and procedures to facilitate the availability of MCMs, including safeguarding MCMs from adulteration or disruption of supplies during public health emergencies and enabling access to MCMs through an appropriate mechanism such as [Emergency Use Authorization \(EUA\)](#).

Accomplishments in 2016 that support MCMs include:

- establishment of an [international confidentiality commitment](#) with the Saudi Food and Drug Authority to facilitate communications on medical products used for Middle East respiratory syndrome coronavirus (MERS-CoV)
- issuance of guidance that explains FDA's general recommendations and procedures applicable to the authorization of the emergency use of certain medical products
- establishment a Memorandum of Understanding with CDC for developing and issuing Emergency Use Instructions ([EUI](#)) for MCMs
- issuance of [emergency dispensing orders](#) for doxycycline and ciprofloxacin for anthrax preparedness
- finalization of revised draft guidance [Product Development Under the Animal Rule](#).

FDA HQ facilitated international coordination of response activities to emerging public health threats including the Ebola outbreak in West Africa and the [Zika virus](#) outbreak in the Americas.

FDA HQ facilitated the expedited development and availability of MCMs – including vaccines, drugs, protective equipment, and diagnostic tests – and authorized the use of 11 Ebola diagnostic tests and 14 Zika virus diagnostic tests under EUA authority.

FDA HQ also developed policies for the development, use, and export of investigational MCMs as necessary and helped to design clinical trials to evaluate investigational MCMs for Ebola and Zika virus. FDA HQ also:

- supported monitoring for products with unsubstantiated or fraudulent claims for the diagnosis, treatment, or prevention of Ebola and Zika
- led domestic and supported international policy development activities related to Ebola and Zika virus response.
- provided technical support to the World Health Organization and international regulatory counterparts (including West African and Brazilian counterparts).⁹⁵
- provided public information and education on response activities via events, press releases and interviews, the FDA website and social media (see Communications with Stakeholders for more information).

Regulatory Policy and Guidance

Below are examples of regulations, guidances, and final rules issued by FDA HQ in 2016. This list does not represent any degree of importance or priority ranking among these items.⁹⁶

FRDTS#	Type	Formal Title	Date of Publication
2016-228	Guidance	Draft Food and Drug Administration Tribal Consultation Policy; Availability; Request for Comments	2/29/2016
2015-917	Guidance	Emergency Use Authorization of Medical Products and Related Authorities; Draft Guidance for Industry and Public Health Stakeholders; Availability	4/4/2016
2016-726	Final Rule	Submission of Food and Drug Administration Import Data in the Automated Commercial Environment	11/29/2016

FDA HQ coordinated with the National Institutes of Health (NIH) on the September 21, 2016 final rule for clinical trial registration and submission of trial results information to ClinicalTrials.gov (42 CFR Part 11). FDA HQ is coordinating with the Centers and ORA to develop its compliance and enforcement program for violations of Title VIII of the Food and Drug Administration Amendments Act (FDAAA).

⁹⁵ FDA signed a joint statement of continued cooperation between FDA and the Brazilian Health Regulatory Agency (ANVISA) to offer mutual support and to collaborate to address the public health emergency presented by the Zika virus disease outbreak in the Americas.

⁹⁶ For more information on guidance, please visit <http://www.fda.gov/RegulatoryInformation/Guidances>.

FDA HQ is leading joint efforts with the Office for Human Research Protections to review public comments and finalize two guidance documents intended to assist institutional review boards (IRBs).

In 2016, FDA HQ reviewed and analyzed over 2100 public comments and provided comments to HHS on various drafts of the final rule. FDA HQ continues to review the final rule to determine its impact on FDA regulations and guidance, and determine areas for potential harmonization, given the FDA's and HHS's different legislative and regulatory mandates.

FDA HQ continues to collaborate with the Clinical Trials Transformation Initiative (CTTI) effort on several projects. Examples⁹⁷ include efforts to improve:

- Antibacterial Drug Development
- Clinical Trial Recruitment
- Data Monitoring Committees.

International Inspections

FDA's Office of International Programs (OIP) works with regulatory counterparts and stakeholders abroad to improve global product development and manufacturing standards and ultimately ensure that products coming to the US market are safe, effective and of high quality. OIP oversees four FDA country or regional offices (China, Europe, India, and Latin America) in seven locations abroad. Engagements involving other countries and regions are covered from OIP's headquarters. These offices expand FDA's decision-making and actions by:

- expanding FDA inspectional capacity targeting firms of highest risk;
- building relationships and partnering with foreign regulators and other stakeholders; and
- sharing information and expertise to strengthen foreign regulatory systems for the benefit of the U.S. consumer.

In FY 2016, 38 percent of inspections conducted in China were performed by investigators based in the China Office or on short term assignments to China from ORA. In India and Latin America, on site FDA investigators also continued to provide significant contributions towards inspectional accomplishments (14 percent and six percent, respectively).

On site relationships with foreign regulatory counterparts enable FDA to leverage their respective authorities and efforts. The following items are examples of these relationships.

⁹⁷ For more information, visit CTTI's website: <https://www.ctti-clinicaltrials.org>.

The Latin America Office regularly shares information with Mexico about products that do not conform to FDA standards and may pose a risk to human health if they enter the United States. In response, Mexico has implemented a process to follow up and prevent the commercialization of risky products. With this activity, the foreign regulatory authority provides in-country follow-up on FDA information.

Another example is provided in China, where Chinese regulators conducted a year-long investigation after FDA's China Office notified them of a firm that FDA alleged was manufacturing and distributing counterfeit drugs to multiple countries via internet sales. In October 2016, the Chinese government reported that several suspects were arrested, many processing sites were shut down and fake labels found on site were seized. The estimated income generated from these illegal activities was \$1.8 billion.

In another example, after the China Office notified China's Food and Drug Administration (CFDA) of potential contamination in a drug shipment examined by FDA at the U.S. port of entry, CFDA worked with the local Chinese regulatory authority to inspect the production facility within 24 hours. CFDA reported that all products in the firm were destroyed and production was suspended until a cleaning validation had occurred.

Finally, the Europe Office collaborated with FDA's Division of Enforcement and Import Operations and others to engage multiple UK authorities in a complex set of strategic activities that halted large shipments of violative medicines from Europe to the U.S.

International Partnerships

In FY 2016, FDA implemented five new Confidentiality Commitments with:

- The Saudi Food and Drug Authority, to permit information sharing related to the Middle East Respiratory Syndrome Coronavirus
- the United Kingdom's Human Fertilization & Embryology Authority, to facilitate information-sharing regarding biological products
- the Danish Medicines Agency, to update existing confidentiality commitments with the Danish Health and Medicines Authority
- the Export Inspection Council of India, to allow FDA to share non-public information regarding foods manufactured in India
- the College of Pharmacists of British Columbia to facilitate collaboration and information sharing related to the investigation of online pharmacies.

FDA signed three Cooperative Arrangements in 2016 to facilitate regulatory activities:

- a food safety systems recognition arrangement with Health Canada and the Canadian Food Inspection Agency
- a renewed arrangement with Ireland's Department of Agriculture, Food and the Marine for certification of casein exports to the United States
- a Memorandum of Understanding with the Pan American Health Organization to develop a secure platform for the exchange of regulatory information.

In other partnership activities, OIP Europe and China Offices, working with CFSAN and OFVM, established a trilateral mechanism in 2016 with the Directorate General of Health and Food Safety of the European Commission, and China's General Administration of Quality Supervision, Inspection and Quarantine (AQSIQ) to enhance cooperation and exchange regarding food safety.

In addition, as part of the implementation of the Canada United States Regulatory Cooperation Council (RCC), a presidential initiative to promote economic growth and job creation through increased regulatory transparency and cooperation, FDA's collaboration with Health Canada on three simultaneous approvals of veterinary drugs lead to quicker availability of those drugs in the Canadian and US markets.

Further, under the U.S.-Mexico Produce Safety Partnership (PSP), the Latin America Office (LAO) worked with Mexican regulatory authorities to secure bacterial isolates to add to the whole genome sequence library maintained by FDA, enhancing the food-borne pathogen illness database for more effective outbreak strain identification.

International Exchange of Information and Sharing of Expertise

FDA Foreign Offices work closely with FDA product Centers and the Office of Regulatory Affairs to exchange regulatory knowledge and expertise. For example, Foreign Offices trained foreign regulatory authorities on topics such as:

- inspectional techniques
- good manufacturing practices
- good clinical practices
- techniques for detecting problems in data integrity
- new rules under the Food Safety Modernization Act (FSMA).

After a series of China Office workshops on data integrity, the China Food and Drug Administration (CFDA) requested FDA's collaboration on a set of Chinese data integrity guidance documents to ensure that it is aligned with FDA's 2016 guidance. The Europe Office facilitates work of over a dozen technical working groups –“clusters”– with the European Medicines Agency, Canada, Australia and Japan, to share strategies and technical information

to enhance development of medical products, including assessing post market safety signals, pediatric drug development and vaccines.

In 2016, two new clusters were launched based on a decision by FDA, the European Medicines Agency (EMA), and the European Commission (EC), focusing on patient engagement and drug development for rare diseases, areas of high priority for FDA and public health.

China Safety Initiative

FDA continues to expand its efforts to regulate the quality, safety and, as applicable, efficacy of FDA-regulated products entering the United States from China through the China Safety Initiative (CSI), with a primary focus being expansion of the number of FDA investigators, which was accomplished through agreement with the Chinese government.

Through an increase in full-time investigators and those on temporary detail (TDY) to the China Office, the number of drug inspections completed from the China Office has seen a more than three-fold increase from FY 2013 to FY 2016. Furthermore, inspections of food facilities conducted by the China Office increased ten-fold between 2008 and 2015.

In addition, the China Office works closely with FDA product Centers and ORA by providing monitoring and reporting on conditions, trends and events that could affect the safety, quality, and effectiveness of FDA-regulated products exported to the United States from China.

Improve and Safeguard Access

FDA HQ serves as the agency focal point for special programs and initiatives that are cross-cutting and clinical, scientific, and regulatory in nature. FDA HQ promotes high standards of scientific integrity to ensure ethical and responsible research practices such as human subject protection. FDA supports accelerated research and development for medical products to improve greater access to safe and effective medical products for children, and rare disease populations.

FDA HQ plays a vital role in the coordination of:

- review of pediatric science to advance the development of pediatric therapeutics
- product development and an effective and efficient product review process
- data standardization and integrity
- consideration of health disparities and outcomes in regulatory decision making.

The following selected accomplishments demonstrate FDA HQ's delivery of its regulatory and public health responsibilities within the context of current priorities.⁹⁸

Rare Disease Designations, Rare Pediatric Disease Determinations, and Grants

In FY 2016, FDA HQ:

- reviewed a record 569 first-time requests for orphan drug designation and designated 340 promising drugs and biological products for rare diseases
- reviewed 18 first-time requests for Humanitarian Use Device designations and designated 14 promising devices for rare diseases and conditions
- reviewed 45 Rare Pediatric Disease Designation and Consultation Requests and designated or granted 20 drugs and biologics for rare pediatric diseases⁹⁹
- funded 21 new grant awards and 85 ongoing grants funding clinical studies of promising therapies for rare diseases
- funded 8 pediatric device consortia to provide multidisciplinary advice and funding to assist pediatric device innovators Development of Neonatal Program.

FDA HQ, working with CDER, has worked to stimulate product development for neonates, a vulnerable population which has not benefited from existing legislative incentives. These efforts include:

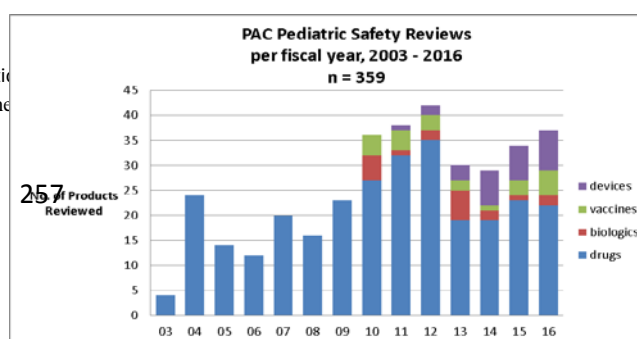
- enhancing communication on specific scientific issues between FDA scientists and external neonatal groups
- developing a research program with academic researchers on endpoints for neonates with pulmonary arterial hypertension
- establishing a neonatology team, led by a board-certified neonatologist,
- establishing a consultation service
- supporting the development of a public-private partnership to foster neonatal product development (International Neonatal Consortium).

Premarket and Postmarket Support

In FY 2016, FDA HQ responded to approximately 700 requests for combination product premarket review assistance from the FDA staff and regulated industry (including products that are on the shortage list). FDA HQ issued 4 formal combination product requests for designation decisions with 100 percent of these decisions meeting the 60-day statutory decision time requirement. FDA HQ provided timely informal jurisdictional assistance for approximately 157

⁹⁸ Please visit <http://www.fda.gov/> for additional program information

⁹⁹ For more information regarding product designations please see the



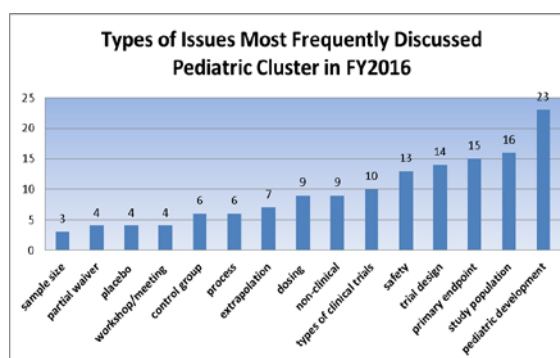
separate Pre-RFD (informal inquiries). FDA HQ provided clarification and support for 350 premarket applications, 1,130 intercenter consults and 71 separate combination product post market activities.

FDA HQ promoted high standards of scientific integrity by providing expert ethical opinions to agency Centers and Offices for more than 100 pediatric ethics issues, more than 600 pediatric development programs, and nearly 50 adult ethics issues. These ethical consultations included issues related to the development of FDA policies for emergencies and crises as seen in the recent Ebola epidemic, the Zika outbreak and research involving the exception from informed consent requirements for emergency research.

FDA HQ enhanced the efficiency of its pediatric safety review process which examines and provides the post market pediatric adverse events and safety reporting issues to the Pediatric Advisory Committee (PAC). Over 300 products have been reviewed by the PAC. In FY 2016, 37 pediatric-focused product safety reviews (drugs, biologics, vaccine and device reviews) were reviewed by FDA's PAC. All CDER products with mandated pediatric safety reviews undergo the same FDA review process. Through the risk-based assessment, low safety risk products will have their mandated pediatric-focused safety reviews posted on FDA's website. Over the last five years the PAC's workload has increased as a result of the legislatively mandated safety assessments on Humanitarian Device Exemptions that have asked for an exclusion from the limitation on profit-making and this will become an increasing part of the workload required to be performed by this committee.

Pediatric Coordination

FDA HQ, working in conjunction with Center subject matter experts through the Pediatric Cluster, met to resolve pediatric scientific differences between European Medicines Agency (EMA) and FDA on 175 issues in FY 2016. Of the 175 issues discussed with the EMA, harmonization was achieved for 77 percent. Examples of the most frequent issues discussed included study design, endpoints, and safety concerns (see graphic).



Promote Informed Decisions

FDA HQ leads the effort to enhance FDA's communications to better serve the public. FDA HQ manages the communications to key stakeholders including the media, Congress, health

professionals, patient advocates, and the general public. FDA HQ ensures important information about the benefits and risks of products is readily available in plain language using different communication methods, such as social media and the FDA website. FDA HQ also educates the public and encourages healthy choices by providing more general information about nutrition and tobacco prevention.

Within the area of Promote Informed Decisions, FDA provides Smart Regulation, Safety and Quality, and Regulatory Science. The following, selected accomplishments demonstrate FDA HQ's delivery of its regulatory and public health responsibilities within the context of current priorities.¹⁰⁰

Helping Reduce Opioid Abuse

In October 2014, based in part on analyses conducted by the Office of Public Health Strategy and Analysis (OPHSA), the Drug Enforcement Administration moved hydrocodone combination drugs from Schedule 3 to the more restrictive Schedule 2, thus effectively eliminating refills. In FY 2016, OPHSA evaluated the impact of this regulatory change and found it produced a 17 percent reduction in hydrocodone combination drug prescriptions and an overall 5 percent reduction in total opioid prescribing, perhaps the largest national impact of any single intervention since the advent of the opioid crisis. This analysis was published January 2016 in the Journal of the American Medical Association (JAMA) Internal Medicine.

Naloxone, a drug that immediately reverses the deadly effects of an opioid overdose, is an important tool in reducing the harm caused by the epidemic of opioid abuse. OPHSA published an article in the American Journal of Public Health in 2016 demonstrating a 1,170 percent increase in naloxone prescribing between 2013 and 2015. In October 2016, OPHSA conceptualized and led a first-of-its-kind naloxone app competition under the America Competes Act. This competition sought to spur the development of a crowd-sourced mobile phone app that would connect people experiencing opioid overdoses with those carrying naloxone, including lay carriers. A \$40,000 prize was awarded to the winning entry. Funding to help bring these products to market will be available through the National Institute on Drug Abuse.

Leading FDA's Engagements with the Government Accountability Office (GAO) and the Office of the Inspector General (OIG)

In this role, OPHSA staff coordinates the Agency response to all these engagements. For each of the several dozen engagements that are ongoing at any moment in time, this requires the identification of appropriate subject matter experts, coordination of FDA responses at a series

¹⁰⁰ Please visit <http://www.fda.gov/> for additional program information and detailed news items.

of meetings and in writing, submission of data in response to requests, and assembly and editing of Agency responses to draft reports. In addition, all responses must be consistent with Agency legal and policy initiatives. The staff also coordinates the annual updates to recommendations contained in the final reports and the Agency's responses to GAO's High Risk List. In recent years, OPHSA staff has assured that a greater number of these recommendations have been closed, and that a greater proportion of those have been closed as implemented.

Support for FDA's Priority Rulemakings

FDA HQ provided crucial support, including developing and drafting the rules and the regulatory impact analyses, to ensure the publication of a number of key proposed and final rules in 2016. These rules included the Final Rule on Produce Safety and the Foreign Supplier Verification Program (FSVP) final rule.

Economic Analysis and Support for Primary FSMA Regulations Published

In 2015, along with the publication of the final rules themselves, FDA HQ Economics published the Economic Analyses for five Food Safety Modernization Act (FSMA) related rules, including Preventive Controls for Human Foods, Preventive Controls for Animal Food and Feed, Foreign Supplier Verification, Produce Safety, and Third-party Accreditation. The support provided via economic analysis spanned more than five years and informed policy decisions throughout the rulemaking process. The outcomes of data analyses and economic modeling provided vital inputs foundational to the publication of the final rules. The result was a complete overhaul of the nation's approach to ensuring food safety that will potentially eliminate millions of foodborne illnesses each year.

21st Century Cures Initiative: Innovation for Healthier Americans

As part of the 21st Century Cures Initiative and the Innovation for Healthier Americans effort, Congress is considering potential legislation that could impact medical product approval standards and regulatory pathways in an effort to expedite getting innovative products onto the market. FDA's work with respect to the initiatives has involved consolidating input from Centers and Offices across the Agency. 21st Century Cures and Innovation for Healthier Americans are priorities for FDA's authorizing committees, and the Agency has worked diligently to provide timely feedback to Congressional offices.

Communication with Stakeholders – Improvements to fda.gov

More than 40 percent of all fda.gov visitors access the site from a mobile device. Since FY 2016, FDA HQ optimized more than 62,000 of the most popular fda.gov pages to better enhance fda.gov visitor experience.

The Patient Network (PN) webpages on fda.gov had more than one million visitors over the past 18 months. The PN web pages also feature the newly developed Expanded Access Form FDA

3926, which provides a streamlined method for submitting an Investigational New Drug Application (IND) for use in cases of individual patient expanded access. Expanded access, sometimes called "compassionate use," is the use outside of a clinical trial of an investigational medical product (i.e., one that has not been approved by FDA).

In February 2016, FDA HQ rapidly established a web page to centralize information about the agency's Zika response activities and includes information on the safety of the blood supply, Emergency Use Authorizations for diagnostic tests, and development of investigational products. The page is updated frequently to help stakeholders easily find the newest information on the FDA's Zika response efforts. The information is also available in [Spanish](#) and [Portuguese](#). As of December 12, 2016, the [Zika Virus Response Updates from FDA web page](#) has received more than 34,000 page views, and the [Emergency Use Authorization](#) page has received 17,500 page views during the Zika response. FDA also sent 18 e-mail updates to approximately 40,000 subscribers; these messages have been opened more than 122,000 times, and recipients have clicked links –mostly to Zika-related information during this timeframe–nearly 11,000 times. FDA Zika-related social media posts have generated at least 4,000 views for FDA web content, in addition to views generated for content from our sister agencies, including CDC.

Communication products to consumers, health care professionals and others

FDA HQ regularly develops communication products about FDA-regulated products, key issues, and other news for consumers, medical professionals, patients, journalists and others.

Since FY 2016, FDA HQ published:

- +225 MedWatch Safety Alerts, which is the FDA's second most popular e-list with more than 350,000 subscribers;
- 191 News Releases and other press announcements in English and/or Spanish with a reach of more than 101,000 subscribers;
- 132 FDA Voice Blogs, which saw a 13 percent increase in readership;
- 77 Consumer Updates in English and Spanish with more than 200,000 subscribers; and
- more than 100 newsletters that reach approximately 700,000 patients and health care professionals.

During National Consumer Protection Week in 2016, FDA HQ launched a multimedia and multilingual initiative to educate at-risk populations against health fraud. YouTube videos, written consumer material and graphics were developed in six languages, and targeted news media and social media outreach was conducted. FDA HQ reached an estimated potential audience of close to 88 million in English and more than 76 million in Spanish.

Meetings with Stakeholders

Since October 2015, FDA HQ conducted approximately 170 meetings with stakeholders and trained and recruited more than 200 patient representatives to advise the FDA. In addition, FDA HQ managed the crosscutting MedWatch Council, which shares best practices across centers related to product safety and safety reporting.

FDA HQ held six Commissioner's Listening Sessions from August through December 2016 with national stakeholder organizations bringing together diverse health professional and patient advocacy organizations across various disciplines. In each of the meetings, the Commissioner provided an overview of FDA's top priorities and emphasized a focus on public health and safety. The Commissioner also engaged with stakeholders on good regulation, innovation, and research. FDA HQ acknowledged the organizations for their prior agency input and expressed an interest in hearing their ideas for best practices to ensure stakeholders' voices are heard within the agency.

FDA HQ also created a new "cluster" on patient engagement with the European Medicines Agency (EMA). The cluster allows FDA and EMA to meet on a regular basis to exchange information on how the organizations engage with and involve patients in regulatory decisions and on ways to enhance future engagement with patients.

Annually, FDA HQ responds to approximately 1,500 inquiries on human subject protection, informed consent, and best practices for the conduct of clinical trials. Archives of these questions and answers are available on fda.gov.

Opioids – State Tours

FDA HQ was instrumental in coordinating and organizing a multi-state (Tennessee, West Virginia and Kentucky) listening tour for the FDA Commissioner to improve understanding of the challenges faced by those who are most affected by the growing opioid epidemic. By listening to stakeholders at the community level, FDA HQ demonstrated its support and commitment to those on the frontlines of the opioid epidemic. The purpose of these visits was to listen, learn, and connect with local health care providers, county medical societies and/or local public health clinics/hospitals.

Stakeholder Outreach Activities

In addition to issuing 225 MedWatch Safety Alerts, two new MedWatch videos were released for consumers and health care professionals. Seven articles on the topic of boxed warning highlights were published in the American Journal of Health-System Pharmacy and the Hospital Pharmacy Journal during FY2016. One article was also published in the official news magazine of the Oncology Nursing Society (ONS), ONS Connect. FDA also collaborated with Medscape on five high-priority topics.

Strengthen Organizational Excellence

FDA HQ ensures the timely and effective implementation of operations and the high quality delivery of services across FDA. FDA HQ plans and manages all resources including:

- budget and financial management
- human resources
- information technology and cybersecurity
- facilities, security and safety
- ethics and equal employment opportunity
- acquisitions activities.

Within the area of Organizational Excellence, FDA provides Stewardship. The following selected accomplishments demonstrate FDA HQ's delivery of its regulatory and public health responsibilities within the context of current priorities.¹⁰¹

FDA HQ is committed to developing its workforce, recruiting, retaining, and strategically managing diversity. FDA HQ invests in infrastructure, evolving management systems and practices to ensure accountability for accomplishing meaningful results to enhance productivity and workforce capabilities. For example, in FY 2016, FDA retained 81 percent of the 10 Commissioner's Fellowship Program graduates.

OpenFDA

OpenFDA is an FDA initiative to provide software developers and researchers Application Programming Interfaces (APIs) to a number of high-value structured datasets, including adverse events, product labeling, and recall enforcement reports.

Since the launch, on June 2, 2014, OpenFDA has received more than 45 million data calls. Half of the calls came from outside the US. There are more than 6,000 registered users, 21,000 connected systems worldwide, and dozens of new software applications that the community has built. During the summer of 2016, FDA held a public meeting to have a robust and interactive discussion with openFDA users to obtain feedback on the openFDA platform.

OpenFDA provides access to:

¹⁰¹ Please visit <http://www.fda.gov/> for additional program information and detailed news items.

- adverse events such as FDA's publically available drug adverse event and medication error reports – over 7.1 million records
- medical device adverse event reports – over 6.1 million records
- unique device identifiers – over 1.3 million records
- device registration and listing – over 230,000 records
- recalls and enforcement report data, containing information from public notices about recalls of FDA-regulated products – over 100,000 recalls records
- Structured Product Labeling for FDA-regulated human drugs – prescription or over the counter – and biologics with over 105,000 records.

FDA Laboratory Modernization

Modernizing FDA's aged, inflexible and unreliable laboratories is critical to FDA's ability to effectively carry out its mission and respond to food safety and medical product emergencies. A large majority of FDA's owned labs were transferred to FDA from other federal agencies, and these buildings as well as the associated site infrastructure were constructed between 30 to 60 years ago.

Similarly, many of FDA's leased lab facilities were constructed over 20 years ago. All of these labs are aged and the building systems, finishes, and layouts are past their useful life, creating unsafe and unhealthy work environments, which in turn compromises FDA's ability to meet scientific needs. The facilities and budget organizations within FDA's Office of Operations (OO) have developed and started implementing a strategy to modernize FDA's laboratories. The strategy consists of:

- assessing facility conditions
- collaborating with the program utilizing the laboratories to fully understand mission impact
- prioritizing laboratories as needing replacement, relocation within the same geographic area, or repairs and improvements
- requesting resources needed to carry out high priority projects.

These efforts have resulted in FDA receiving a total of \$129 million in Non-recurring Expense Fund (NEF) resources to complete a major laboratory project that is a critical first step at implementing the Master Plan at FDA's owned Jefferson Labs Complex (JLC), replace FDA's Winchester Engineering and Analytical Center (WEAC) lab, and relocate the Kansas City and SE Regional labs to new, modern and flexible leased lab space. In addition, FDA was successful in utilizing FDA appropriated funding in FY 2016 to begin the relocation of the leased San Francisco lab.

FDA HQ continues to work to:

- identify ongoing laboratory replacement, relocation, repair, and improvement projects;
- prioritize these projects
- develop resource requests to implement the highest priority projects.

FUNDING HISTORY¹⁰²

<u>FISCAL YEAR</u>	Program Level	Budget Authority	User Fees
FY 2014 Actual	\$244,990,000	\$172,021,000	\$72,969,000
FY 2015 Actual	\$261,099,000	\$173,292,000	\$87,807,000
FY 2016 Actuals	\$301,574,000	\$191,374,000	\$110,200,000
FY 2017 Annualized CR	\$293,259,000	\$191,201,000	\$102,058,000
FY 2018 President's Budget	\$322,486,000	\$125,432,000	\$197,054,000

BUDGET REQUEST

The FY 2018 Budget Request is \$322,486, 000 of which \$125,432, 000 is budget authority and \$197,054,000 is user fees. This level provides a net increase of \$29,227,000. Budget authority decreases by \$65,679, 000 compared to the FY 2017 Annualized CR level and user fees increase by \$94,996, 000.

FDA HQ will continue to provide policy direction and oversight, advance scientific development, and provide oversight of the global supply chain. FDA HQ will continue working to increase transparency and accountability in the supply chain, developing better enforcement and regulatory tools, encouraging greater responsibility by industry, and enhancing collaboration with international regulatory counterparts and other third parties. FDA HQ along with the Centers and Offices, will evaluate and improve the effectiveness of preventive control standards, and advance the development of predictive safety models. FDA HQ will coordinate across FDA to develop improved methods for rapidly detecting, investigating, and stopping foodborne contaminants, as well as develop comprehensive regulatory approaches for integrating pre- and post-approval and compliance functions. In addition, FDA HQ will continue to provide program direction and administrative services, ensuring FDA's public health mission is managed effectively and efficiently. FDA HQ is committed to delivering cutting-edge technology, innovation, and support to all stakeholders.

¹⁰² FY 2016 and FY 2017 do not reflect the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2018, FDA proposes to discontinue the transfer.

BUDGET AUTHORITY**Reductions (-\$7.2 million)**

As part of the FY 2018 budget, FDA HQ will reduce investments in risk analysis and regulatory science activities in order to support higher priorities for food and medical product safety. In FY 2016 and 2017, FDA HQ received \$5 million to bolster the important ongoing development and utilization of a targeted, risk-based, and efficient inspection model for foreign high risk facilities; however, these funds are no longer required in FY 2018. In addition, FDA will reduce funding for regulatory science programs, for the Reagan-Udall Foundation, FDA Fellowship Programs, and other special initiatives lead by FDA HQ.

Medical Product Budget Authority Recalibration (-\$57.1 million)

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees.

USER FEES**Medical Product User Fee Recalibration and Regulatory Efficiencies (+\$95.0 million)**

The FY 2018 President's Budget recalibrates FDA funding for medical product review and approval processes from budget authority to user fees. The budget also includes a package of administrative actions designed to achieve greater regulatory efficiency and speed the availability of innovative, safe, and effective medical products in the market.

PERFORMANCE

The FDA Headquarters' performance measures focus on emergency response, women's health, science, global cooperation, premarket application review of orphan, pediatric and combination products, outreach, and organization efficiency, as detailed in the following table.

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2017 Target	FY 2018 Target	FY 2018 +/- FY 2017
<p><u>292201</u>: Improve FDA's ability to respond quickly and efficiently to crises and emergencies that involve FDA regulated products. (Output)</p>	<p>Maintained 99.45% efficiency on response to calls to the FDA After Hours Call Center.</p> <p>Successfully coordinated 42 incidents involving FDA regulated products during the year.</p> <p>Participated in eleven exercises during the year.</p> <p>(All Targets Met or Exceeded)</p>	<p>Develop 50 mapping products in support of FDA's emergency preparedness, response, and recovery activities.</p> <p>Successfully coordinate 20 incidents involving FDA regulated products during the year.</p> <p>Participate in nine exercises during the year.</p>	<p>Develop 50 mapping products in support of FDA's emergency preparedness, response, and recovery activities.</p> <p>Successfully coordinate 20 incidents involving FDA regulated products during the year.</p> <p>Participate in four exercises during the year.</p>	NA
<p><u>293206</u>: Promote innovation and predictability in the development of safe and effective nanotechnology-based products by establishing scientific standards and evaluation frameworks to guide nanotechnology-related regulatory decisions. (Outcome)</p>	<p>FY 2016: FDA completed annual milestones on 7 more intramural research projects under the Nanotechnology CORES program to promote cross-center and external collaborative regulatory science research opportunities, focusing on studies evaluating nano-materials. (Target Met)</p>	<p>38 CORES projects with completed annual milestones</p>	<p>45 CORES projects with completed annual milestones</p>	+7 projects

<u>291101</u> : Percentage of Fellows retained at FDA after completing the Fellowship program. <i>(Outcome)</i>	FY 2016: 81% Target: 40% (Target Exceeded)	50%	50%	Maintain
<u>293205</u> : Percentage of requests for combination product designations processed within the 60 day statutory requirement. <i>(Output)</i>	FY 2016: 100% Target: 95% (Target Exceeded)	95%	95%	Maintain
<u>293203</u> : Number of pediatric scientific, ethical, product, and product class issues identified through collaboration with the 27 European Union countries coordinated with the EMA, Japan, and Canada, with Australia as observers. <i>(Output)</i>	FY 2016: 54 Target: 40 (Target Exceeded)	50	50	Maintain
<u>293204</u> : Number of medical products studied in children with labeling changes and safety reviews completed and presented to FDA's Pediatric Advisory Committee. <i>(Output)</i>	FY 2016: 37 Target: 30 (Target Exceeded)	30	30	Maintain
<u>292301</u> : The number of new multi-faceted educational programs for patient advocates and health professionals on major FDA public health issues. <i>(Output)</i>	FY 2016: 4 Target: 4 (Target Met)	4	3	-1
<u>291306</u> : The number of targeted engagements, which are strategic interactions between FDA and stakeholders that produce a tangible result in support of FDA's global mission. <i>(Outcome)</i>	FY 2016: 25 Target: 25 (Target Met)	25	25	Maintain

<u>291406</u> : Percentage of invoices issued on time within predefined dates in the month. <i>(Output)</i>	FY 2016: 100% Target: 98% (Target Exceeded)	98%	98%	Maintain
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INFRASTRUCTURE – GSA RENT, OTHER RENT, AND WHITE OAK

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
FDA White Oak Consolidation	52,346	48,944	51,765	56,882	5,117
<i>Budget Authority.....</i>	<i>48,044</i>	<i>48,044</i>	<i>47,953</i>	<i>12,561</i>	<i>-35,392</i>
<i>User Fees.....</i>	<i>4,302</i>	<i>900</i>	<i>3,812</i>	<i>44,321</i>	<i>40,509</i>
<i>Prescription Drug (PDUFA).....</i>	<i>4,302</i>	<i>900</i>	<i>3,812</i>	<i>25,548</i>	<i>21,736</i>
<i>Medical Device (MDUFA).....</i>				<i>8,072</i>	<i>8,072</i>
<i>Generic Drug (GDUFA).....</i>				<i>5,571</i>	<i>5,571</i>
<i>Biosimilars (BsUFA).....</i>				<i>662</i>	<i>662</i>
<i>Animal Drug (ADUFA).....</i>				<i>80</i>	<i>80</i>
<i>Animal Generic Drug (AGDUFA).....</i>				<i>17</i>	<i>17</i>
<i>Family Smoking Prevention and Tobacco Control Act....</i>				<i>4,371</i>	<i>4,371</i>
Other Rent and Rent Related	119,560	119,059	115,794	132,894	17,100
<i>Budget Authority.....</i>	<i>73,484</i>	<i>73,484</i>	<i>73,344</i>	<i>59,889</i>	<i>-13,455</i>
<i>User Fees.....</i>	<i>46,076</i>	<i>45,575</i>	<i>42,449</i>	<i>73,005</i>	<i>30,556</i>
<i>Prescription Drug (PDUFA).....</i>	<i>29,724</i>	<i>26,302</i>	<i>26,340</i>	<i>34,848</i>	<i>8,508</i>
<i>Medical Device (MDUFA).....</i>	<i>4,558</i>	<i>5,158</i>	<i>4,174</i>	<i>12,679</i>	<i>8,505</i>
<i>Generic Drug (GDUFA).....</i>	<i>6,862</i>	<i>6,862</i>	<i>6,962</i>	<i>17,702</i>	<i>10,740</i>
<i>Biosimilars (BsUFA).....</i>	<i>617</i>	<i>617</i>	<i>633</i>	<i>1,203</i>	<i>570</i>
<i>Animal Drug (ADUFA).....</i>	<i>228</i>	<i>228</i>	<i>236</i>	<i>2,101</i>	<i>1,865</i>
<i>Animal Generic Drug (AGDUFA).....</i>	<i>97</i>	<i>97</i>	<i>113</i>	<i>252</i>	<i>139</i>
<i>Family Smoking Prevention and Tobacco Control Act....</i>	<i>3,502</i>	<i>6,311</i>	<i>3,495</i>	<i>3,724</i>	<i>229</i>
<i>Food and Feed Recall.....</i>	<i>43</i>	<i>---</i>	<i>43</i>	<i>43</i>	<i>---</i>
<i>Food Reinspection.....</i>	<i>204</i>	<i>---</i>	<i>204</i>	<i>204</i>	<i>---</i>
<i>Voluntary Qualified Importer Program.....</i>	<i>170</i>	<i>---</i>	<i>170</i>	<i>170</i>	<i>---</i>
<i>Third Party Auditor Program.....</i>	<i>45</i>	<i>---</i>	<i>45</i>	<i>45</i>	<i>---</i>
<i>Outsourcing Facility.....</i>	<i>26</i>	<i>---</i>	<i>34</i>	<i>34</i>	<i>---</i>
GSA Rental Payments	224,105	220,122	235,570	249,783	14,213
<i>Budget Authority.....</i>	<i>161,683</i>	<i>161,683</i>	<i>176,347</i>	<i>128,490</i>	<i>-47,857</i>
<i>User Fees.....</i>	<i>62,422</i>	<i>58,439</i>	<i>59,223</i>	<i>121,293</i>	<i>62,070</i>
<i>Prescription Drug (PDUFA).....</i>	<i>25,512</i>	<i>25,512</i>	<i>22,607</i>	<i>53,640</i>	<i>31,033</i>
<i>Medical Device (MDUFA).....</i>	<i>7,978</i>	<i>7,978</i>	<i>7,306</i>	<i>25,591</i>	<i>18,285</i>
<i>Generic Drug (GDUFA).....</i>	<i>14,705</i>	<i>14,705</i>	<i>14,920</i>	<i>20,213</i>	<i>5,293</i>
<i>Biosimilars (BsUFA).....</i>	<i>1,080</i>	<i>---</i>	<i>1,107</i>	<i>3,076</i>	<i>1,969</i>
<i>Animal Drug (ADUFA).....</i>	<i>1,141</i>	<i>1,141</i>	<i>1,184</i>	<i>3,156</i>	<i>1,972</i>
<i>Animal Generic Drug (AGDUFA).....</i>	<i>583</i>	<i>583</i>	<i>681</i>	<i>1,327</i>	<i>646</i>
<i>Family Smoking Prevention and Tobacco Control Act....</i>	<i>10,592</i>	<i>8,520</i>	<i>10,572</i>	<i>13,444</i>	<i>2,872</i>
<i>Food and Feed Recall.....</i>	<i>73</i>	<i>---</i>	<i>73</i>	<i>73</i>	<i>---</i>
<i>Food Reinspection.....</i>	<i>348</i>	<i>---</i>	<i>348</i>	<i>348</i>	<i>---</i>
<i>Voluntary Qualified Importer Program.....</i>	<i>290</i>	<i>---</i>	<i>290</i>	<i>290</i>	<i>---</i>
<i>Third Party Auditor Program.....</i>	<i>77</i>	<i>---</i>	<i>77</i>	<i>77</i>	<i>---</i>
<i>Outsourcing Facility.....</i>	<i>43</i>	<i>---</i>	<i>58</i>	<i>58</i>	<i>---</i>

Authorizing Legislation: The Federal Food Drug and Cosmetic Act (21 U.S.C. 321-399); Radiation Control for Health and Safety Act (21 U.S.C. 360hh-360ss); The Federal Import Milk Act (21 U.S.C. 142-149); Public Health Service Act (42 U.S.C. 201, et seq.); Foods Additives Amendments of 1958; Color Additives Amendments of 1960; Animal Drug Amendments (21 U.S.C. 360b); Controlled Substances Act (21 U.S.C. 801-830); The Fair Packaging and Labeling Act (15 U.S.C. 1451-1461); Safe Drinking Water Act (21 U.S.C. 349); Saccharin Study and Labeling Act; Federal Anti-Tampering Act (18 U.S.C. 1365); Medical Device Amendments of 1976; Infant Formula Act of 1980; Drug Enforcement, Education, and Control Act of 1986; Generic Animal Drug and Patent Term Restoration Act; Prescription Drug Marketing Act of 1987; Clinical Laboratory Improvement Amendments of 1988 (42 U.S.C. 201); Nutrition Labeling and Education Act of 1990; Prescription Drug Amendments of 1992; Safe Medical Device Amendments of 1992; Dietary Supplement Health and Education Act of 1994; Animal Medicinal Drug Use Clarification Act of 1994; Animal Drug Availability Act of 1996; Food Quality Protection Act of 1996; Federal Tea Tasters Repeal

Act (42 U.S.C. 41); Safe Drinking Water Act Amendments of 1996 (21 U.S.C. 349); Food and Drug Administration Modernization Act of 1997; Antimicrobial Regulation Technical Corrections Act of 1998; Medical Device User Fee and Modernization Act of 2002; Public Health Security and Bioterrorism Preparedness and Response Act of 2002; Animal Drug User Fee Act of 2003 (21 U.S.C. 379j-11 - 379j-12); Project Bioshield Act of 2004 (21 U.S.C.360bbb-3); Minor Use and Minor Species Animal Health Act of 2004; Food Allergy Labeling and Consumer Protection Act of 2004 Medical Device User Fee Stabilization Act of 2005; Sanitary Food Transportation Act of 2005 Dietary Supplement and Nonprescription Drug and Consumer Protection Act (21 U.S.C. 379aa-1); Food and Drug Administration Amendments Act of 2007; The Family Smoking Prevention and Tobacco Control Act of 2009 (P.L. 111-31); Protecting Patients and Affordable Care Act of 2010; The Federal Cigarette Labeling and Advertising Act (15 U.S.C. 1333); FDA Food Safety Modernization Act, Public Law 111-353 (January 4, 2011); The Food and Drug Administration Safety and Innovation Act (P.L. 112-144); and the Drug Quality and Security Act (2013)

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The Infrastructure Program supports FDA's mission of protecting the public health by providing secure and cost-effective office and laboratory space to perform mission-critical work. The Infrastructure Program consists of:

- General Services Administration (GSA) Rental Payments
- Other Rent and Rent Related Activities
- White Oak.

The Infrastructure Program ensures that FDA's offices and labs across the country and its fully integrated headquarters Campus in White Oak, Maryland, are functioning to enable FDA to carry out its mission and respond to food safety and medical product emergencies. Investing in FDA's facility priorities provides the infrastructure and scientific capabilities necessary to ensure FDA can achieve the regulatory responsibilities, strategic priorities, and program initiatives outlined in this document. Programmatic funds may also support improvements critical to FDA's mission.

As FDA strategically manages its infrastructure, it focuses on creating high-quality work environments, optimizing the use of taxpayer dollars, enhancing productivity, and ensuring efficient operations to protect the public's health. For example, FDA ensures that the appropriate information regarding the space required to support its escalating responsibilities is communicated to the Department in the FDA Five-Year Timeline for inclusion in the "Reduce the Footprint" Plan that HHS submits to the Office of Management and Budget.

FDA also promotes maximum utilization of Federal workspace. FDA's energy saving projects decreased long-term energy usage and operating and maintenance costs while increasing

facility life span and efficiency to support Executive Order 13514 – Federal Leadership in Environmental, Energy, and Economic Performance.

As another example, FDA replaced and centralized existing geographically disparate facilities with new, state-of-the-art laboratories, office buildings, and support facilities as part of the White Oak Campus consolidation. FDA is working with GSA to develop a housing strategy and migration plan for FDA headquarters functions and will consider using Federal space near the Campus, to complete FDA's geographic consolidation, including FDA-owned and GSA-owned locations, as well as leasing space in close proximity to the Campus. In addition, a new master plan will be developed for the Federal Research Center and necessary updates will be made to the Muirkirk Road Complex master plan in order to finalize the housing strategy and ensure that environmental impacts have been considered.

GSA Rental Payments

The GSA Rental Payments account includes rental payments for FDA's GSA-managed office and laboratory facilities. FDA occupies almost seven million rentable square feet of GSA-owned and GSA-leased office, laboratory, and warehouse space. More than 60 percent of the GSA rent charges for GSA-owned or GSA-leased space are for facilities in the Washington, D.C. area. FDA occupies GSA space in approximately 270 buildings, including district offices, regional offices, laboratories, resident posts, and border stations across the nation and in Puerto Rico and the Virgin Islands.

The GSA Rental Payments account ensures that the FDA workforce has the space necessary to carry out FDA's public health mission.

During FY 2016, FDA:

- vacated one office building in Rockville, MD, as part of a headquarters lease consolidation
- completed decommissioning and released space for a relocated CDER lab in St. Louis, MO
- vacated two ORA resident posts
- relocated one ORA resident post.

In FY 2017, FDA plans to:

- receive Congressional approval for the relocation of the ORA laboratory in Atlanta, GA

- coordinate design and construction for the relocation of ORA laboratories near Kansas City, KS and San Francisco, CA
- relocate three ORA resident posts and two OCI field locations
- vacate one office building in Rockville, MD as part of a headquarters lease consolidation
- lease office space close to White Oak Campus for office headquarters functions that cannot be accommodated on Campus until additional Federal construction is funded.

FDA strives to be cost effective and energy efficient when it acquires the space required to meet its mission in accordance with nationally recognized standards.

Other Rent and Rent Related Activities

The Other Rent and Rent Related Activities account includes commercial rent and rent related charges that are not part of the GSA Rental account. These funds cover costs for operating and maintaining FDA and GSA facilities located nationwide. Costs include:

- commercial rent
- operation and maintenance contracts
- janitorial and grounds maintenance contracts
- above standard security and guard services contracts
- standard utilities in FDA owned facilities
- essential overtime utilities in laboratories and data centers
- other above-standard level services not provided by GSA in GSA-managed facilities.

This account ensures that FDA's offices and labs are functional and supports the FDA workforce in meeting its public health mission by providing safe, efficient, and secure facilities.

Additionally, FDA is implementing energy efficiencies that will result in significant savings in the Other Rent and Rent Related Activities account. These projects support:

- Executive Order 13693, Planning for Federal Sustainability in the Next Decade
- HHS' Efficient Energy Management Assessments
- Energy Policy Act of 2005
- HHS Sustainable and High Performance Buildings Policy
- HHS Sustainable Buildings Plan
- 2006 Federal Leadership in High Performance and Sustainable Buildings Memorandum of Understanding
- Energy Independence and Security Act of 2007.

For the White Oak Campus, GSA entered into Energy Savings Performance Contracts (ESPCs) with Honeywell Corporation to build a Central Utility Plant (CUP), provide utilities, and perform operations and maintenance activities in a phased approach consistent with the construction and occupancy of the Campus. FDA entered into a memorandum of understanding with GSA and committed to a long-term occupancy of the Campus, including an agreement to pay a share of the costs associated with the ESPCs. Under this agreement, FDA's share of these costs is less than they would be otherwise due to the energy saving features provided by the ESPC.

When each ESPC phase begins to provide benefits to the Campus, including utilities to FDA-occupied buildings, FDA is required to pay the agreed-upon share. The most recent example is GSA's "ESPC III," which covers the expansion of the CUP. The CUP expansion provides the utilities needed to occupy and operate the new Life Sciences – Biodefense Laboratory Complex (LSBC).

FDA awarded a fourth Utility Energy Service Contract (UESC) with Washington Gas at the Muirkirk Road Campus with a capital investment of \$2,921,064 and utility cost savings of approximately \$313,700 annually at a simple payback of 9.31 years. Construction is underway.

The UESC for the FDA owned site in Irvine, California, with Southern California Edison Electric Power Company, with a capital investment of \$2,570,000 and cost savings of about \$254,741 per year with a simple payback of 10.1 years is complete, energy conservation measures are operational, and savings are underway.

FDA awarded a second UESC contract with California Southern Edison Electric Power Company at Irvine with a capital investment of \$5,287,314, utility cost savings of approximately \$351,150 annually, and a simple payback of 15 years. Construction is underway.

FDA has also begun an investment grade audit for our facilities at the Muirkirk Road Campus and in Dauphin Island, Alabama. We anticipate these studies will result in implementation of energy efficiency projects.

GSA is performing audits in FDA-occupied leased facilities, such as the Queens, New York lab. UESCs in GSA-leased buildings will provide energy savings if implemented.

Awarding additional UESCs and procuring renewable energy will contribute to HHS sustainability goals established in the HHS Strategic Sustainability Plan developed in accordance with Executive Order 13514, Federal Leadership in Environmental, Energy, and Economic Performance. FDA's activities related to UESCs and renewable energy will help reduce greenhouse gas emissions.

White Oak

Congress' intent for geographically consolidating the majority of FDA Headquarters on the White Oak Campus was to speed operational excellence and ensure a scientifically stronger FDA. Toward that goal, the White Oak Campus replaced and centralized existing geographically disparate facilities with new, state-of-the-art laboratories, office buildings, and support facilities into one location. While the GSA appropriation funds the design and construction of the new buildings at White Oak, FDA's budget authority and various user fees fund building infrastructure, fit-out, specialized equipment, move costs, and operations and logistics at the Campus.

White Oak funding supports campus operations and requirements including:

- relocation activities, including surplus of furniture and equipment, and decommissioning of FDA vacated laboratories
- FDA information technology and security infrastructure, equipment, cabling and audiovisual
- commissioning and certification of the specialized laboratories
- support services, including conference center management and labor and loading dock services, and operations and maintenance services, including maintenance of vital specialized laboratory equipment
- transportation services, including parking management and a campus shuttle and circulator bus program
- a centralized safety program to support expanded lab operations and Campus occupancy.

FDA initiated relocation activities to White Oak in FY 2002. The total number of employees currently assigned to the White Oak Campus is approximately 9,000 as a result of completing the occupancy of the Biodefense Laboratory Complex (two office and two lab buildings) in FY 2014.

FDA provided funding to GSA to develop an FDA Headquarters housing strategy and migration plan as well as develop a new master plan for the Federal Research Center. This planning will include possible options to house staff at FDA's other two Headquarters consolidated locations – the Muirkirk Road Complex in Laurel, Maryland and FDA's College Park, Maryland facilities. FDA also completed new projects in support of commissioning and certification of the laboratories and other critical facilities on Campus, which are considered above standard by GSA guidelines.

In FY 2017, in addition to funding Campus operations, FDA will initiate above GSA standard repair and improvement projects in support of our program requirements.

FUNDING HISTORY – GSA RENTAL PAYMENTS

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2014 Actual	\$209,372,000	\$162,076,000	\$47,296,000
FY 2015 Actual	\$219,966,000	\$168,882,000	\$51,084,000
FY 2016 Actuals	\$220,122,000	\$161,683,000	\$58,439,000
FY 2017 Annualized CR	\$235,570,000	\$176,347,000	\$59,223,000
FY 2018 President's Budget	\$249,783,000	\$128,490,000	\$121,293,000

FUNDING HISTORY - OTHER RENT AND RENT RELATED ACTIVITIES

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2014 Actual	\$109,416,000	\$74,674,000	\$34,742,000
FY 2015 Actual	\$115,424,000	\$72,943,000	\$42,481,000
FY 2016 Actuals	\$119,059,000	\$73,484,000	\$45,575,000
FY 2017 Annualized CR	\$115,794,000	\$73,344,000	\$42,450,000
FY 2018 President's Budget	\$132,894,000	\$59,889,000	\$73,005,000

FUNDING HISTORY - WHITE OAK

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2014 Actual	\$61,603,000	\$58,044,000	\$3,559,000
FY 2015 Actual	\$46,687,000	\$43,044,000	\$3,643,000
FY 2016 Actuals	\$48,944,000	\$48,044,000	\$900,000
FY 2017 Annualized CR	\$51,765,000	\$47,953,000	\$3,812,000
FY 2018 President's Budget	\$56,882,000	\$12,561,000	\$44,321,000

BUDGET REQUEST

The FY 2018 Total Budget with Adjustments is \$439,559,000, of which \$200,940,000 is budget authority and \$238,619,000 is user fees. This level provides a net increase of 36,431,000. Budget authority decreases by \$96,704,000 compared to the FY 2017 Annualized CR level and user fees increase by \$133,135,000. The request will cover rent increases the agency anticipates in FY 2018 that are related to market changes, including new Occupancy Agreements replacing those expiring for 37 buildings that will cause rental rates to reset to

market rates. In addition, FDA will also occupy expansion space in an existing GSA-leased building and two new GSA-leased buildings in FY 2018 to address user fee growth. The increase in OR&RR is needed to meet cost escalations associated with operations and maintenance contracts, utilities and Energy Savings Performance Contract payments for its owned and leased buildings nationwide. In addition, the OR&RR increase is also needed to address more demands for repairs and non-standard maintenance requests as FDA's owned buildings continue to age and equipment and systems failures occur. Operating costs at the White Oak Campus continue to increase with inflation, and due to the fact that several of the buildings on Campus are 10 or more years old. Additional funding is needed to address ongoing above GSA standard repairs and improvements and meet program needs.

The Infrastructure Program ensures that FDA's offices and labs across the country and its fully integrated headquarters Campus are optimally functioning to enable FDA to carry out its mission and respond to food safety and medical product emergencies. Further, it supports:

- FDA's mission of protecting the public health by providing secure and cost-effective office and laboratory space to perform mission-critical work
- FDA's Strategic Goal to Strengthen Organizational Excellence and the FDA Strategic Priority of Stewardship
- enhanced productivity and capabilities needed to achieve FDA's expanding public health mission.

Proposed Appropriations Language Changes to Rent Cost

The FY 2018 President's Budget proposes striking the "not to exceed" (NTE) language from FDA's appropriation language for rent costs. A large majority of FDA's owned buildings, including laboratories, were transferred to FDA from other federal agencies and these buildings as well as the associated site infrastructure were constructed between 30 to 60 years ago. Many of the buildings, including critical research and regulatory laboratories, are aged and the building systems, finishes, and layouts are past their useful life, creating unsafe and unhealthy work environments, which in turn compromises FDA's ability to meet scientific needs. Historically funding for necessary major improvements for site infrastructure and building systems and equipment has been very limited and below the amount needed to even sustain the current poor condition. Accordingly, operations and maintenance costs are continuing to increase as more equipment and systems fail and more maintenance is needed to keep buildings operational. Major equipment failures could occur and the current "not to exceed" restriction severely limits FDA's ability to address these needs as well as other increased maintenance costs to ensure FDA's mission critical facilities remain operational. Without this flexibility, equipment and system failures will likely result in closing

these critical buildings, which will have an immediate and significant impact on the FDA mission and the public health.

GSA Rental Payments

The FY 2018 Budget request for GSA Rental Payments is \$249,783,000, of which \$128,490,000 is budget authority and \$121,293,000 is user fees. The budget authority decreases by \$47,857,000 compared to the FY 2017 Continuing Resolution level and user fees increase by \$62,070,000.

The GSA-managed properties that provide office and laboratory space for FDA employees are essential facilities. The FY 2018 Budget Request for GSA Rental Payments covers the cost of rental payments to GSA for FDA's almost seven million square feet of GSA-managed office and laboratory space.

Other Rent and Rent Related

The FY 2018 Budget request for Other Rent and Rent Related is \$132,894,000, of which \$59,889,000 is budget authority and \$73,005,000 is user fees. The budget authority decreases by \$13,455,000 compared to the FY 2017 Continuing Resolution level and user fees increase by \$30,556,000.

The FY 2018 Budget will allow FDA to operate, maintain, and secure its facilities in an appropriate and sustainable manner to support over 16,000 staff members.

White Oak

The FY 2018 Budget request for White Oak consolidation and operations activities is \$56,882,000, of which \$12,561,000 is budget authority and \$44,321,000 is user fees. The budget authority decreases by \$35,392,000 compared to the FY 2017 Continuing Resolution level and user fees increase by \$40,509,000.

The FY 2018 Budget provides the necessary resources for ongoing above GSA standard repairs and improvements, and mission support services for the almost 9,000 employees occupying the White Oak Campus on a daily basis. The FY 2018 Budget request will fund support services, transportation services, labor, and loading dock services, and a centralized safety program.

BUILDINGS AND FACILITIES

(Dollars in Thousands)	FY 2016 Final	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018	
				President's Budget	President's Budget +/- FY 2017 CR
Buildings and Facilities (Budget Authority).....	8,788	7,539	8,771	8,771	-

Authorizing Legislation: Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321-399); Public Health Service Act (42 U.S.C. §238); Federal Property and Administrative Services Act of 1949, as amended (40 U.S.C. §§471 *et seq.*); National Historic Preservation Act of 1966 (P.L. 89-665; 16 U.S.C. 470 *et seq.*); Chief Financial Officers Act of 1990 (P.L. 101-576); Federal Financial Management Act of 1994 (P.L. 103-356); Energy Policy Act of 2005 (P.L. 109-058); Energy Independence & Security Act of 2007 (P.L. 110-140, 121 Stat. 1492)

Allocation Methods: Direct Federal/Contract

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

As with the Infrastructure Program, the Buildings and Facilities (B&F) Program ensures that FDA's offices and labs across the country are optimally functioning to enable FDA to carry out its mission and respond to food safety and medical product emergencies. Investing in FDA's facility priorities provides the infrastructure and scientific capabilities necessary to ensure FDA can achieve the regulatory responsibilities, strategic priorities, and program initiatives outlined in this document.

Strengthen Organizational Excellence

The B&F Program is a critical element of FDA's real property asset management program and directly supports FDA's public health mission. FDA recruits, develops, retains and strategically manages a world-class workforce, improves the overall operation and effectiveness of FDA, and invests in infrastructure to enhance productivity and capabilities.

Under the goal of Organizational Excellence, FDA has demonstrated stewardship by striving to provide high quality, reliable buildings that support FDA's mission critical work. B&F funding is used to:

- construct new mission-critical laboratory, office, and support space
- renovate, repair site infrastructure and buildings – an inventory of 85 existing FDA-owned facilities at six sites in the United States and Puerto Rico.

HHS developed a Real Property Asset Management Plan (AMP) to outline a framework and holistic approach for acquiring, managing, and disposing of real property assets.

The AMP contains performance measures and benchmarks that monitor key real property asset management criteria, including:

- mission criticality
- utilization
- facility condition
- operating costs.

The physical condition of FDA assets is critical. A safe, suitable, and reliable work environment is essential for FDA to protect the nation's health, security, and economy. Improving and maintaining facilities often results in a positive effect on associated utilization and operating costs.

An important component of FDA real property asset management is conducting facility condition assessments on a 5-year cycle to evaluate:

- site infrastructure – utility distribution systems, roads, and sidewalks
- buildings, including physical systems – architectural, civil, mechanical, electrical
- code compliance
- life and other safety conditions
- finishes and aesthetics.

The assessments result in:

- a list of maintenance and repair deficiencies with associated costs known as the Backlog of Maintenance and Repair (BMAR)
- a plant replacement value – the cost to replace an infrastructure item or a facility
- a Facility Condition Index (FCI) score.

The BMAR identifies and estimates costs associated with addressing needed maintenance, repairs, and replacement of equipment and building systems that are approaching – or past – their useful life. The BMAR also identifies and prioritizes short- and long-term projects using B&F funding.

At the end of FY 2016, the BMAR for the six FDA-owned sites, including renewals, was approximately \$141.8 million. Approximately 71 percent of FDA-owned assets have an FCI score below the HHS-established goal of 90 and require significant repairs and improvements.

FDA uses funds to accomplish both mission and BMAR-driven projects. The goal is to improve the condition of these assets and the site infrastructure and to ensure the suitability and reliability of FDA-owned assets.

FDA has 22 labs located at the following six owned sites:

- Gulf Coast Seafood Laboratory, Dauphin Island, AL
- Jefferson Labs Complex (JLC), Jefferson, AR
- Muirkirk Road Complex, Laurel, MD
- Pacific Regional Laboratory SW, Irvine, CA
- San Juan District Office and Laboratory, San Juan, PR
- Winchester Engineering & Analytical Center (WEAC), Winchester, MA.

Activities in FY 2016 and Planned for FY 2017

Gulf Coast Seafood Laboratory – Dauphin Island, Alabama

The Gulf Coast Seafood Laboratory is FDA's sole marine laboratory and represents 80 percent of FDA research capacity for addressing seafood safety.

In FY 2016, FDA initiated projects to design and construct a new Algal Culture System Room to support the local mission, perform an energy audit, and complete a study to design and reconstruct the seawall that protects the site, which is located on the Gulf of Mexico.

In FY 2017, FDA will construct a new seawall, implement energy conservation measures, and complete a study and design to improve the efficiency of the electrical power at the site.

Jefferson Laboratories Complex (JLC) – Jefferson, Arkansas

The Jefferson Laboratories Complex houses the National Center for Toxicological Research (NCTR) and the Office of Regulatory Affairs (ORA) Arkansas Regional Laboratory (ARL).

Additional details of the vital scientific research that takes place at the Complex can be found in the NCTR Narrative.

ARL provides analytical laboratory support to FDA's regulatory mission in the Southwest Region.

In FY 2016, FDA initiated site infrastructure projects including:

- designing projects to replace chillers in a critical animal research building
- completing the installation of a new water well
- replacing a chiller starter.

FDA also initiated building improvement projects that include:

- completing concept studies to renovate the pathology and archive storage areas, and designing projects to replace critical equipment in an animal processing area and to create an auditorium needed to facilitate scientific collaboration

- completing two additional phases of the project to replace the HVAC controls in a critical laboratory building
- renovating a second processing facility to modernize equipment and the HVAC system that will support animal research on the campus
- funding construction administration services for the renovation of three key laboratories – Buildings 14, 53A and 62
- completing minor renovations to an animal quarantine facility.

In FY 2017, FDA will complete designs to:

- replace chillers in two site chiller plants
- replace building roofs
- renovate the data center
- replace electric service and standby generation
- repair building envelopes
- replace critical animal processing area equipment
- consolidate warehouse buildings
- renovate existing administrative space to create a large auditorium needed to facilitate scientific collaboration
- replace two backup emergency generators servicing animal research buildings

FDA will also provide funding for contingencies associated with the project to renovate laboratories in Buildings 14 and 53A, and install new roofs on the dormitory and commons buildings. FDA will also repair Campus roadways and sidewalks and design improved drainage features. In addition, FDA will make several building improvements including:

- updating water treatment controls
- upgrading a sample preparation room
- constructing a new walk-in cooler and freezer
- addressing ADA compliance issues
- replacing variable frequency drives on exhaust fans
- replacing preheat coils.

Muirkirk Road Complex (MRC) – Laurel, Maryland

The Muirkirk Road Complex is a campus shared by the Foods and Animal Drugs and Feeds programs to conduct research on:

- food and animal drug safety
- toxicology
- microbiology

- molecular biology.

In FY 2016, FDA initiated projects to:

- install a fire resistant shaft enclosure to ensure adequate fire safety, and a backup generator in two critical lab buildings, respectively
- replace a reverse osmosis tank servicing research laboratories and a clean steam generator
- paint ceilings and walls, and replace flooring in a critical animal research area to ensure animal research accreditation
- create additional workstations for laboratory support personnel
- expand conference room and add divider to ensure space supports increased scientific meetings
- replace tile walkway to main entrance that is aged and cracking to eliminate the trip and fall hazard, and pave the road to a large emergency generator for more efficient access.

In FY 2017, FDA will replace four air handling units that service the animal research portion of a main laboratory building.

Pacific Regional Laboratory Southwest – Irvine, California

The Pacific Regional Laboratory Southwest provides analytical laboratory support to FDA's regulatory mission in the Pacific Region.

In FY 2016, FDA initiated projects to:

- design chemical fume hood exhaust modifications for the lab
- install additional local exhaust ventilation in the lab
- correct a humidity issue in the lab
- construct a firewall in the electrical switchgear room.

In FY 2017, FDA will renovate the Biosafety Level 3 lab to include an independent HVAC system, enlarge the anteroom and add an autoclave. This is a high containment lab designed to isolate dangerous biological agents in an enclosed laboratory room, and these improvements are necessary to ensure employee safety and support required procedures.

San Juan District Office and the National Drug Servicing Laboratory – San Juan, PR

The National Drug Servicing Laboratory specializes in pharmaceutical analysis.

In FY 2016, FDA initiated projects to:

- replace the floor finishes in the main administration building
- perform a structural evaluation of the Maintenance Building and make necessary repairs, if possible.

In FY 2016, FDA also initiated projects to improve the main laboratory by:

- designing, replacing and upgrading the electrical distribution wiring system
- balancing the ventilation system to ensure proper pressurization for safety
- replacing the vacuum system
- installing a distilled water recirculation system.

In FY 2017, FDA will replace and upgrade the electrical distribution wiring system for the main laboratory and replace or repair the sidewalks and building access ramps on Campus.

Winchester Engineering and Analytical Center (WEAC) –Winchester, Massachusetts

The Winchester Engineering and Analytical Center is a specialty laboratory used to:

- test the safety and performance of medical devices, microwaves, and radiopharmaceuticals
- conduct radionuclide testing with food samples
- ensure seafood freshness.

In FY 2016 FDA initiated projects to:

- make needed improvements to the parking lot
- provide humidity control in one lab
- replace an exhaust fan in a laboratory support room.

In FY 2017, FDA will provide construction administration and additional support for the laboratory replacement project.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2014 Actual	\$7,808,000	\$7,808,000	\$0
FY 2015 Actual	\$8,997,000	\$8,997,000	\$0
FY 2016 Actuals	\$7,539,000	\$7,539,000	\$0
FY 2017 Annualized CR	\$8,771,000	\$8,771,000	\$0
FY 2018 President's Budget	\$8,771,000	\$8,771,000	\$0

BUDGET REQUEST

The FY 2018 Budget Request is \$8,771,000, consisting solely of budget authority. This amount is equal to the FY 2017 Annualized CR level.

The funding level requested attempts to sustain the current condition of FDA's owned buildings at its six mission-critical sites and will fund the projects noted below.

At the Gulf Coast Seafood Laboratory facility, FDA will replace the hot water piping system and an air handling unit in the main laboratory building, and complete work associated with the replacement of the seawall.

At the Jefferson Labs Complex, FDA will:

- complete designs for several projects that will replace air compressors and two backup generators, and a renovation for IT space
- install new processing equipment for an animal research building
- repair infrastructure items to include improving campus roads, sidewalks and drainage
- repair windows in the main administration building, building envelopes, and several roofs on campus
- complete the first phase of chiller replacements in a main chiller plant.

At the Muirkirk Road Complex, FDA will:

- replace four air handling units that service the main laboratory building replace obsolete electrical panel boards at the site substation and one of the main lab buildings
- install tempered water for emergency eyewash stations
- provide necessary exhaust systems for two animal rooms.

In the Pacific Regional Laboratory Southwest, FDA will:

- renovate laboratories to address a safety hazard and meet additional laboratory space needs
- re-commission the building.

In the San Juan District Office and Laboratory, FDA will replace HVAC equipment and other equipment associated with aging building systems in the main laboratory building.

At the Winchester Engineering & Analytical Center, FDA will support the ongoing operation of the existing facility during the construction of the replacement building.

The following table provides an allocation plan by site for use of the FY 2018 funds.

FY 2018 BUILDINGS AND FACILITIES ALLOCATION PLAN

Site	Total
CFSAN Gulf Coast Seafood Laboratory	\$1,000,000
Jefferson Laboratories Complex (NCTR & ARL) – Jefferson, AR	4,385,500
Muirkirk Road Complex (MOD1, MOD2, BRF) – Laurel, MD	2,195,000
ORA Pacific Regional Laboratory SW – Irvine, CA	690,500
San Juan District Office and Laboratory – San Juan, PR	400,000
Winchester Engineering and Analytical Center – Winchester, MA	100,000
B&F Project Total	\$8,771,000

In FY 2018, sustaining the condition of FDA-owned real property assets and site infrastructure will continue to be a priority. Completion of these projects is necessary for FDA to achieve its critical mission. In addition, several of these projects will contribute to HHS sustainability goals established in the HHS Strategic Sustainability Performance Plan.

More specifically, projects planned in FY 2018 will help reduce Scope 1, 2, and 3 greenhouse gas emissions¹⁰³ by:

- replacing aged, inefficient chillers and HVAC controls and equipment
- re-commissioning a large lab building
- repairing windows.

PROGRAM ACTIVITY DATA TABLE

Facility ¹	Average Facility Condition Index (FCI) Score		
	FY 2016 Enacted	FY 2017 CR	FY 2018 Request

¹⁰³ More information can be found in the HHS Strategic Sustainability Performance Plan at: <http://www.hhs.gov/sites/default/files/2015-sustainability-plan.pdf>.

BUILDINGS AND FACILITIES

CFSAN Gulf Coast Seafood Laboratory ²	93	93	93
Jefferson Laboratories Complex ³	69	70	71
Muirkirk Road Complex ⁴	82	82	86
ORA Pacific Regional Laboratory Southwest ⁵	99	99	99
San Juan District Office and Laboratory ⁶	76	76	76
Winchester Engineering And Analytic Center ⁷	65	65	65

¹ The Backlog of Maintenance and Repairs (BMAR) at each site is significant. Approximately 69 percent of FDA-owned assets have an FCI score below the HHS-established goal of 90 and require significant repairs and improvements. Funding is allocated to projects at each site in an effort to reduce the BMAR and improve the average Facility Condition Index (FCI) for the site. Without ongoing repair and improvement projects, the increase in BMAR each year would result in no change or a decrease in the FCI rather than an increase. Improvements may not be realized in the fiscal year the funds are received due to timing and complexity of the project.

² Based on funding levels in FY 2017 and FY 2018, the BMAR for this site will decrease by \$4K. Remaining BMAR for this site is approximately \$346K.

³ Based on funding levels in FY 2017 and FY 2018 the BMAR for this site will decrease by approximately \$9.2M. Remaining BMAR total will be approximately \$106.6M.

⁴ Based on funding levels in FY 2017 and FY 2018 the BMAR for this site will decrease by approximately \$2.17M. Remaining BMAR total will be approximately \$14.6M.

⁵ Based on funding levels in FY 2017 and FY 2018, the BMAR for this site will not decrease. Remaining BMAR for this site is approximately \$49K.

⁶ Based on funding levels in FY 2017 and FY 2018 the BMAR for this site will decrease by approximately \$103K. Remaining BMAR total will be approximately \$3.4M.

⁷ Based on funding levels in FY 2017 and FY 2018, the BMAR for this site will not decrease. Remaining BMAR total will be approximately \$5.2M

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OBJECT CLASSIFICATION TABLES

BUDGET AUTHORITY BY OBJECT CLASS

(Dollars in Thousands)	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget	FY 2018 +/- FY 2017
<u>Personnel Compensation and Benefits:</u>				
Personnel Compensation:				
Full-time permanent (11.1).....	907,285	922,664	638,028	-284,636
Other than full-time permanent (11.3).....	91,887	93,444	64,617	-28,827
Other personnel compensation (11.5).....	39,844	40,519	28,019	-12,500
Military personnel (11.7).....	63,765	64,779	65,799	1,020
Special personnel services payments (11.8).....	767	780	539	-241
Subtotal, Personnel Compensation.....	1,103,548	1,122,186	797,002	-325,184
Benefits:				
Civilian benefits (12.1).....	337,985	343,714	237,680	-106,034
Military benefits (12.2).....	32,621	33,140	33,662	522
Benefits to former personnel (13.0).....	501	501	501	---
Subtotal, Benefits.....	371,107	377,355	271,843	-105,512
Total Personnel Compensation and Benefits.....	1,474,655	1,499,541	1,068,845	-430,696
<u>Contractual Services and Supplies</u>				
Contractual Services:				
Travel and transportation of persons (21.0).....	49,666	48,516	31,426	-17,090
Transportation of things (22.0).....	3,193	3,120	2,021	-1,099
Rental payments to GSA (23.1).....	161,683	176,347	128,490	-47,857
Rent payments to others (23.2).....	2,703	2,641	1,711	-930
Communication, utilities, and misc. charges (23.3).....	18,572	18,142	11,751	-6,391
Printing and reproduction (24.0).....	1,633	1,595	1,033	-562
Subtotal, Contractual Services.....	237,451	250,361	176,432	-73,929
Other Contractual Services:				
Consulting services (25.1).....	53,637	52,395	33,938	-18,457
Other services (25.2).....	360,775	352,422	228,278	-124,144
Purchase of goods and svcs from Govt Acts. (25.3).....	133,206	130,122	84,285	-45,837
Operation and maintenance of facilities (25.4).....	104,202	101,789	65,933	-35,856
Research and Development Contracts (25.5).....	19,417	18,967	12,286	-6,681
Operation and maintenance of equipment (25.7).....	90,825	88,722	57,469	-31,253
Subsistence and support of persons (25.8).....	6	5	4	-1
Subtotal, Other Contractual Services.....	762,067	744,422	482,193	-262,229
Supplies and Materials:				
Supplies and materials (26.0).....	46,707	45,626	29,554	-16,072
Equipment (31.0).....	46,710	45,629	29,556	-16,073
Land and Structures (32.0).....	3,183	3,109	2,014	-1,095
Grants, subsidies, and contributions (41.0).....	155,572	151,970	98,437	-53,533
Insurance claims and indemnities (42.0).....	2,257	2,205	1,428	-777
Interest and dividends (43.0).....	48	47	30	-17
Subtotal, Supplies and Materials.....	254,477	248,586	161,019	-87,567
Total Contractual Services and Supplies.....	1,253,994	1,243,369	819,644	-423,725
Total Budget Authority by Object Class.....	2,728,649	2,742,910	1,888,489	-854,421

*FY 2016 and FY 2017 funding levels reflect the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2018, FDA proposes to discontinue the transfer.

USER FEE BY OBJECT CLASS

(Dollars in Thousands)	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget	FY 2018 +/- FY 2017
<u>Personnel Compensation and Benefits:</u>				
Personnel Compensation:				
Full-time permanent (11.1).....	536,195	576,418	927,668	351,250
Other than full-time permanent (11.3).....	76,032	81,736	131,543	49,807
Other personnel compensation (11.5).....	57,080	61,361	98,753	37,392
Military personnel (11.7).....	41,668	42,374	43,042	668
Special personnel services payments (11.8).....	185	199	320	121
Subtotal, Personnel Compensation.....	711,160	762,088	1,201,326	439,238
Benefits:				
Civilian benefits (12.1).....	206,514	222,005	357,288	135,283
Military benefits (12.2).....	22,368	22,747	23,106	359
Benefits to former personnel (13.0).....	32	32	32	---
Subtotal, Benefits.....	228,914	244,784	380,426	135,642
Total Personnel Compensation and Benefits.....	940,073	1,006,872	1,581,752	574,880
<u>Contractual Services and Supplies</u>				
Contractual Services:				
Travel and transportation of persons (21.0).....	18,035	11,928	21,370	9,442
Transportation of things (22.0).....	690	179	320	141
Rental payments to GSA (23.1).....	58,439	59,223	121,293	62,070
Rent payments to others (23.2).....	1,209	149	268	119
Communication, utilities, and misc. charges (23.3)....	8,162	2,786	4,992	2,206
Printing and reproduction (24.0).....	919	2,609	4,674	2,065
Subtotal, Contractual Services	87,455	76,874	152,917	76,043
Other Contractual Services:				
Consulting services (25.1).....	75,691	55,323	99,115	43,792
Other services (25.2).....	370,083	348,595	624,530	275,935
Purchase of goods and svcs from Govt Acts. (25.3).....	187,400	195,961	351,076	155,115
Operation and maintenance of facilities (25.4).....	38,887	23,002	41,209	18,207
Research and Development Contracts (25.5).....	28,988	13,436	24,071	10,635
Operation and maintenance of equipment (25.7).....	29,030	32,836	58,827	25,991
Subsistence and support of persons (25.8).....	---	---	---	---
Subtotal, Other Contractual Services.....	730,078	669,153	1,198,828	529,675
Supplies and Materials:				
Supplies and materials (26.0).....	15,743	12,694	22,742	10,048
Equipment (31.0).....	29,731	19,971	35,779	15,808
Land and Structures (32.0)	---	---	---	---
Grants, subsidies, and contributions (41.0).....	134,238	131,508	235,605	104,097
Insurance claims and indemnities (42.0).....	6	5	9	4
Interest and dividends (43.0).....	---	---	---	---
Subtotal, Supplies and Materials.....	179,981	164,178	294,135	129,957
Total Contractual Services and Supplies.....	997,514	910,205	1,645,880	735,675
Total Reimbursable by Object Class.....	1,937,587	1,917,077	3,227,632	1,310,555

TOTAL PROGRAM LEVEL BY OBJECT CLASS

(Dollars in Thousands)	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget	FY 2018 +/- FY 2017
Personnel Compensation and Benefits:				
Personnel Compensation:				
Full-time permanent (11.1).....	1,443,481	1,499,082	1,565,696	66,614
Other than full-time permanent (11.3).....	167,919	175,180	196,160	20,980
Other personnel compensation (11.5).....	96,923	101,880	126,772	24,892
Military personnel (11.7).....	105,433	107,153	108,841	1,688
Special personnel services payments (11.8).....	952	979	859	-120
Subtotal, Personnel Compensation.....	1,814,708	1,884,274	1,998,328	114,054
Benefits:				
Civilian benefits (12.1).....	544,498	565,719	594,968	29,249
Military benefits (12.2).....	54,990	55,887	56,768	881
Benefits to former personnel (13.0).....	532	532	532	---
Subtotal, Benefits.....	600,021	622,138	652,268	30,130
Total Personnel Compensation and Benefits.....	2,414,728	2,506,412	2,650,596	144,184
Contractual Services and Supplies				
Contractual Services:				
Travel and transportation of persons (21.0).....	67,701	60,444	52,796	-7,648
Transportation of things (22.0).....	3,884	3,299	2,341	-958
Rental payments to GSA (23.1).....	220,122	235,570	249,783	14,213
Rent payments to others (23.2).....	3,912	2,790	1,979	-811
Communication, utilities, and misc. charges (23.3)....	26,734	20,928	16,743	-4,185
Printing and reproduction (24.0).....	2,552	4,204	5,707	1,503
Subtotal, Contractual Services.....	324,905	327,235	329,349	2,114
Other Contractual Services:				
Consulting services (25.1).....	129,328	107,718	133,053	25,335
Other services (25.2).....	730,858	701,017	852,809	151,791
Purchase of goods and svcs from Govt Acts. (25.3).....	320,606	326,083	435,361	109,278
Operation and maintenance of facilities (25.4).....	143,089	124,791	107,142	-17,649
Research and Development Contracts (25.5).....	48,405	32,403	36,357	3,954
Operation and maintenance of equipment (25.7).....	119,855	121,558	116,296	-5,262
Subsistence and support of persons (25.8).....	6	5	4	-1
Subtotal, Other Contractual Services.....	1,492,145	1,413,575	1,681,022	267,446
Supplies and Materials:				
Supplies and materials (26.0).....	62,450	58,320	52,296	-6,024
Equipment (31.0).....	76,441	65,600	65,335	-265
Land and Structures (32.0).....	3,183	3,109	2,014	-1,095
Grants, subsidies, and contributions (41.0).....	289,809	283,478	334,042	50,564
Insurance claims and indemnities (42.0).....	2,263	2,210	1,437	-773
Interest and dividends (43.0).....	48	47	30	-17
Subtotal, Supplies and Materials.....	434,458	412,764	455,154	42,390
Total Contractual Services and Supplies.....	2,251,508	2,153,574	2,465,525	311,950
Total Program Level by Object Class.....	4,666,236	4,659,986	5,116,121	456,135

*FY 2016 and FY 2017 funding levels reflect the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2018, FDA proposes to discontinue the transfer.

SALARIES AND EXPENSES

(Dollars in Thousands)	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget	FY 2018 +/- FY 2017
<u>Personnel Compensation and Benefits:</u>				
Personnel Compensation:				
Full-time permanent (11.1).....	907,285	922,664	638,028	-284,636
Other than full-time permanent (11.3).....	91,887	93,444	64,617	-28,827
Other personnel compensation (11.5).....	39,844	40,519	28,019	-12,500
Military personnel (11.7).....	63,765	64,779	65,799	1,020
Special personnel services payments (11.8).....	767	780	539	-241
Subtotal, Personnel Compensation.....	1,103,548	1,122,186	797,002	-325,184
Benefits:				
Civilian benefits (12.1).....	337,985	343,714	237,680	-106,034
Military benefits (12.2).....	32,621	33,140	33,662	522
Benefits to former personnel (13.0).....	501	501	501	---
Subtotal, Benefits.....	371,107	377,355	271,843	-105,512
Total Personnel Compensation and Benefits.....	1,474,655	1,499,541	1,068,845	-430,696
<u>Contractual Services and Supplies</u>				
Contractual Services:				
Travel and transportation of persons (21.0).....	49,666	48,516	31,426	-17,090
Transportation of things (22.0).....	3,193	3,120	2,021	-1,099
Rent payments to others (23.2).....	2,703	2,641	1,711	-930
Communication, utilities, and misc. charges (23.3)....	18,572	18,142	11,751	-6,391
Printing and reproduction (24.0).....	1,633	1,595	1,033	-562
Subtotal, Contractual Services.....	75,768	74,014	47,942	-26,072
Other Contractual Services:				
Consulting services (25.1).....	53,637	52,395	33,938	-18,457
Other services (25.2).....	360,775	352,422	228,278	-124,144
Purchase of goods and svcs from Govt Acts. (25.3).	133,206	130,122	84,285	-45,837
Operation and maintenance of facilities (25.4).....	104,202	101,789	65,933	-35,856
Research and Development Contracts (25.5).....	19,417	18,967	12,286	-6,681
Operation and maintenance of equipment (25.7).....	90,825	88,722	57,469	-31,253
Supplies and materials (26.0).....	46,707	45,626	29,554	-16,072
Total Contractual Services and Supplies.....	884,536	864,057	559,685	-304,372
Rental payments to GSA (23.1).....	161,683	176,347	128,490	-47,857
Grand Total, Salaries and Expense and Rent.....	2,520,874	2,539,945	1,757,020	-782,925
Direct FTE.....	10,279	10,453	7,348	-3,105

*FY 2016 and FY 2017 funding levels reflect the transfer of \$1.5 million from FDA Headquarters to the HHS Office of Inspector General to support oversight of FDA's expanded authorities. For FY 2018, FDA proposes to discontinue the transfer.

DETAIL OF FULL-TIME EQUIVALENT EMPLOYMENT (FTE)

	FY 2016 Actual			FY 2017 Estimate			FY 2018 Estimate		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Center for Food Safety and Applied Nutrition	963	38	1,001	1,009	39	1,048	962	39	1,001
Center for Drug Evaluation and Research	4,172	476	4,648	4,339	484	4,823	4,913	484	5,397
Center for Biologics Evaluation and Research	1,039	63	1,102	1,069	64	1,133	1,110	64	1,174
Center for Veterinary Medicine	582	13	595	595	13	608	583	13	596
Center for Devices and Radiological Health	1,633	85	1,718	1,657	86	1,743	1,741	86	1,827
National Center for Toxicological Research	299	---	299	304	---	304	304	---	304
Office of Regulatory Affairs	4,668	335	5,003	4,794	340	5,134	4,554	340	4,894
Headquarters and Office of the Commissioner.....	1,142	67	1,209	1,205	68	1,273	1,264	68	1,332
Export Certification	26	---	26	26	---	26	26	---	26
Color Certification	36	---	36	36	---	36	37	---	37
Family Smoking Prevention and Tobacco Control Act...	716	29	745	831	29	860	851	29	880
Total.....	15,275	1,106	16,381	15,864	1,124	16,988	16,344	1,124	17,468

Five Year History of GS/GM Average Grade

Year	Grade
FY 2014	13
FY 2015	13
FY 2016	13
FY 2017	13
FY 2018	13

* FTE figures do not include an estimated 81 reimbursable, 2 CRADA, 2 FOIA, 44 PEPFAR, and 17 EBOLA.

DETAIL OF POSITIONS

	FY 2016 Actuals	FY 2017 Annualized CR	FY 2018 President's Budget
Executive Level			
Executive Level I.....	---	---	---
Executive Level II.....	---	---	---
Executive Level III.....	---	---	---
Executive Level IV.....	1	1	1
Executive Level V.....	---	---	---
Total Executive Level	1	1	1
Executive Service (ES)			
Executive Service.....	66	68	70
Total Executive Service.....	66	68	70
General Schedule (GS)			
GS-15.....	1,649	1,713	1,765
GS-14.....	3,492	3,627	3,737
GS-13.....	4,606	4,784	4,930
GS-12.....	2,039	2,118	2,182
GS-11.....	763	793	817
GS-10.....	11	11	12
GS-9.....	632	656	676
GS-8.....	112	116	120
GS-7.....	439	456	470
GS-6.....	70	73	75
GS-5.....	127	132	136
GS-4.....	58	60	62
GS-3.....	29	30	31
GS-2.....	6	6	6
GS-1.....	1	1	1
Total General Schedule.....	14,034	14,576	15,020
Administrative Law Judges (AL)	1	1	1
Scientific/Senior Level (ST/SL).....	3	3	3
Senior Biomedical Research Service (RS).....	50	52	53
Scientific Staff Fellows (RG) (Title 42)	936	971	998
Distinguished Consultants/Senior Science Managers (RF) (Title 42)	151	157	161
Commissioned Corps (CC):			
Commissioned Corps - 08/07/06.....	243	247	247
Commissioned Corps - Other	863	877	877
Total Commissioned Corps.....	1,106	1,124	1,124
Administratively Determined (AD) (includes Title 42) ²	---	---	---
Wage Grade	15	16	16
Consultants ²	18	19	21
Total Mandatory Resources - Directed Transfer.....	---	51	51
Total FTE (End of Year)¹.....	16,381	16,988	17,468
Average ES Level	3	3	3
Average ES Salary	\$177,917	\$181,653	\$185,195
Average GS grade	13	13	13
Average GS Salary	\$108,080	\$110,350	\$112,501

¹ Does not include an estimated 81 reimbursable, 2 CRADA, 2 FOIA, and 44 PEPFAR FTE. Also excludes 17 FTE for the emergency Ebola fund.

² Includes consultants appointed under 5 U.S.C. 3109, those appointed under similar authorities, and those appointed to serve as advisory committee members. However, scientists hired under Title 42 are now included in the Distinguished Consultants/Senior Science Managers (RF) category.

PHYSICIANS' COMPARABILITY ALLOWANCE (PCA) WORKSHEET

Food and Drug Administration

	FY 2016 (Actuals)	FY 2017* (Estimates)	FY 2018* (Estimates)
1) Number of Physicians Receiving PCAs	1	0	0
2) Number of Physicians with One-Year PCA Agreements	0	0	0
3) Number of Physicians with Multi-Year PCA Agreements	1	0	0
4) Average Annual PCA Physician Pay (without PCA payment)	\$153,702	0	0
5) Average Annual PCA Payment	\$26,000	0	0
6) Number of Physicians Receiving PCAs by Category (non-add)	Category I Clinical Position	0	0
	Category II Research Position	1	0
	Category III Occupational Health	0	0
	Category IV-A Disability Evaluation	0	0
	Category IV-B Health and Medical Admin.	0	0

*The one remaining employee's PCA was terminated at the beginning of FY 2017, as of October 20, 2016.

- 7) If applicable, list and explain the necessity of any additional physician categories designated by your agency (for categories other than I through IV-B). Provide the number of PCA agreements per additional category for the PY, CY and BY.

FDA does not have a need for the additional physician categories other than Category II identified in number 6.

- 8) Provide the maximum annual PCA amount paid to each category of physician in your agency and explain the reasoning for these amounts by category.

FDA utilizes the Category II to hire physicians that are not eligible for Title 38 PDP. The maximum annual PCA for FY 2016 was reduced to \$26,000 for the employee receiving PCA based upon the agreement. Effective October 20, 2016, the employee's PCA was terminated and the PCA that the employee received in FY 2017 was \$2,846.11.

- 9) Explain the recruitment and retention problem(s) for each category of physician in your agency (this should demonstrate that a current need continues to persist).

FDA made a decision in 2008 to convert all eligible physicians to Title 38 PDP which is useful in allowing the agency to effectively recruit and retain medical officers across the FDA. The minimal continued use of PCA allowed FDA the ability to recruit physicians who are not eligible for Title 38 PDP. Effective October 1, 2016 (FY 2017), the FDA will no longer use PCA as a recruitment and retention incentive.

- 10) Explain the degree to which recruitment and retention problems were alleviated in your agency through the use of PCAs in the prior fiscal year.

FDA did not experience recruitment or retention problems of physicians and dentists in FY 2016. FDA used PCA as a means to recruit candidates that are not eligible for Title 38 PDP prior to FY 2016.

- 11) Provide any additional information that may be useful in planning PCA staffing levels and amounts in your agency.

FDA used PCA as an additional authority to hire and compensate physicians that are not eligible for Title 38 PDP.

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HOUSE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

HOUSE COMMITTEE REPORT (114-531)

1. Animal Drug Compounding

The Committee is concerned that the FDA has proposed draft guidance for industry (#230) for animal drug compounding that applies Sections 503A and 503B of the FDCA to animal health even though these provisions were written in regard to compounding of human drugs. The Committee is concerned that this will result in confusion in the industry and may result in a misallocation of the resources Congress makes available to the FDA to oversee compounding activities. The Committee expects that any final guidance on animal drug compounding will reference statutory provisions that specifically relate to veterinary practices.

FDA Response:

FDA issued the draft Guidance for Industry (#230), “Compounding Animal Drugs from Bulk Drug Substances,” to provide clarity regarding the conditions under which FDA generally would not intend to take action against state-licensed pharmacies, licensed veterinarians, and outsourcing facilities for compounding animal drugs from bulk drug substances. Animal drugs compounded from bulk drug substances do not have legal marketing status under the Federal Food, Drug, and Cosmetic Act (FD&C Act); however, FDA recognizes that such drugs may be a necessary and appropriate treatment option for animals in certain circumstances. Thus, this draft Guidance provides FDA’s thinking on our enforcement discretion in this area.

In the draft guidance, FDA is not proposing to apply sections 503A or 503B of the FD&C Act to the compounding of animal drugs from bulk drug substances. However, some of the conditions proposed in the draft guidance appear similar to conditions in section 503B, where appropriate. FDA proposed this approach because many of the concepts embodied in sections 503A and 503B may be appropriate for animal drugs, as well as for human drugs. Additionally, many compounders who compound human drugs also compound animal drugs and are already familiar with this framework and can readily implement it. The approach taken in the draft guidance reflects FDA’s intent to strike the proper balance between the need to provide access to compounded drugs, when necessary, and the need to preserve the integrity of the animal drug approval process, which provides assurances that drugs are safe and effective, properly manufactured, and appropriately labeled.

In regard to finalizing the draft guidance, FDA received more than 150 comments on the draft guidance. FDA will carefully consider these comments and other information received before finalizing the draft guidance.

2. Antibiotics

The Committee urges the FDA to work to foster the development of new antibiotics by supporting greater collaboration between industry and the FDA around adaptive clinical trials and labeling changes. The President's Council of Advisors on Science and Technology has recommended this proposal to help support the type of robust drug development that will be needed to ensure patients are protected from bacterial resistance.

FDA Response:

FDA considers mitigation and prevention of antibiotic resistance a top priority. FDA will continue to collaborate with experts from academia, the pharmaceutical industry, professional societies, patient advocacy groups, and other Public Health Service agencies to find solutions to scientific challenges in the development of new antibacterial drugs.

A draft Guidance for Industry document on possible streamlined drug development pathways for drugs intended for the treatment of serious bacterial diseases in patients who have an unmet medical need has been published that includes recommendations for clinical trial designs and labeling. The Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD) established as part of the 21st Century Cures Act allows FDA, at an applicant's request, to approve an antibacterial or antifungal drug as a limited population drug. Some antibacterial drugs that are candidates for a streamlined development program may also be candidates for LPAD. In certain circumstances, LPAD will allow FDA to conclude that the benefits of a drug outweigh its risks in a particular limited population, despite greater uncertainty. FDA is developing draft guidance describing the criteria, processes, and other general considerations for demonstrating the safety and effectiveness of limited population drugs.

Cooperation between FDA and industry, along with our partners in other Public Health Service agencies, could facilitate advancements in the field. These efforts should help to facilitate the development of new antibacterial drugs to address patient needs.

3. Biological Products

The Committee commends the FDA for issuing draft guidance to address the mixing, diluting, or repackaging of biological products outside the scope of an approved biologics license application. The Committee urges the FDA to finalize the guidance without delay following the public comment period and continues to emphasize the need for close FDA inspection and supervision of large-scale compounding and repackaging of sterile injectable drugs and biological products, particularly products that are administered into areas of the human body where there is tempered immunity, such as the eye or spinal column, to ensure that they are processed in keeping with current good manufacturing practice for sterile products, in particular 21 CFR 200.50 regarding ophthalmic preparations.

FDA Response:

FDA shares the Committee's concern about the public health risks associated with improper manipulation of sterile, injectable drug products, including biological products. FDA has been working to balance minimizing public health risks with ensuring that patients have access to medicines appropriate for their health needs. In January 2017, FDA issued a revised draft guidance concerning mixing, diluting, and repackaging biological products by state-licensed pharmacies, federal facilities, physicians, and outsourcing facilities. The revised draft guidance, published for public comment, includes changes to address comments that FDA received on the initial draft guidance. The comment period on the revised draft guidance closed on March 14, 2017, and FDA received 11 comments. FDA intends to review the comments and finalize the guidance document as quickly as possible.

4. Biosimilars

The Committee recognizes that biosimilars offer an important opportunity for expanding the market and reducing costs for patients. The Committee urges the FDA to partner with external stakeholders including patient organizations on educating patients and professionals about biosimilars, with a focus on populations for which approved biosimilars are indicated.

FDA Response:

FDA remains committed to working with stakeholders, including drug manufacturers, prescribers, pharmacies, hospitals and health systems, informatics providers, and patient groups on this important issue.

5. Blood Donor Policies

The Committee commends the FDA on updating their blood donor policy in the December 2015 Guidance to Industry from a lifetime ban to a one year deferral, however it continues to encourage a permanent policy change based on scientifically supported risk factors and not time passed. The Committee remains concerned that certain questions on the FDA blood donor questionnaire are outdated and discriminatory. This questionnaire should not ask about sexual orientation, rather it should assess risk factors that might expose a potential blood donor to blood-borne illness. The Committee encourages FDA to find an adequate replacement question for the blood donor questionnaire that is cognitively appropriate and will maintain a safe donor pool without discrimination.

FDA Response:

FDA is committed to reevaluating and updating its blood donor deferral policies to reduce the risk of HIV transmission as new scientific data become available. FDA changed its recommendations from an indefinite deferral for men who have sex with men (MSM) to a 12-month deferral from the last sexual contact as described in the December 2015 guidance. This change has been implemented widely by blood collection establishments since that time. In July 2016, FDA established a public docket for comment on the Agency's blood donor deferral recommendations for reducing the risk of HIV transmission by blood and blood products. Specifically, with regard to the 12-month deferral for MSM, FDA invited the submission of scientific evidence on the feasibility of moving from the existing time-based deferrals related to risk behaviors to alternate options, including the use of individual risk assessments. To date, 670 comments were received (many against further policy change), a number of comments provided recommendations, some of which were supported by scientific evidence.

Over the next years, FDA plans to study the feasibility, effectiveness, and operational impact of alternative donor history questionnaires. These alternatives would include individual risk assessment questionnaires that do not ask about sexual orientation.

Additionally, FDA has launched initiatives to facilitate new “real time” monitoring of markers of transmissible infectious diseases and related risk factors in donors of blood components. In September 2016, FDA in collaboration with the National Heart, Lung and Blood Institute, and the Department of Health and Human Services (HHS) Office of the Assistant Secretary for Health, established the Transfusion-Transmissible Infections Monitoring System (TTIMS). This system should provide invaluable data for estimating the incidence and prevalence of HIV,

hepatitis B virus, and hepatitis C virus infection in blood donors. TTIMS is actively assessing transfusion-transmitted infection markers, behavioral risk factors for positive donors, and other epidemiologic variables among voluntary U.S. blood donors that may be useful to assess changes in the donor base including the impact of the change made to the MSM deferral.

6. Centers of Excellence

The Committee is encouraged by the ongoing research and collaboration underway at the Centers of Excellence in Regulatory Science and Innovation (CERSI) program. The Committee believes that these programs will help the agency improve public health, address scientific challenges presented by revolutions in medical product development, and improve food safety and quality. The Committee commends the agency for launching this program in 2011 and expanding it in 2014. For this reason, the Committee believes that the agency should continue to invest in the existing four locations in the CERSI network at their original funding level to ensure their efficacy and to capitalize on existing studies.

FDA Response:

FDA appreciates the recognition of the importance of the CERSIs, their contributions to regulatory science, and identification of support for them. FDA plans to support four CERSIs under the new grant awards that were made in FY 2016. Three of these are existing CERSIs and one is new.

7. Compassionate Use

The Committee is aware of GAO's current plans to conduct a review of the FDA's work with patient stakeholder groups as it relates to Expanded Access or Compassionate Use of human drugs. The Committee encourages the FDA to work with GAO in order to provide them with all the necessary information they need to complete their review of the program.

FDA Response:

FDA is committed to working with GAO and providing the necessary information they need to complete their review.

8. Continued FDA Approval of Drug Safety Labeling

The Committee is deeply concerned with the FDA's failure to resolve issues with and finalize its proposed rule entitled "Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products." The proposed rule, as currently drafted, has the potential to threaten public health and create unprecedented patient and provider confusion by allowing multiple versions of safety labeling for the same bioequivalent product. The Committee urges the FDA to establish in the final rule a system where safety information in prescription drug labeling in a multisource environment (i.e., when there is both an innovator and a generic manufacturer or more than one generic manufacturer) is always FDA-approved, grounded in scientific evidence, and presents no opportunity for mismatched safety information between the innovator and generic versions of a drug. The FDA should be the final decision maker regarding whether a manufacturer should change its labeling in a multisource environment. The FDA is the only entity that possesses all of the clinical trial, safety, and post-marketing data submitted by all manufacturers. Only the agency has all of the necessary tools to make an informed decision when it comes to making safety labeling changes, and, as a result, consistent with the FDA's responsibility to approve drug applications and labeling prior to marketing, only the FDA should determine whether a safety labeling change should occur.

FDA Response:

The proposed rule was intended to improve the communication of important drug safety information to healthcare professionals and patients. FDA has received a great deal of public input from stakeholders during the comment period on the proposed rule regarding the best way to accomplish this important public health objective.

FDA is carefully considering comments submitted to the public docket established for the proposed rule from a diverse group of stakeholders including: consumers and consumer groups, academia (including economists), health care associations, drug and pharmacy associations, brand and generic drug companies, law firms, state governments, and Congress, including comments proposing alternative approaches to communicating newly acquired safety-related information in a multi-source environment (see FDA-2013-N-0500). These comments include a summary of FDA's meeting with the Generic Pharmaceutical Association (GPhA) on September 8, 2014, to listen to their comments and views regarding the proposed rule.

In addition, FDA held a public meeting at which any stakeholder had the opportunity to present or comment on the proposed rule, or on any alternative proposals intended to improve communication of important, newly acquired drug safety information to healthcare

professionals and the public. In the February 18, 2015, notice announcing the public meeting, FDA reopened the docket for the proposed rule until April 27, 2015, to allow the submissions of written comments concerning proposals advanced during the public meeting. FDA will determine next steps based on our analysis of comments on the proposed rule and additional information submitted as part of the public meeting.

9. Crop Biotechnology & Biotech Ingredients

Plants, food, and food ingredients developed using genetic engineering were introduced into the U.S. food supply in the 1990s. Public and private sector scientists knowledgeable in genetic engineering, toxicology, chemistry, nutrition, and other scientific areas have carefully evaluated and assessed the safety of these products and have determined that such products are safe for human and animal consumption. The Committee provides a total of \$3,000,000 for the FDA to coordinate with the U.S. Department of Agriculture (USDA) to provide education and outreach to the public on the safety and benefits of crop biotechnology and food and animal feed ingredients derived from biotechnology. The Committee expects this educational information to be posted on both agency websites and through other social media and communications platforms within 60 days of enactment of this Act.

FDA Response:

FDA continues to work with USDA and the U.S. Environmental Protection Agency (EPA), under the [Coordinated Framework for the Regulation of Biotechnology](#), to promote public confidence in the oversight and development of safe biotechnology products. In an ongoing effort to [modernize the regulatory system for biotechnology products](#), FDA (along with EPA and USDA) is reviewing existing communication tools and, as appropriate, may revise existing or develop new user-friendly sources of regulatory information for product developers and the general public.

FDA's communications materials discuss the Agency's regulatory role in ensuring that foods from genetically engineered (GE) plants meet the same food safety requirements as foods derived from traditionally bred plants. The materials encourage GE plant developers to participate in FDA's voluntary Plant Biotechnology Consultation Program to foster collaboration and transparency and enhance regulatory compliance. FDA and industry coordination and cooperation increases public trust in the safety of foods from GE plants – and confidence in regulatory and industry communications about food safety evaluations.

FDA does not address potential agricultural, environmental (e.g., pest control, weed control, land use, irrigation, yield, etc.) or humanitarian benefits which are beyond the scope of its mandate or expertise. To help maintain public confidence in FDA's role in conducting food

safety reviews, FDA believes it is more appropriate for other agencies to take the lead in conveying messages regarding the benefits of biotechnology within their purview and expertise. Additionally, to conduct an educational campaign of the magnitude envisioned in the House report would require significantly more than 60 days to produce, pilot test, and disseminate the necessary consumer outreach materials.

If provided an additional \$3,000,000 in budget authority above FY 2016 funding levels to carry out education and outreach on crop biotechnology oversight, FDA would do so in cooperation with partners such as USDA and EPA. Funds likely would be provided to an outside contractor to assist in the education campaign. Wherever possible, FDA would leverage existing subject matter experts to support this effort. However, without additional funding in FY 2017, this requirement will impose a significant burden on existing staff and will divert resources away from other important biotechnology initiatives (e.g., consideration of new biotechnology methods and the safety of foods derived from them), as well as other education and outreach efforts.

10. Date Labels on Food

The Committee is concerned by the amount of food waste resulting from consumer confusion around date labels on food. The Committee notes that there is currently no federal uniform system for food date labels, which are currently determined by the food company to indicate quality rather than the safety of the food. The Committee urges FDA to study current and potential date labeling language and formats to determine what language and/or format is most effective in reducing consumer confusion and communicate such voluntary options to food producers.

FDA Response:

A principle of U.S. food law is that foods in U.S. commerce must be fit for consumption. The FD&C Act places a legal duty on manufacturers, processors, and distributors to ensure that the foods they market to consumers are safe and comply with all legal requirements. A "best by," "use by," or expiration date does not relieve a firm from this obligation. A product that is dangerous to consumers would be subject to potential action by FDA to remove it from commerce regardless of any date printed on a label. With the exception of infant formula, the laws and regulations enforced by FDA leave to manufacturers the decision whether to place and what criteria to use in placing "expired by," "use by," or "best before" dates on food products; however, FDA regulations that prohibit manufacturers from labeling food in a manner that is misleading or deceptive apply to the use of such statements.

Parties seeking solutions to the problem of food waste in the United States often point to the absence of a national uniform system for date labeling for packaged foods as a key factor that contributes to food waste. Advocates for more uniform date labels cite data suggesting that consumers mistakenly believe that these dates are indicators of safety, and therefore report throwing food away once the date passes, due to fear of safety risks. In recent years, a National Food Waste Reduction Goal has served as a mechanism for bringing greater attention to food waste. FDA has been working to explore ways to reduce food waste while not compromising the safety of the U.S. food supply as part of this effort, and has engaged with the designated lead federal agencies (USDA and EPA) and various trade associations and non-governmental organizations.

11. Drug Compounding

The Committee believes patient access to the right drug at the right time is of utmost importance. In instances where a commercially manufactured drug is not appropriate for a patient for a specific reason, a compounded drug may be the difference between life and death. Since passage of the Drug Quality and Security Act (DQSA) of 2013, the Committee has had concerns that the FDA interpreted provisions of Section 503A of the FDCA in a manner that might jeopardize the availability of compounded medications for “office use.” The practice of “office use” occurs when a compounder will compound a batch of drugs in anticipation of receiving patient-specific prescriptions at a later time. It may also be the case of a doctor in his or her office maintaining compounded drugs on site because it is unsafe or impractical to issue a traditional prescription. This practice is authorized in the vast majority of states and was intended to be allowable under DQSA. The Committee is aware that on April 15, 2016, FDA released a new Draft Guidance on the issue of “office-use” compounding. The Committee directs the FDA to issue a Final Guidance that provides for “office-use” compounding of drugs, in appropriate circumstances as well as including drugs compounded in anticipation of a prescription for an identified individual patient. Such “anticipatory” compounded drugs must be based on the history of previous valid compound prescription orders, and on an established history between the prescriber and the patient and the compounder.

FDA Response:

FDA shares the Committee’s concern about protecting access to compounded drugs for “office use.” FDA is committed to implementing policies in a way that preserves access to compounded drugs, while protecting patients from poor quality compounded drugs that could cause death or serious injury. The policies set forth in FDA guidance documents implement the statutory provisions that provide for compounding and distribution of drugs for office use by outsourcing

facilities under section 503B of the FD&C Act and anticipatory compounding by compounders under section 503A of the FD&C Act.

As you noted, in April 2016, FDA issued draft guidance for public comment titled *Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act*. FDA issued the final guidance in December 2016. As discussed in this guidance, compounding under section 503A of the FD&C Act must occur either after the receipt of a prescription for an identified individual patient (section 503A(a)(1)), or in limited quantities before the receipt of a prescription for an identified individual patient (section 503A(a)(2)). Section 503A does not provide for the distribution of a compounded drug without the compounder first receiving a prescription for an identified individual patient (e.g., for office use).

In contrast, entities that are registered with FDA as outsourcing facilities under section 503B of the FD&C Act can distribute compounded drugs for office use without receiving patient-specific prescriptions (section 503B(d)(4)(C)). FDA is not aware of specific drug products needed for office use that are not supplied by outsourcing facilities.

The prescription requirement in section 503A of the FD&C Act is critical to protecting patients. Although compounded drugs can serve an important need, they pose a higher risk to patients than FDA-approved drugs. Compounded drug products are not FDA-approved, which means they have not undergone FDA premarket review for safety, effectiveness and quality. In addition, although drugs compounded by licensed pharmacists and licensed physicians in accordance with section 503A are subject to certain requirements of the FD&C Act, such as the prohibition on preparing drugs under insanitary conditions, they are not subject to manufacture according to CGMP requirements. Because such compounders generally do not register their compounding facilities with FDA and are not under routine FDA surveillance, FDA is often not aware of potential problems with their compounded drug products or compounding practices unless it receives a complaint such as a report of a serious adverse event or visible contamination. When FDA has conducted inspections of state-licensed pharmacies because of serious adverse events or contamination, we have observed serious deficiencies in drug production practices and conditions that could put patients at risk.

For these reasons, patients should only receive compounded drugs if their needs cannot be met by an FDA-approved drug product. The prescription requirement is critical to ensure that compounding by state-licensed pharmacies and physicians under section 503A is based on individual patient need, to differentiate such compounding from conventional manufacturing, and to differentiate compounding by pharmacists and physicians who are primarily subject to state regulation from compounding by outsourcing facilities, which are primarily subject to FDA regulation. Compounding for office stock by 503A facilities would undermine the incentive for compounders to become outsourcing facilities, a critical measure that Congress put in place in

the DQSA to prevent another outbreak on the scale of the 2012 fungal meningitis outbreak, which resulted in over 60 deaths and 750 cases of infection.

12. Drug Compounding Inspections

The Committee understands that the FDA is interpreting provisions of Section 503A of the FDCA to inspect state licensed compounding pharmacies under current Good Manufacturing Practices (cGMPs) instead of under the standards contained in the United States Pharmacopeial Convention (USP) for sterile and non-sterile pharmaceutical compounding or other applicable pharmacy inspection standards adopted by state law or regulation. The Committee reminds the FDA that compounding pharmacies are not drug manufacturers, but rather, are state licensed and regulated health care providers that are inspected by state boards of pharmacy pursuant to state laws and regulations that establish sterility and other standards for the pharmacies operating within their states. Compounding pharmacies are more appropriately inspected using USP standards or other pharmacy inspection standards adopted by state law or regulation in the state in which a pharmacy is licensed.

FDA Response:

After the 2012 fungal meningitis outbreak, and until August 2016, FDA investigators had been listing on Forms FDA-483 inspectional observations relating to deviations from drug production practices that could lead to quality problems without regard to whether the observations related to current good manufacturing practice (CGMP) requirements deficiencies or other deficiencies.

Only after the inspection did FDA determine whether the state-licensed pharmacies failed to meet the conditions of section 503A of the FD&C Act, and, as a result, the drugs compounded in their facilities were ineligible for the exemption from CGMP requirements in section 503A. This practice led to the perception that FDA was imposing CGMP requirements on state-licensed pharmacies even if they met the conditions of section 503A.

In response to stakeholder input, FDA changed its practice. As of August 2016, FDA only includes on the Form FDA-483 observations related solely to CGMP requirements if, based on the FDA investigator's preliminary assessment, the compounder produces drugs that are not eligible for the exemptions under section 503A. This change in practice has reduced the number of state-licensed pharmacies receiving Forms FDA-483 listing observations related solely to CGMP requirements. Yet, FDA continues to issue Forms FDA-483 listing observations related solely to CGMP requirements because FDA investigators find that the majority of state-licensed pharmacies they inspect are not meeting the conditions of section 503A and,

therefore, preliminarily assess that the pharmacies' drug products are subject to CGMP requirements.

Furthermore, although drugs compounded by pharmacies that meet the conditions of section 503A qualify for exemptions from three provisions of the FD&C Act, including CGMP requirements, they remain subject to all other applicable provisions of the FD&C Act related to the production of drugs. For example, drugs compounded by pharmacies operating under section 503A must not be prepared, packed, or held under insanitary conditions whereby the drug may have been contaminated by filth, or whereby it may have been rendered injurious to health. Section 501(a)(2)(A).

When FDA finds that a pharmacy compounds drugs in accordance with section 503A and does not violate other applicable Federal laws, FDA generally defers regulatory oversight of the pharmacy to the state, but when a pharmacy fails to produce drugs in accordance with section 503A or violates other Federal laws, such as preparing, packing, or holding drugs under insanitary conditions, FDA may pursue regulatory action.

With respect to the Committee's statement that "compounding pharmacies are more appropriately inspected using USP standards or other pharmacy inspection standards adopted by state law or regulation in the state in which a pharmacy is licensed," FDA inspects compounding facilities for compliance with applicable Federal requirements, not "inspection standards adopted by state law or regulation." FDA cannot tailor each inspection to the unique standards of 50 different states, and a pharmacy may be licensed in many states, each with different requirements. For example, some states require compliance with USP Chapters 795 and 797, but many do not.

FDA collaborates with its state partners on regulation of compounding. However, we also have an obligation to take our own action to protect the American public from adulterated, misbranded, and/or unapproved new drugs produced by compounding facilities in violation of Federal law. If we do not, it will become more likely that another outbreak could occur like the 2012 fungal meningitis outbreak, which resulted in over 60 deaths and over 750 cases of infection.

13. Drug Compounding of Allergen Extracts

The Committee is concerned that proposed changes to general chapter 797 of the USP contradicts the legislative intent of Section 503A of DQSA regarding the practice of "office-use" compounding of allergen extracts. The FDA recognizes USP general chapter 797 as federal policy on the practice of drug compounding. The Committee is concerned that the proposed changes to USP general chapter 797 would be inconsistent with its legislative intent of Section

503A and with the agency's own previous positions on the practice of office-use compounding of allergen extracts. It is the sense of the committee that the practice of office-use compounding of allergen extracts by physicians is proven to be both safe and effective for the diagnosis and treatment of allergic conditions. The Committee suggests that the USP work with organizations from the physician and patient communities that represent physicians who regularly engage in office- use compounding of allergen extracts or patients who benefit from such compounding of allergen extracts, to ensure that any changes to USP general chapter 797 regarding office-use compounding of allergen extracts are reflective of the clear legislative intent of Section 503A of the DQSA.

FDA Response:

At the outset, the Committee should be aware that the USP is an independent, non-governmental standard-setting organization. Representatives of FDA serve as liaisons to certain USP expert committees to provide recommendations and guidance on scientific and public health matters, but FDA liaisons are not voting members of USP expert committees and do not control the standards that the USP establishes.

Section 503A of the FD&C Act does not apply to biological products, including allergenic extracts that are subject to licensure under section 351 of the PHS Act. Section 503A describes the conditions that must be met for certain compounded drug products to qualify for exemptions from three provisions of the FD&C Act, including new drug approval requirements in section 505. Although section 503A provides an exemption for certain compounded drugs from the requirement to obtain premarket approval under section 505 of the FD&C Act, it does not provide an exemption from the requirement to obtain premarket approval under section 351 of the PHS Act. Manufacturers of biological products, including allergenic extracts, are required to obtain an approved license under section 351 of the PHS Act. Because section 503A does not provide an exemption from the licensure requirement under section 351 of the PHS Act, for purposes of section 503A, the term *drug* does not include any biological product that is subject to licensure under section 351 of the PHS Act. Accordingly, such biological products are not eligible for the exemptions for compounded drugs in section 503A of the FD&C Act.

Combinations of licensed allergenic extracts as prescription sets for subcutaneous treatment of individual patients who have allergies have not been reviewed for safety, purity, and potency and licensed by FDA. Nevertheless, FDA recognizes the importance of preserving patient access to such products when they meet appropriate quality standards to prevent patient harm. In January 2017, FDA published for public comment a revised draft guidance document titled, "Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved

Biologics License Application.” Among other things, this revised draft guidance will, when finalized, describe FDA’s current thinking regarding State-licensed pharmacies, Federal facilities, outsourcing facilities, and physicians that prepare prescription sets of allergenic extracts. The revised draft guidance states, in part, that FDA does not intend to take action for violations of section 351 of the PHS Act or sections 502(f)(1), 582, or 501(a)(2)(B) of the FD&C Act if prescription sets are prepared by a State-licensed pharmacy, Federal facility, or physician in accordance with certain conditions. One of these conditions is that the prescription set be prepared in accordance with USP Chapter 797, with the exception of the beyond use date, which is addressed separately in the guidance.

The revised draft guidance refers to the current USP Chapter 797 (USP 39-NF 34 (2016)), and not to USP’s proposed revision. The revised draft guidance further explains that FDA intends to consider whether to update its guidance document to refer to the revised chapter once USP issues a final revision to Chapter 797. FDA received 11 comments on the revised draft guidance, including one comment from allergy organizations. In their submission, the allergy organizations stated that they are very pleased that FDA has clarified, in the revised draft guidance that its reference to USP Chapter 797 refers to the current version of that chapter and not any future chapter. The allergy organizations’ other comments, such as those relating to allergen extracts used for intradermal testing and the distribution of prescription sets, will be taken into consideration as FDA works on finalizing its guidance.

14. Duchenne Muscular Dystrophy

The Committee is encouraged that the FDA has the tools, authorities, and latitude necessary to review and approve safe and effective treatments for rare diseases, such as Duchenne Muscular Dystrophy, as efficiently as possible. In particular, the Committee is aware that the use of intermediate clinical endpoints (ICE) may be an appropriate approach as it has been in similar deadly diseases with dire unmet needs, such as HIV and cancer.

FDA Response:

FDA is committed to engaging with patient groups to receive valuable input during the evaluation of the medical needs of patients with rare diseases whenever appropriate. We appreciate the proposed guidance that members of the Duchenne muscular dystrophy (DMD) community submitted to FDA in June 2014. FDA announced the DMD community’s guidance through a Federal Register notice (September 4, 2014) to seek additional input and public comment. FDA carefully considered the community’s guidance and public comments received in response to it in writing the agency’s own draft guidance.

The draft guidance for industry, “Duchenne Muscular Dystrophy and Related Dystrophinopathies: Developing Drugs for Treatment,” was released in June 2015, and a 60-day

comment period was provided. We are currently reviewing the comments received and plan to issue a final guidance following review of those comments. The purpose of the guidance to industry is to assist sponsors in the clinical development of drugs for treating X-linked Duchenne muscular dystrophy and related dystrophinopathies, discuss various pathways to approval including the use of intermediate clinical endpoints, and to serve as a focus for continued discussions on this topic.

15. Emerging Public Health Threat Funding

In order for the FDA to mount as rapid a response as possible to the spread of the Zika virus, the Committee reinforces its position that the agency obligate unobligated Ebola funds for the higher threat of Zika. The legislative text of the fiscal year 2015 emergency supplemental provided the FDA with such flexibility to deal with future public health emergencies such as those threats associated with the Zika viruses. Due to ongoing threats, the bill includes an appropriation of \$10,000,000 to support needs related to work on Ebola and Zika, such as support for FDA staff conducting ongoing response activities; support for regulatory science research to develop the tools, standards, and approaches to characterize investigational medical product safety, efficacy, quality, and performance; and support to expedite the development and availability of medical products for Ebola and Zika.

FDA Response:

The FDA reallocated \$4,975,000 of its Ebola emergency funding resources to support its response to the Zika virus outbreak. The FDA appreciates the inclusion of \$10,000,000 to support needs related to work on Ebola and Zika and would use this funding for further response activities including supporting the development and availability of medical countermeasures.

16. FDA and Centers for Medicare and Medicaid Services (CMS) Parallel Review Pilot

The Committee directs the FDA to provide a report within 60 days of enactment of this Act on whether it plans to once again extend the pilot and steps the agency will take to encourage more manufacturers to utilize the pilot, including considerations for manufacturers choosing the 510(k) approval pathway and for novel products deemed covered by CMS but that warrant evaluation to ensure the appropriate level of coverage. The Committee also directs the FDA to report on efforts to work with CMS to balance each agency's evidentiary needs with the burden on manufacturers, including the consideration and use of alternative trial designs.

FDA Response:

FDA and CMS have made the pilot Parallel Review Program into a permanent program, as stated in the published guidance 81 FR 73113-15 (Oct. 24, 2016). CMS, rather than FDA, determines the appropriate level of coverage. FDA and CMS continue to work together to balance sponsor evidence requirements to find the least burdensome approach to evidence collection.

17. FDA Partnerships under FSMA

The purpose of FSMA is to reform the nation's food safety laws to ensure a safe public food supply. As the FDA continues implementation of FSMA, the Committee encourages the FDA to work in partnership with existing government food safety programs, including the use of MOUs, to verify compliance with FSMA rules once they are finalized as a way to eliminate duplication of activities under the law. In addition, the Committee continues to provide \$5,000,000 for the Food Safety Outreach Program under NIFA and expects that NIFA will serve as the sole agency providing food safety training, education, outreach, and technical assistance at the farm level.

FDA Response:

FDA agrees that a strong partnership with other Federal, State, local, tribal, and territorial food programs is critical to achieving high rates of compliance with the FDA Food Safety Modernization Act (FSMA) and other existing food safety laws and regulations. FDA is committed to continuing our strong partnership with existing government food safety programs to implement FSMA and achieve an Integrated Food Safety System. FDA will continue to use Memoranda of Understanding with regulatory partners such as state, local, territorial, and tribal officials, in addition to contracts, grants, and cooperative agreements and other vehicles for partnership. FDA and NIFA have provided funding through grants for the National Food Safety Training, Education, Extension, Outreach, and Technical Assistance Grant Program. Grants to establish Regional Centers for Food Safety Training, Outreach and Technical Assistance were awarded to University of Florida Gainesville, Oregon State University, Iowa State University, and University of Vermont and State Agricultural College to provide food safety training, education, outreach, and technical assistance at the farm level. A grant to establish the National Coordination Center, coordinating with the Regional Centers, was awarded to the International Food Protection Training Institute in Battle Creek, Michigan. Both FDA and NIFA will continue to work with Regional Centers and the National Coordination Center to advance knowledge among food producers to meet FSMA requirements.

18. Federal Employee Conduct

The federal government grants federal employees with tremendous responsibility and trust to carry out their duties. They must do so free from conflicts of interest and without seeking private gain. Employees are public servants charged with implementing federal programs in a legal and ethical manner. Federal employees are reminded that they shall not advance a personal agenda or give preferential treatment to any outside organization or individual within government programs in which they administer. Information that is received by the employee, including information from the employees, offices, or Committees of the Congress of the United States, should be handled in a professional and confidential manner according to the federal government's code of conduct, standards, regulations, and statutes. The Committee is aware of recent conduct in violation of these principles, and the Committee believes that it is incumbent upon agency officials to take immediate disciplinary action when they confirm such behavior.

FDA Response:

The agency continues to strengthen its ethics and integrity program to help employees avoid conflicts of interest. The agency is committed to preventive activities, such as continuing awareness campaigns of ethics standards for employees and in depth training to supervisors and managers to avoid conflicts. Additionally, the agency has established recommended actions when behavior in violation of these principles has been confirmed.

19. Food Contact Notification User Fees

The funds made available by this Act include sufficient monies to fund the FDA's Food Contact Notification Program and shall be deemed to satisfy the requirements of 21 U.S.C. 348(h)(5)(A). The Committee recommendation does not include proposed user fees.

FDA Response:

FDA acknowledges the Committee's recommendation on the proposed user fees.

20. Genomic Editing

The Committee understands the potential benefits to society in the genetic modification of living organisms. However, researchers do not yet fully understand all the possible side effects of editing the genes of a human embryo. Editing of the human germ line may involve serious and unquantifiable safety and ethical issues. Federal and non-federal organizations such as the National Academy of Sciences and National Academy of Medicine continue to understand the potential risks of genome editing and a broader public discussion of the societal and ethical

implications of this technique is still ongoing. In accordance with the current policy at the National Institutes of Health, the Committee includes bill language that places a prohibition on the FDA's use of funds involving the genetic modification of a human embryo. The Committee continues to support a wide range of innovations in biomedical research, but will do so in a fashion that reflects well-established scientific and ethical principles.

FDA Response:

FDA currently does not accept investigational new drug applications in which a human embryo is intentionally created or modified to include a heritable genetic modification. FDA continues to work with organizations, such as the National Academies of Sciences, Engineering, and Medicine, to understand the scientific, medical, societal, and ethical implications of human germ line gene editing.

21. Harm Reduction

It is the Committee recommendation that the FDA consider the benefits of harm reduction as part of evaluations under the Deeming regulations for tobacco products.

FDA Response:

FDA recognizes that there is a continuum of risk for users of tobacco products. The agency will rely on sound science to evaluate the public health impact of new FDA-regulated tobacco products. The Agency has taken multiple actions concerning harm reduction. These actions include issuing draft guidance on modified risk tobacco products and soliciting comments on the continuum of risk and how it should impact regulatory policy. The concept of risk also plays a role in the agency's evaluation of new products. For example, premarket tobacco applications are to include information about investigations on the health risks of the new tobacco product and whether that tobacco product presents *less risk than other tobacco products*. The agency's evaluation of these applications includes an assessment of the risks and benefits to the population as a whole including users and nonusers of the tobacco product, and takes into account the increased or decreased likelihood of initiation and cessation. FDA reviewed premarket tobacco applications and issued marketing orders for eight snus smokeless tobacco products marketed by Swedish Match North America Inc. under the General brand name. FDA determined that these products would result in a low likelihood of new initiation, delayed cessation, or relapse, and that these products would likely provide less toxic options if current adult smokeless tobacco users used them exclusively.

FDA also has a regulatory pathway for tobacco products that are sold or distributed to reduce harm or the risk of tobacco-related disease. This includes products whose label, labeling, or advertising represents – explicitly or implicitly – that the product is less harmful or presents a lower risk of tobacco-related disease than one or more other commercially marketed tobacco products, or that the product or its smoke contains a reduced level of, presents a reduced exposure to, or does not contain, or is free of a substance. Under Section 911 of the Federal Food, Drug, and Cosmetic Act, FDA has authority to issue an order authorizing a product to be marketed as a modified risk tobacco product if the product will, or is expected to, benefit the health of the population as a whole, taking into account a number of factors including the relative health risks to individuals of the product, the likelihood that existing users of tobacco products who would otherwise stop using such products will switch to the product, and the likelihood that persons who do not use tobacco products will start using the product.

Applicants seeking a risk modification order under Section 911(g)(1) must demonstrate that the product, as actually used by consumers, will significantly reduce harm and the risk of tobacco-

related disease to individual tobacco users and will benefit the health of the population as a whole.

Applicants seeking an exposure modification order under Section 911(g)(2) must demonstrate, among other things, that the product as actually used exposes consumers to the specified reduced level of the harmful substances and generally will not expose them to higher levels of other harmful substances, that consumers will not be misled by the product's labeling/marketing into believing the product has been shown to be less harmful and that the issuance of the order is expected to benefit the health of the population as a whole.

If the modified risk tobacco product is a new tobacco product within the meaning of section 910(a)(1), any applicable premarket review requirements under section 910 of the FD&C Act must also be satisfied.

22. Indoor Tanning Devices

Last December, the FDA proposed two rules intended to prevent the use of sunlamp products, including tanning beds, by certain age groups, reduce the risks for adults using these devices, and require manufacturers to take additional safety precautions. While the Committee remains deeply concerned with the deadly threat of melanoma, it questions some elements of the proposed rules. In particular, the Committee requests that the FDA hold a meeting with industry officials as it begins to consider the final regulations to discuss such issues as the number of allowable visits by adults and other similar measures that could create an undue economic burden on the industry.

FDA Response:

Sunlamp products, which include tanning beds and tanning booths, emit UV radiation that can cause skin cancer. According to the American Academy of Dermatology, people who have been exposed to UV radiation from indoor tanning before age 35 experience a 59 percent increase in the risk of developing melanoma, the deadliest type of skin cancer. This risk increases each time a person uses a sunlamp product, and is higher for younger users. FDA's proposed rules are intended to protect Americans, especially those under 18 years, from skin cancer and other illness or injury. The proposed rules are also intended to help ensure that adults make decisions regarding sunlamp product use based on accurate information. The Agency met in person with manufacturers of indoor tanning equipment while it drafted the rules. FDA looks forward to working with the new Administration on this issue and remains open to additional meetings with industry officials.

23. Late Reports

The Committee reminds the Commissioner that the timelines specified by the Committees on Appropriations of the House and Senate for fiscal year 2016 reports are deadlines that must be met. While the Committee notes that the FDA has made progress in providing more timely information and updates, the FDA still has several outstanding reports that are delayed due to long reviews and clearances. The Committee directs the Commissioner to submit these overdue reports.

FDA Response:

FDA will provide the requested reports.

24. Local Port Cooperation

The Committee directs the FDA to work with local governments at high volume ports of entry to explore activities which reduce the risk of food borne illnesses and enhance the capacity of local officials in dealing with food borne threats.

FDA Response:

FDA's Office of Regulatory Affairs (ORA) works extensively with local ports by directly engaging the local port authorities and U.S. Customs and Border Protection (CBP) and other partner government agencies (PGAs) to examine and control FDA-regulated food products at and around ports of entry. ORA also works with state and local governments on foodborne illness outbreaks, investigations, and appropriate follow-up activities. Additionally, FDA looks at not only volume of entries entering through a port, but also at the risk associated with those entries. The development and implementation of the Foreign Supplier Verification Program (FSVP) regulation and the Voluntary Qualified Importer Program (VQIP), both system-focused, risk-based programs adopted in accordance with the FDA Food Safety Modernization Act (FSMA), will help improve the safety of imported food products and maximize resources at all ports of entry.

25. Mammography Exam Reports

More than four years ago, in November 2011, the National Mammography Quality Assurance Advisory Committee approved a change to the mammogram patient report and physician report to include information regarding an individual's breast density. This process has not been completed. The Committee urges the FDA to implement this change in an expedited manner and must report to Congress on the status of this change no more than 60 days from the enactment of this Act.

FDA Response:

FDA is working with the Administration on this issue and will provide any requested report.

26. Medical Countermeasures

The Committee directs that not less than \$24,552,000 shall be available for the FDA's Medical Countermeasures Initiative. This total is in addition to the unobligated funds remaining to support the FDA's emergency response to Ebola and related disease outbreaks.

FDA Response:

FDA intends to spend the amount directed by the Committee on the activities outlined.

27. Medical Gas Rulemaking

The Committee is significantly concerned that the FDA has not initiated rulemaking to address numerous longstanding regulatory issues for medical gases despite the statutory requirement in the Food and Drug Administration Safety and Innovation Act (FDASIA) to issue a final rulemaking addressing all necessary changes for medical gases by July 9, 2016. In fact, the FDA rulemaking on medical gases is not even listed in the most recent Unified Agenda as a priority. Designated medical gases are a unique class of drugs that differ significantly from traditional pharmaceuticals and therefore must be addressed in the federal drug regulations to prevent safety and enforcement issues caused by current regulations. The Committee disagrees with the FDA report to Congress sent on June 30, 2015, which stated that, despite decades of issues created by existing regulations, “the current regulatory framework is adequate and sufficiently flexible to appropriately regulate medical gases.” The bill includes language requiring the FDA to issue final regulations revising the federal drug regulations with respect to medical gases not later than July 9, 2016. If the Commissioner fails to issue final regulations with respect to medical gases by the statutory deadline, the Commissioner shall incorporate by reference voluntary consensus safety and labeling standards developed by an ANSI-accredited standard development organization until such time as the Commissioner issues final regulations consistent with Section 1112 of Public Law 112–144.

FDA Response:

FDA issued the final rule “Medical Gas Containers and Closures: Current Good Manufacturing Practice Requirements,” on November 18, 2016 (81 FR 81685). This final rule (which revised warning statements for medical gases and required measures intended to reduce the likelihood of medical gas mix-ups) satisfies the FDASIA medical gas rulemaking requirement, though FDA may undertake additional rulemaking on medical gases as needed.

FDA understands that industry stakeholders believe that FDA should promulgate a separate regulatory scheme specific to medical gases, despite the Agency’s determination (explained in its 2015 report to Congress on this topic) that extensive rulemaking in this area is unnecessary. However, FDA remains convinced that we can work within the existing regulatory framework to set clear and appropriate regulatory expectations for the production and distribution of medical gases without extensive additional rulemaking. FDA recently made revisions to the medical gas inspection program (completed in 2015), and is very far along in the process of producing revised guidance on current good manufacturing practices applicable to medical gases.

FDA will, of course, undertake targeted rulemaking on medical gases to address any significant public health issues that arise, or to satisfy statutory rulemaking requirements – as demonstrated by the final rule published in November 2016. However, FDA continues to believe that the separate regulatory scheme for medical gases sought by industry stakeholders is unnecessary.

FDA also has significant concerns with any proposal mandating that FDA incorporate medical gas industry standards by reference. First, incorporation by reference requires notice-and-comment rulemaking, with all of the resource burdens rulemaking entails. Furthermore, the proposal to incorporate by reference “voluntary consensus safety and labeling standards” would first require such standards to be developed, as it does not appear that any currently exist. Rather, the safety and labeling standards industry has sought to have FDA incorporate by reference were created entirely by the industry, with no FDA involvement. In fact, these “standards” are largely identical to the dozens of new regulations industry proposed during the 2013 FDASIA regulation review, and which FDA determined were generally not needed. FDA is not opposed to referencing specific targeted standards co-developed by FDA and the medical gas industry (provided FDA agrees such standards meet regulatory and public health needs) and engaging in rulemaking as necessary and appropriate. However, FDA sees significant legal, policy, logistical, and resource concerns with adopting unvetted industry standards by reference.

Finally, FDA is concerned with the precedent that would be set by creating a separate regulatory scheme for a given product class. In general, FDA believes it is much more efficient to rely upon the general regulatory scheme applicable to all drug products and to provide class-specific recommendations through guidance and other non-rule-making means.

Accordingly, FDA’s position continues to be that the extensive rulemaking sought by industry is not necessary.

28. Laboratories Near High Volume Ports (ORA)

The Committee directs the FDA to submit a report within 90 days of enactment of this Act on the potential for implementing pilot programs which will allow for public-private partnerships at high volume ports of entry in an effort to increase the number of FDA-certified public or private labs located near major ports of entry to provide services on weekends and holidays, reduce the risk of food borne illnesses, and enhance the capacity of local officials in dealing with foodborne threats.

FDA Response:

Currently, FDA does not certify laboratories. However, consistent with section 202 of FSMA, FDA is developing a program for the accreditation of laboratories for analyses of foods. FDA is currently engaged in the rulemaking process for this laboratory accreditation program. Establishing a separate laboratory certification program could be duplicative of the FSMA laboratory accreditation program and divert resources from FDA's implementation of this FSMA provision.

Additionally, it is not clear if the intent is to use the results from these laboratories to support FDA regulatory activities, e.g., to institute a seizure action against a product already in U.S. commerce, or to assist in the surveillance sampling and testing performed by FDA laboratories on foods offered for import to determine admissibility. If the intent is for private laboratories to perform analyses used to support regulatory activities by FDA, there would be many issues to consider.

FDA has previously evaluated the proximity to port issue, including the establishment of satellite laboratories co-located in ports of entry, with limited capabilities for analysis. However, given the increasing complexities of required analyses for imported products and the necessity for rapid screening methodologies that also require greater sensitivities and lower limits of detection, most of this work must be done in a larger, fixed-site, fully functioning laboratory. FDA ORA laboratories currently do maintain weekend schedules which provide weekend capacity to address urgent events.

29. Laboratory Developed Tests

The FDA's draft guidance issued on October 3, 2014, titled "Framework for Regulatory Oversight of Laboratory Developed Tests" (LDTs), puts forth a proposed regulatory framework that is a significant shift in the way LDTs are regulated. Such a shift deserves input from the public, and Congress has been working with stakeholders, constituencies, and the FDA to find common ground on regulating LDTs. The FDA's guidance circumvents the normal rulemaking process and changes expectations for patients, doctors, and laboratories for the first time since the Clinical Laboratory Improvement Amendments Act was passed in 1988. The Committee directs the FDA to suspend further efforts to finalize the LDT guidance and continue working with Congress to pass legislation that addresses a new pathway for regulation of LDTs in a transparent manner.

FDA Response:

FDA appreciates that this topic is of great interest to the Committee members and stakeholders. We would welcome the opportunity to review any legislative proposals from Members of Congress.

30. Medical Device Facility Inspections

The Committee is concerned about the lack of transparency and consistency with the medical device facility inspection process. This often leads to inefficiencies and inconsistencies in the inspection process. The Committee urges the agency to work with stakeholders and Congress to improve the facility inspection process. Potential process improvements may include, but are not necessarily limited to, more timely and frequent communications related to inspection observations and remediation plans, as well as changes to the way medical device Export Certificates (e.g., Certificate to Foreign Government, etc.) are affected by FDA Observational Findings following a facility inspection. In addition, the agency shall produce a report to the Committee by September 30, 2016, which provides information on the rates of inspection for facilities across districts and internationally and any FDA efforts to standardize rates of inspections across districts and internationally. The Committee understands that five days is typically sufficient for the FDA to complete an overseas inspection and determine the suitability of the location to provide product into the U.S. market while inspections inside the U.S. can take several weeks or months to complete the same assessment. These discrepancies lead to variations in inspection standards and potentially competitive advantages for those who choose to manufacture outside the U.S.

FDA Response:

A majority of both domestic and foreign device inspections involve four or fewer days on-site. There are many device inspections that conclude on the same day as arrival. Domestic inspections can take longer than foreign inspections. Foreign inspections are planned for consecutive days (excluding weekends) and more hours are spent at the firm per day than a domestic inspection, while on a domestic inspection an investigator may be completing an inspection over non-consecutive days. FDA has indicated its willingness to hold a public meeting to gather input from affected stakeholders about improvements to the device inspections process. FDA is working with HHS to review legislative proposals intended to help streamline the device inspections process.

FDA is currently addressing domestic inspection times through improved internal procedures and through Program Alignment, which will take effect on May 15, 2017. Program Alignment is FDA's reorganization of its inspection program to a commodity-based and vertically integrated

structure such that, for example, only device specialists will inspect device establishments and drug specialists will inspect drug establishments.

31. Menu Labeling

The Committee is concerned about the recent FDA final determination that increased the size and scope of those affected under restaurant menu labeling regulations. Specifically, the final rule attempts to regulate local grocery chains that typically do not qualify as restaurants. The Committee includes bill language which directs the FDA to implement the final rule no earlier than December 1, 2016, at least one-year following agency publication of related guidance to newly regulated stakeholders.

FDA Response:

FDA issued a final guidance document on May 5, 2016, to help covered establishments comply with the menu labeling final rule, which requires calorie information to be listed on menus and menu boards in chain restaurants and similar retail food establishments with 20 or more locations doing business under the same name and offering for sale substantially the same menu items. The final guidance responds to many of the most frequently asked questions the agency has received through extensive input from stakeholders throughout the process of establishing requirements for menu labeling in certain restaurants and other retail food establishments and to the substantive and useful feedback in the stakeholder comments on the draft guidance published in September 2015.

In December 2016, FDA extended the compliance date for these covered establishments to May 5, 2017, one year after FDA issued the menu labeling final guidance, to ensure that companies have adequate time to fully implement the requirements of the rule.

On May 1, 2017, FDA announced it was extending the compliance date for menu labeling requirements from May 5, 2017 to May 7, 2018.

32. Nanotechnology

The Committee recognizes the increased capabilities that the FDA has developed to study environment, health, and safety of nanomaterials within the FDA's Jefferson Laboratory Campus, including the National Center for Toxicological Research, and its consolidated headquarters at White Oak, Maryland. The Committee recommends continued collaborative research with universities and industry on the toxicology of nanotechnology products and processes, in accordance with the National Nanotechnology Initiative Environment, Health, and Safety Research Strategy as updated in October 2011.

FDA Response:

FDA continues to enhance capabilities to understand the health impact and safety of nanomaterials through staff training, continued research into the safety and disposition of nanomaterials in various products, increased collaboration with government agencies — both national and international — and participation in standards-development activities. FDA continues its efforts to enhance its nanomaterials research infrastructure. Since 2011, the Collaborative Opportunities for Research Excellence in Science (CORES) research program funded a total of 36 projects and is part of FDA’s Nanotechnology Regulatory Science Research Plan. Together with the advanced Nanocore infrastructure at the Jefferson Laboratories campus and facilities at the White Oak campus, FDA is able to conduct research to accurately characterize, detect, and quantify nanomaterial in FDA-regulated products to help assess safety and inform risk assessment. FDA’s Nanotechnology Task Force is committed to advancing nanotechnology research and collaboration.

FDA continues to engage with industry and other agencies through the National Nanotechnology Initiative (NNI), including participation in the US-EU Communities of Research, Indo-US Science and Technology Forum, Nanotechnology for Healthcare Conference, and collaborations with the Consumer Protection Safety Commission, National Institute of Environmental Health Sciences/National Toxicology Program, and the National Cancer Institute.

The 2016 Global Summit on Regulatory Science focused on “Nanotechnology Standards and Applications” and was hosted by FDA/NCTR and Arkansas Research Alliance. There were other U.S. government agencies in attendance at the Summit — held on the NIH campus — as well as participants from 19 countries. This annual Summit is held in cooperation with the European Union and global regulatory and standards agencies to discuss the standards methodologies and standards that are helpful for regulatory reviews. The outcome from the 2016 Summit was a list of standards in nanotechnology that are relevant to drugs, devices, and consumer products. FDA will also continue to engage industry through the standards-development organizations to help develop relevant and consensus based standards that can help regulatory reviews.

33. Nutrient Content Claims

The Committee expects the FDA to amend its “healthy” nutrient content claim regulation to be based upon significant scientific agreement. In addition, to ensure that food producers can make truthful and non-misleading statements about the healthfulness of products, the Committee directs the FDA to make such regulatory changes during the rulemaking process and issue guidance to industry no more than six months after the enactment of this Act providing for the use of the word “healthy” in food labeling statements.

FDA Response:

FDA is currently engaged in updating nutrition labeling regulations to reflect the latest consensus nutrition science, including the 2015-2020 *Dietary Guidelines for Americans*. As the first step, in May 2016, FDA published a final rule updating the Nutrition Facts label regulations to reflect the latest science. Among other updates to nutrition labeling regulations, FDA is considering whether and how to redefine the nutrient content claim “healthy.” FDA is aware that the current definition for “healthy” needs to be updated in order to be consistent with the latest science, and will work collaboratively with all stakeholders in this process, including food producers.

As background, on September 28, 2016, FDA started a public process to solicit stakeholder input on whether and how to redefine the “healthy” nutrient content claim. We published a request for information and comments in the *Federal Register* and issued a guidance document stating that while we consider revisions to the claim, we do not intend to enforce certain current eligibility requirements relating to use of the claim if specific criteria are met. For example, the current regulation requires that foods bearing a “healthy” claim limit the amount of total fat. However, current science shows that the type of fat is more important than the total amount of fat. Additionally, the current regulation for a “healthy” claim requires specific criteria for nutrients to limit, in addition to total fat, such as saturated fat, cholesterol, and sodium, as well as requirements for nutrients to encourage, including vitamin A, vitamin C, calcium, iron, protein, and fiber. These criteria are linked to elements in the Nutrition Facts label regulations. However, the 2016 revision to the Nutrition Facts label requires the declaration and Daily Values for potassium and vitamin D; Vitamins A and C are no longer mandated on the label. Consequently, the guidance on “healthy” advises food manufacturers of our intent to exercise enforcement discretion relative to foods that use the implied nutrient content claim “healthy” on their labels which: (1) are not low in total fat, but have a fat profile makeup of predominantly mono- and polyunsaturated fats; or (2) contain at least 10 percent of the Daily Value per reference amount customarily consumed of potassium or vitamin D.

On December 30, 2016, we extended the comment period to allow more time for public comment on the definition of the term “healthy.” On March 9, 2017, FDA held a public meeting to give interested parties an opportunity to discuss and provide feedback on the use of the term “healthy” on food labels. The information shared during the meeting and throughout the comment period, which closed on April 26, 2017, will help us determine how to proceed with this matter.

34. Nutrition Facts Label

The Committee is concerned that proposed rules that have been issued to revise the Nutrition and Supplemental Facts labels may create confusion and misinformation among consumers. The FDA is encouraged to determine how the proposed new label disclosure statements regarding added sugars would be understood and interpreted by consumers before proceeding with a final rule. Additionally, the FDA should evaluate the consumer perception and impact on healthful nutrient dense foods that use added sugar to make the food more palatable.

FDA Response:

In May 2016, FDA published the final rule for the Nutrition and Supplement Facts labels, in which, after consideration of comments, FDA finalized a declaration requirement for added sugars. FDA required the declaration for added sugars, in part, because excess consumption of added sugars makes it difficult to meet nutrient needs while staying within calorie limits, and can lead to an increase in overall caloric intake. Further, healthy dietary patterns with lower amounts of sugar-sweetened foods and beverages, when compared to less healthy dietary patterns, are associated with a reduced risk of cardiovascular disease.

In collaboration with Federal and other partners, FDA plans to engage in educational activities for consumers and health professionals about the use of information on the Nutrition Facts label. Part of that education will include information about added sugars. A key message related to added sugars will be that consumers should consider all of the information on the Nutrition Facts label when constructing a healthful dietary pattern. Further, a key message will be to moderate—rather than eliminate—intake of added sugars. If consumers choose to eat foods with sugars added to them, for example, for palatability, they may do so in moderation, and cut back on added sugars elsewhere in the diet.

35. Office of Cosmetics and Colors

The Committee recommendation includes not less than \$11,700,000 for cosmetics activities, including not less than \$7,200,000 for the Office of Cosmetics and Colors (OCAC) and other supporting offices within the Center for Food Safety and Applied Nutrition (CFSAN). Funding provided for CFSAN is for direct support of operation, staffing, compliance, research and international activities. The Committee notes that every year since fiscal year 2012 it has requested that OCAC respond to a citizen petition setting safety levels for trace amounts of lead in cosmetics. The Committee is disappointed that OCAC has not responded to these requests and urges OCAC to make this a priority. Therefore, the Committee directs OCAC to respond to the petition by September 15, 2016.

The Committee appreciates OCAC's willingness to engage with China in 2016 for a cosmetics regulatory dialogue. In light of China's importance to U.S.-based manufacturers and consumers, the Committee directs the FDA to seek ways to continually enhance engagement with Chinese regulators on cosmetic technical and regulatory issues. The Committee directs the FDA to promote international regulatory harmonization and trade in cosmetic products by supporting international trade negotiations on cosmetics in the Transatlantic Trade and Investment Partnership, the International Cooperation on Cosmetics Regulation (ICCR), and other bilateral and multilateral trade agreements.

FDA Response:

CFSAN will use funding for direct support of the operation, staffing, compliance, research, and international activities.

After completing testing of a selection of cosmetics products and performing an exposure assessment, FDA granted the Personal Care Products Council's Citizen Petition on December 22, 2016. On that same day, FDA issued draft guidance for industry recommending a limit of no more than 10 parts per million (ppm) for lead as an impurity in cosmetic lip products (such as lipsticks, lip glosses, and lip liners) and externally applied cosmetics (such as eye shadows, blushes, compact powders, shampoos, and body lotions), based on our assessment that the recommended maximum lead level would not pose a health risk. FDA considers the recommended maximum lead level to be achievable with the use of good manufacturing practices and consistent with the 10 ppm maximum lead level for similar products recommended by other countries.

In May 2016, FDA, with representation from OCAC, participated in the US-China Joint Commission on Commerce and Trade dialogues with China Food and Drug Administration (CFDA), General Administration of Quality Supervision, Inspection and Quarantine (AQSIQ), and

other agencies in Beijing, China. This meeting was to establish communications among regulators on topics of mutual interest as well as to engage in discussions about trade-related issues. FDA continues to maintain an interactive dialogue with China on technical and regulatory issues, including animal testing and compliance/enforcement issues.

FDA has supported international trade negotiations and regulatory harmonization for several years—e.g., through participation in the international group of cosmetics regulatory authorities called International Cooperation on Cosmetics Regulation (ICCR) and engagement in discussions in support of various trade negotiations and bilateral discussions with other countries, such as China, Brazil, and Canada. FDA will continue to identify opportunities to further these goals—for example, by providing technical assistance in support of the U.S. Government’s international trade negotiations and by engagement with the ICCR to the extent that resources and priorities allow.

36. Olive Oil

The Committee is concerned with reports that consistently describe the prevalence of adulterated and fraudulently labeled olive oil imported into the United States and sold to American consumers. In addition, some products labeled as olive oil may contain seed oil, which poses a serious health risk to consumers who are allergic to seed oil. The Committee directs the FDA to take a sampling of imported olive oil to determine if it is adulterated or misbranded, pursuant to Section 342 or Section 343 of the FDCA, respectively, and report to Congress within 270 days on its findings and what actions the FDA will take to ensure consumer safety and proper labeling of imported olive oil.

FDA Response:

In 2014, FDA performed a survey of olive oil products available to consumers within the United States, and included a cross-section of domestic and imported products in the survey. FDA used USDA grading standards in the assessment and used an analytical methodology capable of detecting 10 percent seed oil adulteration. Out of 88 products surveyed, only three showed evidence of adulteration. This work was published in a peer-reviewed publication^{1,2}. FDA continues to develop better methods that may be able to detect adulteration beyond gross addition of seed oils^{3,4}. FDA plans to continue to monitor the marketplace for adulterated olive oil products to ensure consumer safety and proper labeling of imported olive oil.

1. Authenticity Assessment of Extra Virgin Olive Oil: Evaluation of Desmethylsterols and Triterpene Dialcohols; Srigley, CT; Oles, CJ; Kia, ARF; Mossoba, MM; JOURNAL OF THE

AMERICAN OIL CHEMISTS SOCIETY; 93(2); 2016; pp: 171-181. (DOI: 10.1007/s11746-015-2759-4)

2. Authenticity Assessment of Extra Virgin Olive Oil, part 2. Evaluation of fatty acids and triacylglycerols; manuscript in preparation, 2017.
3. Nontargeted, Rapid Screening of Extra Virgin Olive Oil Products for Authenticity Using Near-Infrared Spectroscopy in Combination with Conformity Index and Multivariate Statistical Analyses; Karunathilaka, SR; Kia, ARF; Srigley, C (Srigley, Cynthia); Chung, JK; Mossoba, MM; JOURNAL OF FOOD SCIENCE; 81(10); 2016; pp C2390-C2397. DOI: 10.1111/1750-3841.13432
4. Developing FT-NIR and PLS1 Methodology for Predicting Adulteration in Representative Varieties/Blends of Extra Virgin Olive Oils; Azizian, H; Mossoba, MM ; Fardin-Kia, AR ; Karunathilaka, SR; Kramer, JKG; LIPIDS; 51(11); 2016, pp 1309-1321 (DOI: 10.1007/s11745-016-4195-0).

37. Opioid Abuse

The abuse, misuse, and diversion of opioid painkillers has precipitated an epidemic in the United States. The CDC indicates that one American loses his or her battle with addiction every twenty minutes. For years, the Committee has encouraged the FDA to utilize the full breadth of its regulatory authority to address this challenge. The Committee is pleased that, with the Opioids Action Plan, the FDA has acknowledged that the agency shoulders some responsibility for turning the tide of abuse. The FDA's recent regulatory changes related to scheduling and labeling of opioids are positive developments, as are efforts to encourage the development of abuse-deterrent formulations (ADF) and new evidence-based medication-assisted therapies (MAT).

The use of opioids as first-line therapies for any form of pain has led to over-prescribing, and the CDC has made clear that clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh the risks to the patient. With respect to prescribing patterns, the Committee supports efforts to incentivize ADF use by clinicians and to increase the number of prescribers who receive training on pain management and safe prescribing of opioid drugs in order to decrease inappropriate opioid prescribing. The Committee notes that 38,370 Extended Release/Long-Acting (ER/LA) opioid analgesic prescribers have been trained through the FDA's Risk Evaluation and Mitigation Strategy (REMS), but is disappointed that this constitutes less than half of the 80,000 prescriber training goal that was established in 2012. Even if the FDA was on track to meet its lofty goal of having 60 percent of ER/LA prescribed take a REMS class by 2017, there will still be some 128,000 prescribers without additional, opioid-specific training. The Committee understands that FDA intends to share these lackluster results with an advisory committee to assess its impact on preventing the misuse and abuse of opioids, and to determine what changes, if any, need to be made to the program.

The Committee notes that treatment is not a "one size, fits all" enterprise and that every patient's treatment regimen should be tailored by his or her doctor to his or her unique needs. The federal government, therefore, ought to be promoting the full suite of available treatment options—including abstinence-based models and non-opioid medications—rather than picking winners and losers. The Committee supports efforts at the FDA and elsewhere to develop MATs that improve efficacy of daily administration, are resistant to diversion and misuse, and/or help patients on a path to abstinence. Finally, the Committee has been supportive of naloxone distribution and training licensed healthcare professionals and emergency responders on its use. When considering the appropriateness of providing naloxone over the counter, the Committee asks the FDA to ensure that the administration of naloxone serves as a point of

intervention to spur an honest conversation between the patient and his doctor about addiction and treatment.

FDA Response:

FDA remains committed to increasing the number of prescribers who receive training on pain management and safe prescribing of opioid drugs in order to decrease inappropriate opioid prescribing. FDA continues to explore potential methods to increase prescriber training, bearing in mind that clinicians may be receiving opioid prescribing education from sources other than training provided under the ER/LA Opioid Analgesics REMS , and accordingly is holding a public workshop, on May 9th and 10th, 2017, to obtain input on issues and challenges associated with Federal efforts to support training on pain management and the safe use of opioids for health care providers.

This workshop has three main goals. Participants will be asked to 1) discuss the role that health care provider training plays, within the broader context of ongoing activities, to improve pain management and the safe use of opioids; 2) comment on how best to provide health care providers, who prescribe or are directly involved in the management or support of patients with pain, appropriate training in pain management and the safe use of opioids; and 3) comment on the issues and challenges associated with possible changes to Federal efforts to educate health care providers on pain management and the safe use of opioids.

FDA remains committed to promoting a comprehensive effort to combat opioid abuse, including supporting the development of MATs and the use of naloxone when appropriate. In May 2016, FDA approved buprenorphine, a first-of-kind subdermal implant for the maintenance treatment of opioid dependence, providing a new treatment option for patients struggling with opioid addiction. FDA has also approved in recent years both an auto-injector and an intranasal form of naloxone, which facilitate use by laypersons. Looking ahead, FDA is identifying ways to assist manufacturers in submitting an application to the FDA for an over-the-counter (OTC) version of a naloxone product. This assistance has included development of a consumer-friendly Drug Facts label (which is required for OTC drug products), and the award of a contract for a study currently being conducted on consumer understanding of how to use naloxone in the OTC setting.

38. Over-the-Counter (OTC) Monograph Resources

The Committee understands that, over the past few years, funding allocated to OTC monograph issues has declined, in part due to stagnation in rulemaking and timely responses to Citizen Petitions related to OTC Monograph ingredients. The FDA is directed to provide an exhibit

within the fiscal year 2018 budget justification with the total obligations and staffing levels associated with OTC Monograph issues for the past 11 years (fiscal years 2006–2016). In addition, the FDA is directed to develop detailed justifications and supporting documentation if the agency proposes to increase funding or staffing levels with regard to reforms of the OTC process in future budget submissions.

FDA Response:

FDA will provide a response to Congress for this Significant Item in a supplemental package.

39. Packaged Ice

The Committee recognizes that packaged ice is produced in the U.S., traded internationally, and consumed as both a packaged food and a food ingredient. The FDA has had a citizen petition regarding a proposed standard of identity for packaged ice for a significant and unacceptable length of time and is directed to provide quarterly status reports to the Committee on this effort until a response has been provided. Further, the Conference for Food Protection recently reviewed issues related to commercial ice machines in the retail environment and found that research is needed to identify the type of microbial growth and locations of concern within these machines. Therefore, the FDA is directed to research the issue more carefully and establish a cleaning and sanitizing frequency standard for commercial ice machines.

FDA Response:

FDA is currently reviewing the citizen petition requesting establishment of a standard of identity and a standard of quality for packaged ice. However, due to other high-priority activities that merit the agency's immediate attention and limited resources, we have not been able to complete our review of the petition and issue a response.

Generally, a facility that manufactures, processes, packs, or holds packaged ice for human consumption is subject to subpart B (Current Good Manufacturing Practice) in FDA's Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food regulations in 21 CFR part 117¹⁰⁴. These regulations provide the appropriate standards for the preparation, packing and holding of packaged ice, including cleaning and sanitizing

¹⁰⁴ The CGMP regulations in 21 CFR part 110 have been updated and included in 21 CFR part 117 as part of FDA's Food Safety Modernization Act rulemaking (see the final rule on "Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food" (80 FR 55908, September 17, 2015)). Compliance dates for the provisions of 21 CFR part 117 are phased in based on size, with very small businesses having to comply on September 17, 2018, small businesses on September 18, 2017, and all other businesses on September 19, 2016. See 21 CFR 117.3 for definitions of business size.

practices by FDA-regulated firms. In addition, under 21 CFR part 117, a facility is also subject to the requirements for hazard analysis and risk-based preventive controls in subpart C, unless an exemption applies. A covered facility must conduct a hazard analysis and implement preventive controls for hazards identified as requiring a preventive control.

FDA has issued a Food Facts sheet that addresses concerns raised by the International Packaged Ice Association (IPIA) regarding the lack of awareness of ice safety and of FDA's role in regulating packaged ice. This document is available at:

www.fda.gov/Food/ResourcesForYou/Consumers/ucm197586.htm.

As explained in the Food Facts sheet, State and local regulators have the primary responsibility for regulating retail establishments and can use the FDA Food Code as a model to develop or update their own food safety regulations and to be consistent with national food regulatory policy. The Food Code contains many provisions relevant to production and handling of food and ice including the cleaning and sanitizing of food contact surfaces, potable water requirements, proper plumbing and backflow prevention for ice machines, proper labeling of packaged foods, and guidance on proper handling of ready-to-eat foods, including to not touch food with bare hands. In April 2016, the Council on Food Protection has recommended that FDA amend the FDA Food Code to address more specifically the cleaning frequency associated with equipment such as ice makers and other such equipment with enclosed components. In response, FDA is reviewing the Food Code language to determine if clarity surrounding the frequency of cleaning is best achieved through an interpretation of the existing Code language and placed in the online database of Food Code interpretations known as the Food Code Reference System (FCRS), or through making a change in the Code's language.

40. Pediatric Devices

The Committee applauds the FDA's support of development of pediatric medical devices through the Pediatric Device Consortia and notes the significant investment of more than \$65,000,000 in non-FDA funding that consortia members have raised to advance pediatric device projects. The program funds consortia to assist innovators in developing medical and surgical devices designed for the unique needs of children that often go unmet by devices currently available on the market. The Committee provides an increase of \$2,500,000 in fiscal year 2017 for the consortium to better leverage federal investments and move more devices to the market. The Committee directs that the agency spend no less than \$6,000,000 in order to attract additional funds for these vital projects.

FDA Response:

The Pediatric Device Consortia (PDC) Grant Program continues to successfully support the development of pediatric medical devices and fulfill unmet needs in the pediatric population. Since the program's inception in 2009, the pediatric device consortia have advised innovators on more than 900 potential pediatric devices – and assisted on more than 300 projects just this past year alone. As a result of funding advice provided by the consortia, more than \$110 million of additional funds have been raised to advance pediatric device projects affiliated with the consortia. In the last 4 years, more than ten PDC-assisted pediatric medical devices have become available for use in pediatric care, including TIVA, a needle-free blood collection device, and SleepWeaver Advance Pediatric CPAP Mask. The FDA recognizes the value of the Pediatric Device Consortia in supporting the pediatric medical device ecosystem toward development and innovation for children. The FDA anticipates funding the PDC at the appropriated level for the upcoming year, consistent with prior years.

41. Pet Food Imports

As of September 2014, the FDA has received more than 5,800 complaints of illness related to consumption of chicken, duck, or sweet potato jerky treats, nearly all of which are imported from China. The reports involve more than 5,800 dogs, 25 cats, three humans and include more than 1,000 pet deaths. These incidents date back to 2007. The Committee requests that the FDA provide it with a timeline of all activities associated with the investigation into the pet illnesses associated these products, including any import alerts and import refusals, within 60 days of the enactment of this Act. In addition, the Committee requests that the agency provide it with semi-annual reports on the status of the investigation into these illnesses beginning in April 2016 and continuing until the issue has been resolved.

FDA Response:

FDA will provide the Committee with the requested timeline and report. We currently are assembling information for the FY 2017 annual report on the status of the investigation, as requested by the Committee. In the past two years, the FDA has noted a significant decline in the number of complaints associated with jerky pet treats, and accordingly is in the process of scaling back the investigation to focus on other pet food issues. We continue to monitor jerky pet treats and other pet food issues. The Agency continues to routinely post updates on the pet jerky treat investigation on its website to inform the public and other interested stakeholders about the Agency's actions and developments in the investigation. Please see the following link for more information related to pet jerky treats:

www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation/ucm360951.htm. For information on our laboratory activities, please see the following link:

www.fda.gov/AnimalVeterinary/ScienceResearch/ucm247334.htm#JerkyPetTreats.

42. Pharmacy Compounding

The Committee remains concerned with the draft MOU that the FDA proposed under Section 503A of the FDCA. Section 503A distinguishes between “distribution” and “dispensing” for the purposes of the MOU. In the DQSA, Congress only allowed the FDA to regulate “distribution”. The MOU appears to exceed the authority granted in the statute by redefining “distribution” in a manner that includes dispensing. Congress did not intend to include dispensing of compounded drugs over state lines within the scope of the MOU. The MOU should not address dispensing of compounded drugs to a patient over state lines if all other requirements of 503A are met.

FDA Response:

Section 503A of the FD&C Act describes the conditions that must be satisfied for a drug compounded by a licensed pharmacist in a State licensed pharmacy or Federal facility, or by a licensed physician, to qualify for exemptions from section 505 (concerning pre-market approval requirements), section 502(f)(1) (concerning labeling with adequate directions for use), and section 501(a)(2)(B)(concerning current good manufacturing practice requirements).

When Congress enacted the DQSA, it left intact as one of the conditions necessary to qualify for the exemptions listed in section 503A of the FD&C Act that:

(1) the drug product is compounded in a State that has entered into an MOU with FDA that addresses the distribution of inordinate amounts of compounded drug products interstate and

provides for appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State

(2) if the drug product is compounded in a State that has not entered into such an MOU, the licensed pharmacist, pharmacy, or physician does not distribute, or cause to be distributed, compounded drug products out of the State in which they are compounded in quantities that exceed 5 percent of the total prescription orders dispensed or distributed by such pharmacy or physician (see section 503A(b)(3)(B)(i) and (b)(3)(B)(ii) of the FD&C Act).

Even though the statute did not direct FDA to obtain public input on the draft standard MOU, other than the consultation with the National Association of Boards of Pharmacy (NABP), FDA has engaged in a public process to obtain comments on the draft standard MOU. FDA has solicited public input from the public generally through written comments to the docket, and has also discussed the proposed MOU with representatives from the 50 states.

FDA discussed the concepts it was considering for the MOU at an Intergovernmental Working Meeting with representatives of the 50 States and NABP in March, 2014. After the draft standard MOU was published for comment, FDA discussed the published draft at Intergovernmental Working Meetings with representatives of the 50 States in March, 2015, and again in November, 2015, after the comment period closed. FDA received over 3,000 comments to the docket on the draft MOU. FDA is considering all of the comments, including comments on the definition of “distribution,” as we work to finalize the MOU.

43. Premium Cigars

The Committee includes statutory language exempting premium and traditional large cigars, in keeping with FDA’s intent under Option 2 of its proposed rule “Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act (TCA); Regulations on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products” (Docket No. FDA–2014–N–0189). The Committee notes that premium cigars are shown to be distinct from other tobacco products in their effects on youth initiation, the frequency of their use by youth and young adults, and other such behavioral and economic factors. Lastly, a large number of participants in this unique business are small and very small operations that might not be able to maintain jobs and a physical presence in the United States due to the financial impact of this pending regulatory burden. Given that there is very little mention of cigars throughout the TCA, it is clear Congress did not intend to focus on the unique subset of premium cigars.

FDA Response:

Left unchanged, Section 749 of H.R. 5054 (114th Congress) would prevent the Agency from using funds to finalize, implement, administer, or enforce the deeming rule if it applies to traditional large and premium cigars. If the language became law, FDA will no longer be able to implement the deeming rule, nor enforce any of the provisions in law or regulation for any of the newly deemed products regardless of the effective and compliance dates set forth by FDA in the rule and its preamble. This means that sales to youth will be legal again, as will free sampling of newly deemed tobacco products. None of the newly deemed products will be subject to FDA premarket review and FDA will be unable to set tobacco product standards for such products to protect public health.

We also note that the definition of “traditional large and premium cigar” is very broad and may include more products than the drafters intend, including products that could be attractive to youth.

44. Prescription Drug Labeling Inserts

The Committee is aware of FDA proposals that would subvert repeatedly expressed Congressional intent by permitting the distribution of prescription drugs without printed prescribing information on or within the packages from which such drugs are to be dispensed. The FDA intends to replace such printed labeling with an electronic labeling system for the majority of prescription drugs. On several occasions Congress has directly declined to provide the FDA the necessary statutory authority to implement this change. As recently as 2012, Congress commissioned a GAO report (GAO–13–592) discussing this issue. The GAO report concluded that such a change could adversely impact public health. Thus, the Committee is very concerned that the FDA is moving to promulgate a regulation that would generally eliminate printed prescribing information inserts for prescription drugs. Therefore, the Committee has included a provision prohibiting the FDA from utilizing any funds to propose or otherwise promulgate any rule that requires or permits any prescription drug or biologic products to be distributed without printed prescribing information on or within the packaging from which such products are to be dispensed, unless such actions are expressly provided by an amendment to the FDCA.

FDA Response:

On December 18, 2014, FDA published a proposed rule that would provide for electronic distribution of prescribing information (professional labeling) for human prescription drugs and biological products. Pursuant to Section 746 of the Omnibus Spending Bill of December 18, 2015 (Pub. Law No. 114-113), the Agency stopped work on finalizing the proposed rule. In FDA’s view, if finalized, the rule would have modernized the system for disseminating drug

information and utilized available technological advancements. Such advancements would make it possible for healthcare providers to access new safety information about the drugs and biological products they are prescribing and dispensing much quicker than the current system, thereby enabling them to make decisions about patient care based on the most up-to-date information possible. Also, the above-referenced GAO report addressed both professional and patient labeling. However, the proposed rule pertained only to professional labeling for prescription drugs — it did not propose any changes to the distribution of patient labeling for prescription drugs.

Additionally, under the proposed rule, FDA on its own initiative or upon request from a manufacturer can exempt a product from the electronic distribution requirements if compliance could adversely affect the safety, effectiveness, purity or potency of the drug, is not technologically feasible, or is otherwise inappropriate. The rule also proposed to require drug manufacturers to provide labeling in paper format to any patient or provider upon request.

45. President’s Budget Submission to Congress

The Administration has submitted the President’s budget request the past two years with a false level of base funding for the agency. Congress provided funds for the Department of Health and Human Services OIG in the FDA’s Salaries and Expenses Appropriation in fiscal years 2015 and 2016. While those funds were transferred to the OIG following an apportionment by the Office of Management and Budget, such a transfer did not alter the Congressional appropriation level for the FDA. The Subcommittee directs the FDA to incorporate the actual funding level approved by Congress when displaying the previous year funding level in the fiscal year 2018 President’s budget.

FDA Response:

FDA will incorporate the actual funding level approved by Congress when displaying the previous year funding level in the fiscal year 2018 President’s budget.

46. Private Accredited Laboratories

As the FDA begins to implement the regulations associated with FSMA and increase sampling of food products, the agency is encouraged to use and contract with, when appropriate, ISO/IEC 17025 certified, and other certified laboratories to advance the goals of FSMA and for other data collection purposes.

FDA Response:

FDA agrees with the importance of obtaining analyses from laboratories using reliable quality management systems. To that end, the FDA Foods and Veterinary Medicine Program will use laboratories accredited under ISO/IEC 17025 and other certified laboratories, as appropriate, for sample collection and analysis.

47. Protecting Proprietary Information

The Committee is concerned about the FDA's ability to protect trade secrets and confidential information the agency obtains from its regulated industries. FDA's access to such information has been expanded under FSMA and other regulatory actions. Recent cybersecurity breaches at the FDA underscore the importance of the FDA's ability to safeguard sensitive information. The agency has a legal obligation under the FDCA to protect confidential information. The Committee directs the FDA to provide a detailed plan on how this information will be protected no later than 60 days after enactment.

FDA Response:

Information security is among the top priorities at the FDA, and we do not take lightly our responsibility for protecting industry and public health information in today's environment of increased cybersecurity risk. The agency recognizes the risks associated with operating this large global IT enterprise and has implemented processes, procedures, and tools to better ensure the prevention, detection and correction of incidents. Since October 2013, FDA is not aware of any recent cybersecurity breaches at the agency. FDA will provide the requested report.

48. Public Disclosure

The FDA's current rules and policies governing what drug and device developers may say about their own products were designed decades ago. Since then, the way that medicine is practiced and delivered and the way that information is communicated have fundamentally changed. The Committee urges the FDA to convene a working group with stakeholders, including representatives from government, industry, health professionals, and patient advocacy groups, in order to solicit information to inform the FDA's evaluation of its rules and policies regarding the appropriate scope of scientific and medical information that can be shared with physicians, insurers, and researchers, with appropriate safeguards, in order to optimize patient care.

FDA Response:

FDA is committed to continuing a robust dialogue regarding scientific and medical information. In furtherance of the commitment the agency in recent years has convened public meetings, opened dockets and issued new guidance. The agency will continue to encourage appropriate discussions and will consider approaches that may further that aim.

49. Ready-to-Eat Foods

The Committee is aware that the FDA is in the process of finalizing guidance documents regarding *Listeria monocytogenes* in ready-to-eat (RTE) foods, which may include frozen vegetables that are not currently considered as RTE foods. Reducing incidents of listeriosis is an important health goal, and the Committee supports the issuance of scientifically based guidance. However, including foods that are not considered RTE should be justified based upon a quantitative risk assessment. The Committee urges the FDA to conduct such an assessment prior to taking any action that would formally consider frozen vegetables or other foods currently not considered RTE as RTE foods.

FDA Response:

FDA determines the risk associated with *Listeria monocytogenes* in a frozen food, such as a frozen vegetable, on a case-by-case basis depending on a number of factors, including whether it supports the growth of the pathogen when thawed and how the frozen food is commonly handled. Some frozen vegetables present minimal risk to consumers because these vegetables are commonly held frozen, cooked from a frozen state, and immediately consumed. By contrast, some frozen vegetables can be thawed and used without cooking in salads, whether in commercial salad bars or in the home; and some recipes available to consumers describe the preparation of products using frozen vegetables that are thawed, but not cooked. Where a frozen food that supports growth of *L. monocytogenes* is thawed and held for considerable time at refrigerated or room temperature, such as on a salad bar, it may pose a risk to consumers because it has not been subject to cooking that would kill the pathogen and it will be held under conditions that allow pathogen growth to occur.

Every few years, FDA identifies new vehicles for *L. monocytogenes* illness among foods with no known prior history of contamination or epidemiological link to listeriosis, and some foods with limited histories of contamination can prove to be higher risk than previously thought. For example, in 2016, CDC identified a multistate outbreak of listeriosis linked to frozen vegetables by epidemiologic and laboratory evidence. We anticipate that the pattern of discovering new food vehicles will continue, if not hasten, with the advancement of whole genome sequencing in connecting known clinical illnesses with the foods responsible for those illnesses.

The Committee's request for an assessment, prior to any other action, would hinder the Agency's efforts to prevent public health problems involving *L. monocytogenes*-contaminated frozen vegetables. Moreover, this would be a costly undertaking because the type of comprehensive up-to-date survey data needed to develop a quantitative risk assessment for foodborne *L. monocytogenes* in frozen vegetables is not presently available; therefore, FDA would have to conduct its own survey prior to conducting such a risk assessment or commission another organization to conduct such an assessment. For example, a 2003 Quantitative Assessment of Relative Risk to Public Health from Foodborne *Listeria monocytogenes* Among Selected Categories of Ready-to-Eat Foods -- jointly developed by FDA, the Centers for Disease Control and Prevention, and the USDA's Food Safety and Inspection Service -- took four (4) years to complete, beginning with a *Federal Register* notice of intent issued in 1999 and culminating in completion of the final assessment in 2003. Given current consumer and retailer practices for using some kinds of thawed, uncooked frozen vegetables without cooking, FDA believes we can scarcely afford this delay.

50. Scientific Integrity

Pursuant to the President's 2009 memorandum and as directed by the Office of Science and Technology Policy, the FDA adopted a scientific integrity policy in 2012. It appears to conform to the President's directive by maintaining a firm commitment to science-based, data-driven decision making, facilitating the free flow of scientific and technical information, and requiring a fair and transparent approach to resolving scientific disputes. The Committee directs the Commissioner to ensure all FDA centers agencies are complying with the policy and using it to guide their policy and regulatory decisions.

FDA Response:

FDA's policies related to scientific integrity currently apply to all Agency components and employees. The Office of Scientific Integrity within the Office of the Commissioner is regularly working with the Agency's centers and other components to ensure compliance with these policies and encourages employees to report deviations from them.

51. Sodium Guidance

The Committee is aware that the FDA is considering issuing guidance to food manufacturers in order to reduce sodium in various food categories. It is imperative that any guidance be issued using the latest sound science. The Centers for Disease Control and Prevention and the IOM are working together to update the Dietary Reference Intake (DRI) report on sodium. The FDA is encouraged to issue any voluntary or mandatory guidance based upon an updated DRI report.

FDA Response:

In June 2016, FDA issued draft guidance for public comment for voluntary sodium reduction goals in commercially processed and prepared food, both in the short-term and over the long-term (81 FR 35363). This draft guidance was based on the latest scientific evidence available, and reflects recommendations in the most recent Dietary Reference Intakes (DRI)¹⁰⁵ for sodium, as well as the recently issued 2015-2020 *Dietary Guidelines for Americans* (which involved expert review of the current body of research by the Dietary Guidelines Advisory Committee). FDA's draft voluntary short-term (two-year) targets are aimed at reducing average sodium consumption from 3,400 to 3,000 mg/day, and the voluntary long-term (ten-year) targets are aimed at reducing average sodium consumption to 2,300 mg/day, which is consistent with current federal recommendations. FDA also strongly supports efforts by the National Academies of Science, Engineering and Medicine (National Academies) to formally review the sodium DRI, and FDA is collaborating with CDC, NIH, and USDA to update the DRI for sodium as expeditiously as possible.

The majority of Americans are trying to take action to reduce their sodium intake (CDC, 2015), and the weight of the scientific evidence supports reducing sodium in the food supply in order to reduce current average sodium consumption levels from 3,400 mg/day—well above the current recommended limit of 2,300 mg/day—, thereby reducing the risks associated with increased blood pressure and cardiovascular disease (CVD). Three quarters of sodium intake comes from processed or prepared food – before it is added at the table, or during cooking. Supporting options for food products lower in sodium therefore increases choices for American consumers. Several major food manufacturers are supportive of FDA's efforts in their recently submitted comments on the draft voluntary sodium reduction targets.

Given the scientific evidence in support of reducing sodium intake from current levels to reduce blood pressure, subsequent CVD, and associated health care costs, as well as recent industry feedback on the targets, the Agency believes that it is reasonable to continue work on voluntary sodium reduction targets, even as the DRI is updated. Once the DRI report is finalized (anticipated to be in 2019), FDA is committed to making any needed adjustments to the long-term targets to align them with the findings of the National Academies Committee. Furthermore, FDA will continue extensive outreach with industry and public health groups on our draft voluntary targets to ensure that they are well understood.

¹⁰⁵ The Dietary Reference Intakes (DRIs) are nutrient reference values developed by the Institute of Medicine of The National Academies of Sciences, Engineering, and Medicine.

52. Spent Grains

The Committee recognizes that the FDA took into consideration public comments and revised some of its proposed regulations on spent grains used for animal food. Processors already complying with FDA human food safety requirements would not need to implement additional preventive controls when supplying a by-product like wet spent grains for animal food.

However, further processing a by-product for use as animal food such as drying spent grains, would require additional compliance under the proposed rule. The FDA has said that potential hazards associated with spent grains are minimal and steps to prevent contamination are likely already in place. The Committee includes bill language to ensure dry and wet spent grains used for animal food are regulated equally.

FDA Response:

Americans purchasing human and animal food expect that the food is safe and not adulterated, and produced in a manner that protects it from contamination. There are two general types of spent grains of the alcoholic beverage production process that are used as animal food: unprocessed spent grains (“wet spent grains”) and processed spent grains (“dried spent grains”). During a recent education and outreach event with the alcoholic beverage manufacturing industry, we learned that for certain segments of the industry there are “intermediary by-products” produced in addition to spent grains that also are used as animal food. The by-product that is more processed (i.e., dried spent grains) may be more likely to be contaminated because additional processing of the by-product allows more opportunities for the introduction of contamination.

In the Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Food for Animals final rule (PCAF rule), FDA established two major sets of new requirements for animal food. FDA established current good manufacturing practice (CGMP) requirements for animal food under section 402 of the FD&C Act to help ensure animal food is manufactured in a manner that protects it from contamination. The PCAF rule also established the hazard analysis and risk-based preventive controls requirements as required by FSMA.

CGMPs are baseline manufacturing standards to protect food against contamination. Alcoholic beverage manufacturing facilities are subject to human food CGMPs for the production of their alcoholic beverages and animal food CGMPs for spent grains for use as animal food. The animal food CGMPs are similar to the human food CGMPs, but include more flexibility for implementation than the human food CGMPs. FDA understands the Committee's concern with respect to the hazard analysis and preventive control requirements of the PCAF rule and does not intend to apply these requirements to alcoholic beverage manufacturers processing spent grains for use as animal food.

As discussed in our education and outreach meetings with the alcoholic beverage industry, FDA wants to ensure all by-products of the alcoholic beverage industry remain subject to the baseline CGMP requirements that protect against contamination of animal food that result in adulteration under the FD&C Act. We will continue to convey this message in further outreach and education efforts to the alcoholic beverage industry.

FDA will use the information gained through our continued outreach with the industry to develop both training material and guidance for our field staffs. Regulators and industry share a common goal of achieving compliance while maintaining standards for food safety and public health.

FDA believes it can achieve this common goal of safe animal food through education and outreach and through the implementation of the CGMPs at these facilities.

53. State Inspections

The Committee is aware of the December 2011 OIG report that outlined vulnerabilities in the agency's oversight of non-FDA food inspections and the agency's intention to further rely on state inspections. The Committee understands that both the federal government and states share authority and responsibility for domestic food facilities and that the FDA will continue to contract with the states to conduct inspections on its behalf, which is critical to performing its mission in an efficient and effective manner. The agency must assure it has strong federal inspection standards that are met by both federal investigators and state inspectors. The FDA must continue its progress in improving federal oversight and monitoring of state inspection programs, reviewing and strengthening internal directives and processes, and identifying new methods to improve oversight capabilities.

The FDA should continue working with states to: (1) build the capacity and effectiveness of their inspection programs through implementation of national program standards, such as the Manufactured Food Regulatory Program Standards and the Animal Feed Regulatory Program Standards; (2) utilize state or private laboratory services with ISO/IEC 17025 laboratory accreditation; and (3) improve federal-state collaboration during investigations and responses to food borne illness outbreaks by supporting the implementation of Rapid Response Teams.

The Committee is aware of the FDA's continuing progress to modernize existing IT systems and infrastructure, allowing for the secure and efficient exchange of data between the FDA and the states, in addition to efforts to add capabilities supporting mobile inspection applications. The FDA should continue work with state partners toward promoting data standards and developing shared database schemas to facilitate secure electronic information sharing.

FDA Response:

FDA did a great deal of work following the 2011 OIG study. Significant resources have been allocated to evaluating the study findings, internal processes and procedures and enhancing FDA operations. FDA is continuing to audit state regulatory programs and implement a quality review of state inspections conducted under contract. FDA also continues to improve federal-state work planning communication, coordination and collaboration to leverage resources and improve efficiency and effectiveness in the prevention of human and animal food contamination and illness.

FDA is continuing to improve its regulatory program standards in collaboration with state partners and to provide training and resources to states as well as FDA investigators to ensure all investigators and inspectors have the knowledge, skills and abilities to competently inspect, conduct investigations, gather evidence, collect samples and take enforcement actions. FDA district offices continue to review state-conducted inspection assignments in accordance with the contract statement of work requirements. Both FDA and state regulatory agencies continue to execute audits of the contract inspection programs in accordance with the FMD-76 audit requirements.

The Agency has collaborated with our state regulatory partners to review, modify and enhance the MFRPS and released an updated version of the standards in 2016. Additionally, a collaborative review of both the MFRPS and the AFRPS is currently underway as part of the three-year review cycle. FDA and the states will work jointly to enhance both programs where possible. FDA continues to provide financial support and technical assistance to states for the implementation of the national program standards, including the MFRPS, AFRPS, and Voluntary National Retail Regulatory Program Standards. We continue to see enhanced participation from the states in the MFRPS program as well as the AFRPS program. In addition, we are collaborating with states to develop new standards for egg and shellfish regulatory programs.

Both FDA and the states continue to leverage resources and abilities through the use of Rapid Response Teams (RRTs), which are utilized when dealing with food outbreaks/emergencies. State and FDA counterparts continue to train together and FDA continues to devote financial and human resources to support, develop and implement RRTs. Both the states and FDA remain invested in RRTs and the continued use and progression of this collaborative resource.

FDA continues to improve its IT capabilities, working with our state partners to enhance existing IT systems that allow for the transmission of information between the Agency and states. FDA is also evaluating other existing Agency IT systems to determine their viability for use in state communications. In FY17, FDA is establishing an Initial Operating Capability (IOC) for a National

Food Safety Data Exchange (NFSDX) platform to conduct a pilot automated electronic sharing of contracted inspection data with a few partner states. As of April 1, 2017, seven states have signed up to participate in the NFSDX pilot testing scheduled for July and August. By September 2017, a plan for a Full Operating Capability (FOC) will be completed to prepare for extending beyond the pilot states to the other partner states in the near future. FDA will continue to work with our state partners to enhance and further the IT infrastructure to advance new mechanisms to allow for the secure and efficient exchange of data between FDA and the states.

54. Staffing at Land Ports of Entry

The Committee is concerned that USDA, FDA, and Customs and Border Protection are relying on historical data in determining their staffing models at Land Ports of Entry. Recent reports on agriculture imports show steep increases in the future, especially along the Southwest border and South Texas in particular. It is the sense of the Committee that these agencies should be utilizing forward looking data for their staffing models to ensure we have an appropriate workforce available in the future to inspect and certify this growth in agriculture imports as efficiently, safely and expeditiously as possible.

FDA Response:

FDA's electronic import processing systems allow the Agency to review import entries without having to physically be at the actual port of entry. These systems interface with CBP's Automated Commercial Environment (ACE) system. FDA's import entry screening tool (PREDICT) calculates a customized risk score based on a wider variety of factors, including, but not limited to, inherent risk of the product, data anomalies, data quality, and the compliance history of firms (e.g., manufacturer, shipper, and consignee) and the product; to get the best use of FDA's limited resources, staffing decisions should assess not only the volume of products entering through a particular port of entry, but also the overall risk of those products compared to other ports of entry.

FDA is developing new system-based, import-centric processes under FSMA, such as the Foreign Supplier Verification Program (FSVP) regulation and the Voluntary Qualified Importer Program (VQIP), that are risk-based and are less reliant on an increased level of surveillance or end product testing. The FSVP regulation requires that importers perform certain risk-based activities to verify that food imported into the United States has been produced in a manner that meets applicable U.S. safety standards. In addition, VQIP will provide for the expedited review and importation of foods from importers who achieve and maintain a high level of control over the safety and security of their supply chains. These programs represent a better use of FDA resources than placing staff at ports of entry without consideration of product risk.

FDA tries to staff ports of entry based on volume and risk associated with the products imported through those ports, in line with the resources available. Adding physical coverage to specific ports of entry without adding additional resources means decreasing capacity in other ports of entry. Additionally, relocating staff from one port to another raises retention and union issues which must be considered.

55. Sunscreen Ingredients

The Committee is significantly concerned that despite the increase in incidence of skin cancer in the United States, the Surgeon General's 2014 Call to Action to Prevent Skin Cancer, unanimous passage of the Sunscreen Innovation Act (SIA) in Congress and President Obama's January 2016 Presidential Memorandum creating the White House Cancer Moonshot Task Force to prevent and cure cancer, the FDA has still not approved a new OTC sunscreen ingredient through the process created by the SIA. For several years, the House and Senate Appropriations Committees have directed the FDA to clear the sunscreen backlog and ensure that Americans have access to the latest skin cancer prevention technology (H. Rept. 113–116, H. Rept. 113–468, H. Rept. 114–205, S. Rept. 114–82). The agency has failed to do so. The Committee directs the FDA to work with stakeholders to develop a benefit-risk testing regimen that appropriately balances the benefit of additional skin cancer prevention tools versus the risk of skin cancer to the 5 million Americans that will be diagnosed with the condition this year. The agency is directed to reach agreement with stakeholders on this testing regimen by June 20, 2016 and publish the summary of the meetings and results of the specific testing requirements on its website. The Committee reminds the FDA that section 4(c) of the SIA requires the FDA to report to the Senate Health, Education, Labor and Pensions Committee and House Energy & Commerce Committee on the implementation of the Act on or before May 26, 2016. The FDA shall include in this report a detailed analysis of how the FDA is balancing the Surgeon General's Call to Action, the President's Moonshot effort to remove administrative hurdles to cancer prevention, the known public health benefits that regular sunscreen use provides to prevent skin cancer and melanoma, and the long history of safe and effective use of sunscreens currently backlogged at the FDA in comparable countries versus the hypothetical risk sunscreens theoretically may pose to human health in FDA's GRAS standard. The funding level for the FDA maintains the \$700,000 increase in Fiscal Year 2016 to help address the critical public health threat resulting from no new sunscreen ingredients being available to the public.

FDA Response:

FDA transmitted the report entitled "Report in Response to Sunscreen Innovation Act (P.L. 113-195) Section 586G" to the Committee on Energy and Commerce on May 23, 2016.

FDA has carefully considered what information is needed to ensure that a particular sunscreen active ingredient is safe and effective for use in OTC sunscreen products. FDA's recommended studies reflect the Agency's scientific expertise, existing technical guidance, experience from reviewing safety and efficacy data submitted for a generally recognized as safe and effective (GRASE) review of sunscreen active ingredients seeking to be added to the OTC Review for Sunscreens under current OTC drug regulations, and input from outside scientific experts (<http://www.fda.gov/AdvisoryCommittees/Calendar/ucm407137.htm>). The recommended studies are not novel and are consistent with FDA's standard data requirements for both nonprescription and prescription topical drugs intended for chronic use.

Information on FDA's recommendations and expectations for the safety data needed to show that an active ingredient is GRASE for use in nonprescription sunscreen products has been publicly shared with industry and other interested parties on multiple occasions, including a public advisory committee meeting held in September 2014, proposed sunscreen orders published in 2014 and early 2015 for the eight sunscreen active ingredients that were under evaluation by FDA when the SIA was enacted, sponsor-requested meetings on the proposed sunscreen orders, and an SIA-required draft guidance for industry published in November 2015, which the FDA finalized in November, 2016.

To date FDA has met all statutorily mandated SIA deadlines and remains committed to achieving that goal in the future.

56. Surrogate Endpoints

The Committee urges the FDA to issue guidance on the use of surrogate and intermediate endpoints for accelerated approval of regenerative medicine products under section 506(c) of the FDCA (21 U.S.C. 356(c)). In the process of issuing guidance, the FDA shall consult with appropriate stakeholders in the development of this guidance.

FDA Response:

The FDA's Center for Biologics Evaluation and Research is committed to helping make regenerative medicine therapies that are shown to be safe and effective available as soon as possible. FDA has an Expedited Programs guidance that addresses the use of surrogate and intermediate endpoints for accelerated approval; this guidance applies to regenerative medicine therapies that are drugs and biologics and that meet the criteria for accelerated approval (Expedited Programs for Serious Conditions – Drugs and Biologics, published in May 2014).

Building on the FDA's existing expedited programs available to regenerative medicine products, the Regenerative Medicine Advanced Therapy (RMAT) Designation was established through the 21st Century Cures Act, signed into law in December 2016. Drugs that are regenerative medicine therapies, as defined in the new law, may obtain the RMAT designation if the drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition and if there is preliminary clinical evidence indicating that the drug has the potential to address unmet medical needs for that disease or condition.

RMAT-designated products are eligible for increased interactions with the FDA, similar to those interactions available to sponsors of breakthrough-designated therapies. In addition, they may be eligible for priority review and accelerated approval. The legislation recognizes that these early meetings between FDA and sponsors of RMAT-designated products may be a suitable time to discuss whether accelerated approval would be appropriate based on surrogate or intermediate endpoints reasonably likely to predict long-term clinical benefit, or reliance upon data obtained from a meaningful number of sites. FDA is committed to continuing to advance the development of drugs and biological products, including by providing more guidance related to surrogate endpoints and implementing the drug development tools provisions of the 21st Century Cures Act, and will continue to engage sponsors and other stakeholders on this issue.

57. User Fee Collections/Obligations

The Committee continues to be concerned about the financial management of the FDA's user fee programs. The Committee directs that not later than 30 days after enactment of this Act, and each month thereafter through the months covered by this Act, the Commissioner to submit to the Committees on Appropriations of the House and Senate a report on user fees collected for each user fee program included in the Act. The report shall also include monthly obligations incurred against such fee collections. The report shall include a distinct categorization of the user fee balances that are being carried forward into fiscal year 2018 for each user fee account as well as a detailed explanation of what accounts for the balance and what the balance will be used for.

FDA Response:

FDA will provide the requested reports.

58. Funding for Food Safety

Funding for Food Safety.--The Committee includes increases of \$33,152,000 for the implementation of FSMA. These increases include \$19,139,000 for the National Integrated Food Safety System (NIFSS) and \$14,013,000 for Import Safety. The increases provided in this bill and the increases provided since fiscal year 2011 should assist the FDA in preparation for the implementation of FSMA prior to the effective dates of the seven foundational proposed rules. While the FDA has not implemented the final rules, the Committee understands that most businesses will not need to comply with the two rules for preventive controls for human food and for animal food until August 2016 and that the other five rules will not be effective until fiscal year 2017 and later. Within the amount provided for NIFSS, the Committee includes \$5,000,000 to allow for the development of a data exchange to maximize standardization and access to farm data across FDA and States.

FDA Response:

FDA will provide a response to Congress for this Significant Item in a supplemental package.

SENATE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

SENATE COMMITTEE REPORT (S. 114-259)

1. Active Pharmaceutical Ingredients

The Committee is concerned that the FDA has not yet approved a list of active pharmaceutical ingredients [APIs] for use by compounding pharmacists pursuant to the Federal Food, Drug, and Cosmetic Act [FDCA]. Within 90 days of the enactment of this act, the FDA is directed to provide a timeline for when the remaining substances will be considered, and in the meantime re-consider its policy with regard to enforcement of the bulk drug substances provisions under section 503A.

FDA Response:

FDA will provide the requested report.

2. Artisanal Cheese

While the Committee appreciates the FDA's willingness to pause enforcement and reevaluate its standard regarding permissible levels of nontoxigenic *E. coli* in raw milk cheese, it remains concerned that this standard was developed in the absence of any published data from controlled studies describing either the process or rate of transfer of bacteria from the environment in the plant to the product. Therefore, the Committee directs the FDA to continue working with stakeholders to benefit from their expertise about safe cheese-making practices to achieve the mutual goal of food safety, and to provide to the Committee on Appropriations the results of the "Surveillance Sampling Program for Raw Milk Cheese."

FDA Response:

As the Committee notes, in February of 2016 the FDA paused its testing for generic *E. coli* in raw milk cheese as we consider the role of the generic *E. coli* standard in identifying and preventing insanitary conditions and food safety hazards for both domestic and foreign cheese producers. In July, we published findings from our FY 2014-2016 microbiological sampling assignment in which we analyzed raw milk cheeses that were aged for 60 days or longer: www.fda.gov/food/complianceenforcement/sampling/ucm510799.htm. Sampling assignments, such as this one, are an important part of our preventive approach to food safety

by helping us identify hazards to minimize and enabling us to determine the prevalence of contamination in instances where we may not otherwise have enough data to do so.

We will use the results obtained under this assignment as part of our review of the role of testing for generic *E. coli* in identifying insanitary conditions for both domestic and imported raw milk cheese. FDA's deliberations include an extensive review of relevant scientific literature and stakeholder dialogue.

FDA looks forward to continuing to engage cheese industry stakeholders and experts in this scientific dialogue, and we welcome the opportunity to continue this dialogue with all stakeholders to discuss the development and implementation of preventive controls for the manufacture of safe cheeses, with particular emphasis on the generic *E.coli* standard.

3. Atypical Actives

The Committee requests that the FDA provide an update on how it regulates "atypical actives."

FDA Response:

FDA will provide the requested report.

4. Biosimilars

The Committee directs the FDA to provide no later than 30 days after enactment an estimated timeline by which the agency will finalize pending draft biosimilars guidance documents and an estimated timeline by which the agency will issue draft guidance on biosimilars topics, including, interchangeability, for which the agency has not published draft guidance.

In addition, the Committee recognizes that biosimilars offer an important opportunity for expanding the market and reducing costs for patients. The Committee urges the FDA to conduct outreach to external stakeholders including patient organizations on educating patients and professionals about biosimilars, with a focus on populations for which approved biosimilars are indicated.

FDA Response:

FDA will provide the requested report.

FDA remains committed to working with stakeholders, including drug manufacturers, prescribers, pharmacies, hospitals and health systems, informatics providers, and patient groups on this important issue.

5. Center for Safety and Nutrition Centers of Excellence

The Committee is aware of the important contribution of the FDA Center for Food Safety and Applied Nutrition's Centers of Excellence [COEs] program in supporting critical basic research as well as facilitating the implementation of the FDA Food Safety Modernization Act. The Committee encourages the Agency to continue to fully utilize the COEs to accomplish these goals, and instructs that it enhance its level of support for FDA Food Safety Modernization Act activities.

FDA Response:

FDA appreciates the recognition of the importance of the COEs, their contributions to regulatory science, and encouragement of support for them.

6. Centers of Excellence in Regulatory Science and Innovation

The Committee is encouraged by the ongoing research and collaboration underway at the Centers of Excellence in Regulatory Science and Innovation program and commends the FDA for launching this program in 2011 and expanding it in 2014. As such, the Committee directs the Office of the Commissioner to use at least \$2,000,000 within existing funds to provide additional funding opportunities for the existing CERSI Centers to allow for the capitalization of ongoing studies and research.

FDA Response:

FDA appreciates the recognition of the importance of the CERSIs, their contributions to science in support of FDA's mission, and identification of resources for them. As directed, the Office of the Commissioner will use at least \$2,000,000 within existing funds to provide additional funding opportunities for the existing CERSI Centers to allow for the capitalization of ongoing studies and research.

7. Cosmetics

The Committee provides not less than \$11,700,000 for cosmetics activities, including not less than \$7,200,000 for the Office of Colors and Cosmetics [OCAC]. Funding for OCAC is for the direct support of the operation, staffing, compliance, research and international activities performed by this office.

FDA Response:

CFSAN will use funding for direct support of the operation, staffing, compliance, research, and international activities.

8. Cotton Ginning

The Committee is concerned about the impact of the “Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Food for Animals” final rule (80 FR 56170; September 17, 2015) on the cotton industry. The Committee notes post-harvest activity of ginning cotton does not transform the resulting cottonseed into a “processed food,” and thus, cottonseed should fall within the definition of a “raw agricultural commodity” for purposes of rules promulgated pursuant to the FSMA. In addition, the Committee is concerned about the rationale for the definitions of “primary production farm” and “secondary activities farm” and how these definitions factor into the determination of operations either being exempt from or covered by certain requirements of the final rule. Therefore, the Committee directs the FDA to provide outreach and technical assistance to cotton ginning operations to assist them in complying with the final rule or subsequent guidance documents.

FDA Response:

FDA worked to harmonize the preventive controls rules for both human and animal food that were finalized in September 2015. In both of those regulations, “harvesting” is conducted by farms (primary production or secondary activities) or farm mixed-type facilities. Not all cotton ginneries are part of a farm, and when not conducted on a farm, the ginning of cotton is considered manufacturing, not harvesting. Because cotton ginning can result in manufacturing of animal food, cotton ginneries that manufacture animal food for consumption in the U.S. are required to register and therefore are subject to certain provisions in the Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Food for Animals rule (PCAF rule).

FDA is aware of the cotton ginning industry's concerns regarding whether certain entities are classified as farms or facilities. We also are aware of their concern related to whether ginning results in a "processed food." FDA is looking at the farm definition, and will consider the concerns of the cotton ginning industry in that evaluation. To facilitate this effort, we extended the compliance dates for several provisions related to the farm definition, including extending compliance dates for the portion of the cotton ginning industry that is subject to the PCAF rule (please see the following webpage for more information about the compliance date extensions: www.fda.gov/Food/GuidanceRegulation/FSMA/ucm517545.htm). Compliance dates for the cotton ginning industry have been extended to January 28, 2019 or later depending on business size to provide FDA time to consider concerns raised by the cotton ginning industry.

FDA will continue to provide outreach and technical assistance, such as through meetings, to the cotton ginning industry to assist them in complying with the PCAF rule.

9. Diabetes

The Committee applauds the FDA for working with the diabetes community on clinical outcomes beyond hemoglobin A1c [HbA1c]. While HbA1c remains a fundamental measurement to assess the benefit of therapy for diabetes mellitus, regulatory decisions should be reached using the full range of outcomes that are important to people with diabetes. The Committee is pleased that the FDA will be holding a workshop focused on this topic in 2016 and encourages the Agency to incorporate the scientific learnings from that workshop into their decision-making so that important new, safe, and effective medical therapies can be made available to people with diabetes.

In addition, the Committee recognizes that being able to identify people at risk of developing type 1 diabetes could provide an opportunity to delay and eventually prevent the disease altogether. The appearance of certain islet autoantibodies in the serum of individuals increases the chance of developing type 1 diabetes at some point in the future. Therefore the Committee encourages the FDA to work with the Type 1 diabetes community on the assessment of potential diabetes biomarkers related to islet autoimmunity, which might help inform the design of clinical studies.

FDA Response:

FDA acknowledges that the benefits of antidiabetic therapies may extend beyond the benefits attributed to HbA1c reduction. FDA held a widely attended public workshop on the topic of

“Outcomes beyond HbA1c” on August 30th, 2016. At this meeting, people with diabetes, patient advocates, healthcare providers, diabetes researchers and manufacturer of diabetes related-products proposed a broad range of measures centered on the patient experience that could potentially serve to detect clinical benefits of antidiabetic therapies not captured by HbA1c. To incorporate the learning from this workshop, the FDA is using the Critical Path Innovation Meeting program and the Drug Development Tools Qualification Program to encourage stakeholders to propose specific measures that could be used to reliably capture one or more benefit with the goal of incorporating these measures in studies used for drug development and in decision-making. Related to benefits of antidiabetic therapies that extend beyond the benefits attributed to HbA1c reduction, the FDA approved, in 2016, the first ever antidiabetic therapy for Type 2 diabetes mellitus that was demonstrated to also reduce the risk of cardiovascular death in patients with Type 2 diabetes and heart disease.

FDA acknowledges that being able to reliably identify people at risk of developing Type 1 diabetes with prognostic immune markers could help inform the clinical studies for development of therapeutics aiming to delay or prevent Type 1 diabetes onset. FDA is partnering with the Critical Path Institute and the Type 1 diabetes community on a project whose objective is to leverage existing data for the purpose of qualifying the use of diabetes biomarkers related to islet autoimmunity as prognostic markers for Type 1 diabetes. Where appropriate, companies may still discuss specific drug development proposals for therapeutics aiming to delay or prevent Type 1 diabetes that involve use of one or more of these biomarkers in the setting of FDA’s formal meetings with industry under the Investigational New Drug application mechanism.

10. Donor Milk Supply

The Committee is aware of the growing commercial human milk industry, and its importance to, in particular, preterm infants. The Committee is also aware that the FDA has had discussions with the industry regarding the need for adequate safeguards to ensure the safety and nutritional quality of the donor human milk supply. The Committee directs FDA to report on its efforts to implement regulations to protect a safe and stable human milk supply.

FDA Response:

Products containing donor human-milk-based products are generally regulated as foods. Certain products may also be regulated under more specific requirements, such as those for exempt infant formula (i.e., infant formula that is represented and labeled for use by infants who have inborn errors of metabolism or low birth weight, or who otherwise have unusual

medical or dietary problems). The FDA Food Safety Modernization Act (FSMA) significantly strengthened FDA's authorities over the food safety system and requires food facilities to establish and implement hazard analysis and risk-based preventive controls for human food.

FDA's rule implementing mandatory preventive controls for human food was finalized in 2015, and the compliance dates for some businesses began in September 2016. Facilities producing human-milk-based food products are subject to FSMA's risk-based mandated inspection frequencies. High-risk domestic facilities will be inspected every three years and non-high risk facilities every five years.

Donor human milk could, in certain circumstances, also be regulated under additional specific requirements, such as those for exempt infant formula. Facilities that produce exempt infant formula are inspected annually.

For non-commercial use, some hospitals have milk banks for use in neonatal intensive care units; other hospitals obtain milk from the Human Milk Banking Association of North America (HMBANA). Although the majority of the donor human milk from HMBANA milk banks is distributed to hospitals, it is also distributed to infants in the home who need donor human milk because of medical conditions such as formula intolerance or feeding issues related to prematurity. When possible, milk banks serve healthy babies who have been adopted or are otherwise not able to get their own mother's milk. HMBANA sets standards and guidelines that its member milk banks can follow. Among other things, those guidelines provide recommendations for donor screening and pasteurization.

11. Drug Shortages

The Committee requests that the FDA report on how it works with manufacturers to facilitate timely communication to the field on the availability of drugs in shortage, as well as its processes for the completion of drug application reviews and facility inspections during times of or risk of critical drug shortage.

FDA Response:

FDA will provide the requested report.

12. Duchenne Muscular Dystrophy

The Committee is encouraged that the FDA has the tools, authorities, and latitude necessary to review and approve safe and effective treatments for rare diseases, such as Duchenne Muscular Dystrophy, as efficiently as possible. In particular, the Committee is aware that the use of intermediate clinical endpoints [ICE] may be an appropriate approach as they have been in similar deadly diseases with dire unmet need, such as HIV and cancer.

FDA Response:

FDA is committed to engaging with patient groups to receive valuable input during the evaluation of the medical needs of patients with rare diseases whenever appropriate. We appreciate the proposed guidance that members of the Duchenne muscular dystrophy (DMD) community submitted to FDA in June 2014. FDA announced the DMD community's guidance through a Federal Register notice on September 4, 2014, to seek additional input and public comment. FDA carefully considered the consortium's guidance and public comments received in response to it in writing the agency's own draft guidance.

The draft guidance for industry, "Duchenne Muscular Dystrophy and Related Dystrophinopathies: Developing Drugs for Treatment," was released in June 2015, and a 60-day comment period was provided. We are currently reviewing the comments received and plan to issue a final guidance following review of those comments. The purpose of the guidance to industry is to assist sponsors in the clinical development of drugs for treating X-linked Duchenne muscular dystrophy and related dystrophinopathies, discuss various pathways to approval including the use of intermediate clinical endpoints, and to serve as a focus for continued discussions on this topic.

13. Drug Vial Sizes

The Food and Drug Administration is responsible for approving vial sizes and fill volumes for injectable drug products before products come to market, in a manner that balances multiple considerations related to safe use and administration of the product. In 2015, the FDA issued guidance documents for industry on this matter. Given that many factors play a role in FDA's assessment of vial sizes for injectable drug products, the Committee directs the FDA to provide a report to Congress within 180 days of enactment with recommendations on how the FDA may assist in addressing concerns about appropriate vial sizes and fill volumes from a safety perspective, to ensure that patients are receiving the appropriate care.

FDA Response:

FDA will provide the requested report.

14. Experimental Drugs for Terminally Ill Patients

The Committee directs the FDA to report on efforts to increase patient access to experimental drugs for terminally-ill patients.

FDA Response:

FDA will provide the requested report.

15. FDA Food Mission

The Committee requests information on FDA's current nutrition activities and resources.

FDA Response:

FDA's Foods and Veterinary Medicine (FVM) Program helps to ensure that the nation's food supply is wholesome, that food is labeled truthfully and in a manner that is not misleading, and that nutrition labeling is informative and accurate. The FVM Program also promotes a nutritious food supply that ultimately contributes to the risk reduction of diet-related chronic disease. The FVM Program, including Center and Field activities, spent \$28.9 million on nutrition-related priorities in FY 2016.

16. Food Contact Notification User Fees

The Committee recommendation does not include proposed user fees.

FDA Response:

FDA acknowledges the Committee's recommendation on the proposed user fees.

17. Food Packaging

The Committee encourages FDA to increase the involvement of experts in endocrinology as FDA continues to evaluate the chemical BPA and similar alternatives such as BPS as it relates to health safety of human exposure through food packaging. Evaluations shall include specific focus on the long-term low dose exposure that these chemicals have on the endocrine system

FDA Response:

FDA agrees that endocrinology is an important discipline for the evaluation of chemical safety. FDA personnel have expertise in a broad range of scientific and medical fields, including endocrinology, for assessment of relevant chemical safety issues. As an example, in the fall of 2014, FDA experts specializing in toxicology, analytical chemistry, endocrinology, epidemiology, and other fields completed a four-year review of more than 300 scientific studies on the safety of BPA. Among other factors, this review evaluated available information on long-term low dose exposure and the endocrine system. Reports from this team of experts can be found at: www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm166145.htm

and

www.fda.gov/Food/IngredientsPackagingLabeling/FoodAdditivesIngredients/ucm064437.htm.

18. Food Traceability

The FDA announced two pilot projects on September 7, 2011 pursuant to section 204 of the Food Safety Modernization Act, which required pilot projects for improving product tracing along the food supply system and establishment of recordkeeping requirements for high-risk foods to help in tracing products. The pilots were conducted by the Institute of Food Technologists, in consultation with industry sectors, USDA, State agencies and consumer groups, and the resulting report was released on March 4, 2013. The Committee notes that industry and government continue to pursue their traceability goals on separate tracks and with little collaboration. The Committee further notes that no report has been issued pursuant to section 204(a) of the act, which directs the Secretary to report to Congress on the findings of the pilot projects, and the Committee directs the Secretary to issue such report. Furthermore, the Committee notes that the Secretary has failed to propose a rulemaking to establish the recordkeeping requirements as required by section 204(d) of the act. The Committee directs the FDA to collaborate with science-based international and industry-led food traceability initiatives of the type recommended by the pilot projects. In addition, the Committee directs the Commissioner to make publicly available information on FDA's efforts to encourage the work of science-based international and industry-led food traceability initiatives.

FDA Response:

FDA provided the report to Congress on the two traceability pilots on January 5, 2017. A copy of the report can be found at:

www.fda.gov/downloads/Food/GuidanceRegulation/FSMA/UCM540940.pdf. In the report,

FDA provides recommendations that cover a broad spectrum of activities including, but not limited to, identifying uniform key data elements, finding ways to link foods as they move through the supply chain, and collaborating with industry and encouraging proactive industry-led efforts to improve traceability. The report also outlines FDA's strong historical engagement with industry on this topic, including collaboration on pilot projects and communications through public meetings. Consistent with our past practices, FDA will continue to share with the public, such as during meetings and conferences – information on traceability projects and other collaborations with our stakeholders. FDA remains committed to working with industry to improve traceability, such that a contaminated food can more rapidly be traced to its source and removed from the marketplace in order to prevent consumers from becoming ill.

19. Foreign High Risk Inspections

The bill provides an additional \$3,000,000 and a total of \$8,000,000 for the FDA's Office of Global Regulatory Operations and Policy to enhance the compliance of foreign manufacturers and exporters of food, medical devices and pharmaceuticals through on-site verification.

FDA Response:

FDA's Office of Global Regulatory Operations and Policy intends to spend the amount directed by Congress to bolster the important ongoing development and utilization of a targeted, risk-based, and efficient inspection model for foreign high risk facilities. The funding will support efforts to develop key systems, processes, and data sources in different commodity areas including food safety and medical products. The funding will also support enhancements to FDA's ability to identify risk indicators in existing data sets.

These efforts may include mutual reliance or other methods to leverage inspection and site data from foreign regulators. Additionally, these efforts will support the incorporation of commercially available information on high-risk establishments for onsite verifications. The increased funding will drive significant progress in achieving these multi-year objectives.

20. Human Tissue Models, Including 3D Models

The Committee is aware that bioengineered human tissue models hold the promise of improving the drug discovery process by enhancing the ability to predict potential safety risks during preclinical testing and post market safety of pharmaceutical products, thereby minimizing the potential risk of adverse toxicological outcomes to patients during clinical trials and post-approval use. The Committee directs the Secretary to prepare a report, with input from the Office of Regulatory Science and Innovation and the National Center of Toxicology Research, on how to accelerate adoption of predictive bioengineered human tissue models when used in combination or in lieu of animal testing models pre and post market approval. The Committee directs the Secretary to report recommendations to the House and Senate Appropriations Committees within 180 days of enactment of this Act.

FDA Response:

FDA is supportive of the Committee's recommendation that a report be developed to address how to accelerate adoption of predictive bioengineered human tissue models when used in combination or in lieu of animal testing models before and after market approval and will support the Secretary in preparation of such a report.

21. In Silico Clinical Trials

In Silico clinical trials use computer models and simulations to develop and assess devices and drugs, including their potential risk to the public, before being tested in live clinical trials. Advanced computer modeling can also be used to predict how a drug or device will behave when deployed in the general population, thereby protecting the public from the unintended consequences of side effects and drug interactions. In Silico trials protect public health, advance personalized treatment and can be executed quickly and for a fraction of the cost of a full scale live trial. The FDA has advocated the use of such systems and utilized them with success in the past. Therefore, the Committee strongly encourages the FDA to make greater use of In Silico trials for devices and drug therapies before they are released for live clinical trials.

FDA Response:

FDA acknowledges the benefits to public health provided by in silico clinical trials, and has previously advocated for their use as one of many research tools. Modeling and simulation play a critical role in organizing diverse data sets and exploring alternate study design strategies, so that safe and effective new therapeutics can advance more efficiently, from preclinical studies through clinical trials to market. The efforts in modeling and simulation are enabled through

multiple collaborations with external parties that provide additional expertise and infrastructure to advance the development of innovative state-of-the-art technologies.

FDA advises sponsors on the use of modeling and simulation to predict clinical outcomes, inform clinical trial designs, support evidence of effectiveness, optimize dosing, predict product safety, and evaluate potential adverse event mechanisms. Some computational models are firmly embedded in the product review process and supported by guidances, while others are used as needed (fit-for-purpose) or in a research capacity to help inform regulatory decisions.

FDA is also collaborating, both internally and externally (with both Investigational New Drug application sponsors and New Drug Application stakeholders, researchers, and other regulatory bodies), to maximize the use of modeling and simulation to complement clinical trials or to improve their design and success, including – but not limited to – comparative predictions of Phase 3 responses across a novel therapeutic class and replacement of clinical studies with in silico modeling for cardiac safety testing.

In addition FDA is actively working to explore modeling approaches and enhance their regulatory impact through the Agency’s Scientific Computing Board whose goal is to advance science, streamline operations, and strengthen FDA’s overall effectiveness. FDA drug modeling reviewers have also actively engaged with device modeling efforts to build regulatory models for product design and evaluation, including the development of a digital library of models and a family of “virtual patients” for device testing.

22. In Vitro Clinical Trials

In vitro clinical trials use specimens collected from patients to test how a particular cancer or disease will react to a specific therapy or combination of therapies. This personalized approach to treatment can improve a patient’s quality of life by increasing the likelihood that physicians and researchers will find the proper combination of drugs uniquely suited to treat that individual’s illness. An emerging new scientific methodology, In Vitro trials allow researchers to test therapeutics and treatment strategies on living human tissues without the risks posed by traditional whole patient clinical trials. Personalized treatment through In Vitro trials dismantles the “one size fits all” approach to care and enables medical professionals to diagnose and treat patients in a more efficient and effective way. Accordingly, the Committee strongly encourages the FDA to make greater use of In Vitro clinical trials for Investigational New Drug applications and general therapeutic indications, especially as it relates to complicated cancers and other common disease States.

FDA Response:

FDA acknowledges the benefits to public health provided by In Vitro trials, and the potential to provide more personalized medical treatment options for patients. The Critical Path Innovation Meeting program, launched by FDA in 2013, allows drug developers and other stakeholders to discuss new and emerging technologies with FDA. These meetings have included topics related to In Vitro trials to identify suitable combination therapies to take into clinical trials. FDA will continue to engage stakeholders through this mechanism to discuss such technologies. Where appropriate, companies may still discuss specific drug development proposals involving these technologies in the setting of FDA's formal meetings with industry under the Investigational New Drug application.

In addition, consortia and other stakeholders may interact with FDA via the Drug Development Tools Qualification Program to the extent that a particular technology platform is being formally developed to support regulatory decision-making. FDA has received submissions involving In Vitro trials, and will continue to engage with sponsors of drug development tools to advance In Vitro trials into drug development.

23. Listeriosis

Listeriosis is a serious illness that is usually caused by eating food contaminated with the bacterium *Listeria monocytogenes*. The disease primarily affects older adults, pregnant women, newborns, and adults with weakened immune systems. To better understand the risk of listeriosis associated with the consumption of certain foods, the FDA has conducted or is conducting risk assessments on ready-to-eat foods, soft ripened cheeses, smoked finfish, and retail delicatessens. These risk assessments have been used to protect and enhance the public health.

The FDA uses risk analysis to ensure that regulatory decisions about foods are science-based and transparent. For the first time, the consumption of certain frozen vegetables has been linked to a multi-state outbreak of listeriosis. Because of this outbreak, the need to protect the public health, and to ensure science-based and transparent regulatory decisions, the Committee encourages the

FDA to conduct a quantitative risk assessment of the relative risk to public health from foodborne *Listeria monocytogenes* among frozen vegetables and other frozen foods currently considered not ready-to-eat.

FDA Response:

FDA determines the risk associated with *Listeria monocytogenes* in a frozen food, such as a frozen vegetable, on a case-by-case basis depending on a number of factors, including whether it supports the growth of the pathogen when thawed and how the frozen food is commonly handled. Some frozen vegetables present minimal risk to consumers because these vegetables are commonly held frozen, cooked from a frozen state, and immediately consumed. By contrast, some frozen vegetables can be thawed and used without cooking in salads, whether in commercial salad bars or in the home; and some recipes available to consumers describe the preparation of products using frozen vegetables that are thawed but not cooked. Where a frozen food that supports growth of *L. monocytogenes* is thawed and held for considerable time at refrigerated or room temperature, such as on a salad bar, it may pose a risk to consumers because it has not been subject to cooking that would kill the pathogen and it will be held under conditions that allow pathogen growth to occur.

Every few years, FDA identifies new vehicles for *L. monocytogenes* illness among foods with no known prior history of contamination or epidemiological link to listeriosis, and some foods with limited histories of contamination can prove to be higher risk than previously thought. For example, in 2016, CDC identified a multistate outbreak of listeriosis linked to frozen vegetables by epidemiologic and laboratory evidence. We anticipate that the pattern of discovering new food vehicles will continue, if not hasten, with the advancement of whole genome sequencing in connecting known clinical illnesses with the foods responsible for those illnesses.

FDA is not aware of the type of comprehensive up-to-date survey data that would be needed to develop a quantitative risk assessment for foodborne *L. monocytogenes* in frozen vegetables; therefore, FDA would have to conduct its own survey prior to conducting such a risk assessment or to commission another organization to conduct such an assessment. For example, a 2003 Quantitative Assessment of Relative Risk to Public Health from Foodborne *Listeria monocytogenes* Among Selected Categories of Ready-to-Eat Foods -- jointly developed by FDA, the Centers for Disease Control and Prevention, and the USDA's Food Safety and Inspection Service -- took four (4) years to complete, beginning with a *Federal Register* notice of intent issued in 1999 and culminating in completion of the final assessment in 2003.

24. Mammography Quality Standards Act

The Committee recommendation includes full funding as requested for implementation of the Mammography Quality Standards Act. This program sets national quality standards for mammography facilities, equipment, personnel and operating procedures, and has improved the quality of mammography and made mammograms a more reliable tool to detect breast cancers.

FDA Response:

FDA intends to fully fund the MQSA program.

25. Medical Devices

The Committee is concerned about the lack of transparency and consistency with the medical device facility inspection process. This often leads to inefficiencies and inconsistencies in the inspection process. The Committee urges the agency to work with stakeholders and Congress to improve the facility inspection process. Potential process improvements may include, but are not necessarily limited to, more timely and frequent communications related to inspection observations and remediation plans, as well as changes to the way medical device Export Certificates (e.g., Certificate to Foreign Government, etc.) are affected by FDA Observational Findings following a facility inspection.

FDA Response:

A majority of both domestic and foreign device inspections involve four or fewer days on-site. There are many inspections that conclude on the same day as arrival. Investigators follow the same procedures, which are publicly available, when conducting a domestic inspection as they do for a foreign inspection. The Investigations Operations Manual, which is publicly available, states that every reasonable effort should be made to discuss all observations with the management of the establishment as they are observed, or on a daily basis, to minimize surprises, errors and misunderstanding when the 483 is issued. Inspectional staff will be reminded of these requirements.

FDA is currently addressing domestic inspection times through improved internal procedures and through Program Alignment, which will take effect on May 15, 2017. Program Alignment is FDA's reorganization of its inspection program to a commodity-based and vertically-integrated structure. It is intended to improve consistency by focusing on investigators' training and workload on one product area; for example, only device investigators will inspect device establishments and drug investigators will inspect drug establishments.

FDA has indicated its willingness to hold a public meeting to gather input from affected stakeholders about improvements to the device inspections process. FDA is working with HHS to review legislative proposals intended to help streamline the device inspections process and to improve the process for issuing export certificates.

26. Medical Device Performance

The Committee is aware that each year the FDA is required to submit a report to Congress regarding performance goals for user fees paid by medical device manufacturers.

However, the Committee is concerned that FDA may not be providing information about how the FDA is meeting timelines established in law by Congress. The Committee directs the FDA to provide a report to the Committee within 90 days of the date of enactment including performance information for statutory timelines for medical devices, specifically: the number of de novo requests under 513(f)(2) for which FDA has met the 120 day statutory requirement, and the total number of de novo requests submitted; the number of requests for classification under 513(g) and the number for which FDA has met the 60 day statutory requirement; and, the number of orders for postmarket device surveillance under 522 for which the FDA has responded within 60 days of receipt of such plan.

FDA Response:

FDA submits an annual report to Congress as well as provides quarterly reporting to the industry and the public. Under the MDUFA IV agreement submitted to Congress in January 2017, FDA would report new information to Congress, industry, and the public, including its performance on de novos.

27. Medical Foods

The Committee urges the FDA to be more active in engaging external stakeholders on best practice standards for medical foods that are based upon the Generally Recognized as Safe [GRAS] status. The Committee requests the FDA work with external stakeholders in forming a framework for a distinct regulatory pathway for medical foods that does not encumber its progress towards approval for patient use.

FDA Response:

FDA recognizes that medical foods serve a critical role in the lives of patients with inherited metabolic disorders such as phenylketonuria (PKU). The agency's goals for medical foods include staying abreast of the science in this rapidly evolving field; working to ensure the availability of safe and appropriately labeled; and providing sound guidance to patients,

healthcare providers, and industry. For example, FDA provided stakeholders an updated medical foods guidance in May 2016.¹⁰⁶

DA prioritizes communication and collaboration with medical food stakeholders on scientific issues. For example, a recent NIH study revealed that a medical food intended for a single specific metabolic disorder was being inappropriately used to treat patients with a combination metabolic disorder, resulting in adverse effects. FDA, NIH, and a manufacturer of one such product collaborated on the matter, which led to the manufacturer changing the product labeling to warn healthcare practitioners against its use for the specific combination disorder at issue. The manufacturer and NIH agreed to continue working in partnership to further study that disorder (and other related metabolic disorders), with FDA providing regulatory knowledge and guidance as needed.

We note that issues pertaining to GRAS status are only some of the many potential issues that can affect medical foods, and that GRAS status has no bearing on whether a product meets the statutory definition of a medical food. Further, we note that medical foods are not subject to an approval process. Rather, medical foods are a type of conventional food.

28. Medical Gases

The Committee is significantly concerned that FDA has not initiated rulemaking, nor listed such rulemaking as a priority in the Unified Agenda, to address numerous longstanding regulatory issues for medical gases despite the statutory requirement section 1112 in FDASIA (Public Law 112–144) to issue a final rulemaking addressing all necessary changes for medical gases by July 9, 2016. The Committee disagrees with the FDA report to Congress sent on June 29, 2015, and believes that FDA must address medical gas regulatory issues with a new rulemaking amending the Federal drug regulations. Therefore, FDA shall issue final medical gas regulations as required by FDASIA not later than July 9, 2016. If FDA determines that it is a more efficient use of resources, it should incorporate by reference a voluntary consensus standard by an ANSI-accredited standard development organization as required by the National Technology Transfer and Advancement Act of 1995 (Public Law 104–113), and the Office of Management and Budget [OMB] Circular A–119. If FDA fails to issue final regulations with respect to medical gases by the statutory deadline, the Agency shall incorporate by reference voluntary consensus safety and labeling standards developed by an ANSI-accredited standard development

¹⁰⁶ Guidance for Industry: Frequently Asked Questions About Medical Foods; Second Edition, www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm054048.htm

organization until such time as the Agency issues final regulations consistent with section 1112 of Public Law 112–144.

FDA Response:

FDA issued the final rule “Medical Gas Containers and Closures: Current Good Manufacturing Practice Requirements,” on November 18, 2016 (81 FR 81685). This final rule (which revised warning statements for medical gases and required measures intended to reduce the likelihood of medical gas mix-ups) satisfies the FDASIA medical gas rulemaking requirement, though FDA may undertake additional rulemaking on medical gases as needed.

FDA understands that industry stakeholders believe that FDA should promulgate a separate regulatory scheme specific to medical gases, despite the Agency’s determination (explained in its 2015 report to Congress on this topic) that extensive rulemaking in this area is unnecessary. However, FDA remains convinced that we can work within the existing regulatory framework to set clear and appropriate regulatory expectations for the production and distribution of medical gases without extensive additional rulemaking. FDA recently made revisions to the medical gas inspection program (completed in 2015), and is very far along in the process of producing revised guidance on current good manufacturing practices applicable to medical gases.

FDA will, of course, undertake targeted rulemaking on medical gases to address any significant public health issues that arise, or to satisfy statutory rulemaking requirements – as demonstrated by the final rule published in November 2016. However, FDA continues to believe that the separate regulatory scheme for medical gases sought by industry stakeholders is unnecessary.

FDA also has significant concerns with any proposal mandating that FDA incorporate medical gas industry standards by reference. First, incorporation by reference requires notice-and-comment rulemaking, with all of the resource burdens rulemaking entails. Furthermore, the proposal to incorporate by reference “voluntary consensus safety and labeling standards” would first require such standards to be developed, as it does not appear that any currently exist. Rather, the safety and labeling standards industry has sought to have FDA incorporate by reference were created entirely by the industry, with no FDA involvement. In fact, these “standards” are largely identical to the dozens of new regulations industry proposed during the 2013 FDASIA regulation review, and which FDA determined were generally not needed. FDA is not opposed to referencing specific targeted standards co-developed by FDA and the medical gas industry (provided FDA agrees such standards meet regulatory and public health needs) and engaging in rulemaking as necessary and appropriate. However, FDA sees significant legal,

policy, logistical, and resource concerns with adopting unvetted industry standards by reference.

Finally, FDA is concerned with the precedent that would be set by creating a separate regulatory scheme for a given product class. In general, FDA believes it is much more efficient to rely upon the general regulatory scheme applicable to all drug products, and to provide class-specific recommendations through guidance and other non-rule-making means.

Accordingly, FDA's position continues to be that the extensive rulemaking sought by industry is not necessary.

29. Nanotechnology

The Committee recognizes the increased capabilities that FDA has developed to study environment, health, and safety of nanomaterials within FDA's Jefferson Laboratory Campus, including the National Center for Toxicological Research, and its consolidated headquarters at White Oak, Maryland. The Committee expects FDA to continue to support collaborative research with universities and industry on the toxicology of nanotechnology products and processes in accordance with the National Nanotechnology Initiative Environment, Health, and Safety Research Strategy as updated in October 2011.

FDA Response:

FDA continues to enhance capabilities to understand the health impact and safety of nanomaterials through staff training, continued research into the safety and disposition of nanomaterials in various products, increased collaboration with government agencies — both national and international — and participation in standards-development activities. FDA continues its efforts to enhance its nanomaterials research infrastructure. Since 2011, the CORES research program funded a total of 36 projects and is part of FDA's Nanotechnology Regulatory Science Research Plan. Together with the advanced Nanocore infrastructure at the Jefferson Laboratories campus and the facilities at the White Oak campus, FDA is able to conduct research to accurately characterize, detect, and quantify nanomaterial in FDA-regulated products to help assess safety and inform risk assessment. FDA's Nanotechnology Task Force is committed to advancing nanotechnology research and collaborations.

FDA continues to engage with industry and other agencies through the National Nanotechnology Initiative (NNI), including participation in the US-EU Communities of Research,

Indo-US Science and Technology Forum, Nanotechnology for Healthcare Conference, and collaborations with the Consumer Protection Safety Commission, National Institute of Environmental Health Sciences/National Toxicology Program, and the National Cancer Institute.

The 2016 Global Summit on Regulatory Science focused on “Nanotechnology Standards and Applications,” and was hosted by FDA/NCTR and Arkansas Research Alliance. There were other U.S. government agencies in attendance at the Summit — held on the NIH campus — as well as from 19 countries. This annual Summit is held in cooperation with the European Union and global regulatory and standards agencies to discuss the standards methodologies and standards that are helpful for regulatory review. The outcome from the Summit was a list of standards in nanotechnology that are relevant to drugs, devices, and consumer products. FDA will also continue to engage industry through the standards-development organizations and develop relevant and consensus based standards that can help regulatory reviews.

30. National Antimicrobial Resistance Monitoring System

The Committee recommendation includes \$10,800,000 for the National Antimicrobial Resistance Monitoring System, equal to the level provided in fiscal year 2016.

FDA Response:

FDA will provide funding equal to FY 2016 levels as recommended by the Committee.

31. Olive Oil

The Committee directs the FDA to take a sampling of off-the-shelf olive oil bottles offered for sale to consumers to determine if it is adulterated with seed oil, pursuant to Section 342 of the FDCA, and report to Congress within 270 days on its findings.

FDA Response:

In 2014, FDA performed a survey of olive oil products available to consumers within the United States, and included a cross-section of domestic and imported products in the survey. FDA used USDA grading standards in the assessment and used an analytical methodology capable of detecting 10 percent seed oil adulteration. Out of 88 products surveyed, only 3 showed evidence of adulteration. This work was published in a peer-reviewed publication^{1,2}. FDA continues to develop better methods that may be able to detect adulteration beyond gross addition of seed oils^{3,4}. FDA plans to continue to monitor the marketplace for adulterated olive oil products to ensure consumer safety and proper labeling of imported olive oil.

1. Authenticity Assessment of Extra Virgin Olive Oil: Evaluation of Desmethylsterols and Triterpene Dialcohols; Srigley, CT; Oles, CJ; Kia, ARF; Mossoba, MM; JOURNAL OF THE AMERICAN OIL CHEMISTS SOCIETY; 93(2); 2016; pp: 171-181. (DOI: 10.1007/s11746-015-2759-4)
2. Authenticity Assessment of Extra Virgin Olive Oil, part 2. Evaluation of fatty acids and triacylglycerols; manuscript in preparation, 2017.
3. Nontargeted, Rapid Screening of Extra Virgin Olive Oil Products for Authenticity Using Near-Infrared Spectroscopy in Combination with Conformity Index and Multivariate Statistical Analyses; Karunathilaka, SR; Kia, ARF ; Srigley, C (Srigley, Cynthia); Chung, JK; Mossoba, MM; JOURNAL OF FOOD SCIENCE; 81(10); 2016; pp C2390-C2397. DOI: 10.1111/1750-3841.13432

4. Developing FT-NIR and PLS1 Methodology for Predicting Adulteration in Representative Varieties/Blends of Extra Virgin Olive Oils; Azizian, H; Mossoba, MM ; Fardin-Kia, AR ; Karunathilaka, SR; Kramer, JKG; LIPIDS; 51(11); 2016, pp 1309-1321 (DOI: 10.1007/s11745-016-4195-0).

32. Opioid Overdose Prevention

The Committee is very concerned about the ongoing prescription opioid abuse epidemic, and is additionally concerned by FDA's decision in August 2015 to approve OxyContin for pain management in children as young as 11 years old. As the Agency that oversees the approval of these drugs, the FDA has a responsibility to consider the public health impact of opioid abuse and overdose death. Therefore, the Committee directs FDA to continue implementing its opioids action plan announced in February 2016 to take concrete steps toward reducing the impact of opioid abuse on American families and communities, and to strongly consider the danger of addiction and overdose death associated with prescription opioid medications when approving and regulating the manufacturing, marketing and distribution of opioid medications. This plan should include policies aimed at reversing the epidemic while still providing patients access to effective pain relief. Finally, the FDA is directed to refer any new drug application for an opioid submitted under section 505(b) of the Federal Food, Drug and Cosmetic Act to an advisory committee for their recommendations prior to approval, unless the FDA finds that holding such advisory committee meeting is not in the interest of protecting and promoting public health.

FDA Response:

FDA will continue to implement its opioid action plan announced in February 2016, and will continue to follow section 106 of the Comprehensive Addiction and Recovery Act (CARA) concerning this action plan. Specifically, FDA will convene an expert advisory committee before approving any New Drug Application for an opioid unless FDA determines that such referral is not required, as provided in CARA section 106(a)(1)(B) ("Public health exemption"). Additionally, the Pediatric Advisory Committee will make recommendations regarding a framework for pediatric opioid labeling before any new pediatric labeling is approved. Finally, FDA will continue to appropriately consider the public health consequences of opioid abuse (including addiction and overdose) when regulating opioid medications.

33. Over-the-Counter Drugs

The Committee directs the FDA provide a report on the funding levels put to OTC Monograph issues for the past 10 years (fiscal year 2006–2016).

FDA Response:

FDA will provide the requested report.

34. Parallel Review Pilot

The Committee directs the FDA to report on plans to extend the pilot and steps the agency will take to encourage more manufacturers to utilize the pilot, including considerations for manufacturers choosing the 510(k) clearance pathway and for novel products deemed covered by CMS but that warrant evaluation to ensure the appropriate level of coverage.

FDA Response:

FDA and CMS have already made the pilot Parallel Review Program into a permanent program, as stated in the published guidance 81 FR 73113-15 (Oct. 24, 2016). CMS, rather than FDA, determines the appropriate level of coverage. FDA and CMS continue to work together to balance sponsor evidence requirements to find the least burdensome approach to evidence collection.

35. Patient Focused Drug Development Initiative

The Committee applauds FDA's efforts to engage external and patient stakeholders through FDA's Patient Focused Drug Development initiative which includes convening disease-specific public meetings, publication of Voice of the Patient reports for each meeting, and welcoming stakeholders to conduct externally-led Patient Focused Drug Development Meetings. The Committee encourages FDA to continue working with external stakeholders to develop a strategic action plan in follow up to these activities.

FDA Response:

FDA values the experiences and perspectives of patients and caregivers. Under PDUFA V, FDA will have conducted 24 disease-specific patient-focused drug development meetings to systematically obtain patient and caregiver input on a range of disease areas. To help expand the benefits of FDA's Patient-Focused Drug Development (PFDD) initiative, FDA is also

welcoming patient organizations to identify and organize patient-focused collaborations (e.g., externally-led PFDD meeting) to generate public input on other disease areas.

FDA will continue efforts to enhance the incorporation of the patient's voice into drug development and regulatory decision-making. For PDUFA VI reauthorization, FDA and industry reached agreement on a set of proposed enhancements to facilitate the advancement and use of systematic approaches to collect and utilize robust and meaningful patient input that can inform drug development. The 21st Century Cures Act also has several FDA requirements on Patient-Focused Drug Development, which are mostly aligned with the PDUFA VI proposed recommendations.

36. Pediatric Device Consortia Grants

The Committee is pleased that the nine FDA-funded Pediatric Device Consortia have assisted in the development of more than 650 proposed pediatric medical devices since its inception in 2009, as well as promoting job-growth in the healthcare sector, and as such, continues to support this critical effort. The program funds consortia to assist innovators in developing medical and surgical devices designed for the unique needs of children that often go unmet by devices currently available on the market. The Committee recommendation includes \$5,000,000 for Pediatric Device Consortia Grants.

FDA Response:

The PDC Grant Program continues to successfully support the development of pediatric medical devices and fulfill unmet needs in the pediatric population. Since the program's inception in 2009, the pediatric device consortia have advised innovators on more than 900 potential pediatric devices – and assisted on more than 300 projects just this past year alone. As a result of funding advice provided by the consortia, more than \$ 110 million of additional funds have been raised to advance pediatric device projects affiliated with the consortia. In the last 4 years, more than ten PDC-assisted pediatric medical devices have become available for use in pediatric care, including TIVA, a needle-free blood collection device, and SleepWeaver Advance Pediatric CPAP Mask. The FDA recognizes the value of the Pediatric Device Consortia in supporting the pediatric medical device ecosystem toward development and innovation for children. The FDA anticipates funding the PDC at the appropriated level for the upcoming year, consistent with prior years.

37. Proprietary Information

The Committee is concerned with requirements in the Nutrition Facts proposed rule that may cause some manufacturers to disclose proprietary records. Therefore, the Committee urges the FDA to ensure that steps are imposed to protect the security of trade secrets and commercial confidential information if it is provided to FDA.

FDA Response:

FDA issued a final rule for the revision of the Nutrition Facts and Supplement Facts labels on May 27, 2016. The final regulation for the Nutrition Facts label does not require firms to submit information to FDA. As a result, the circumstances under which FDA would review company information are limited to inspection activities associated with verifying compliance. However, we are aware of concerns regarding the safeguarding of information that FDA might review or collect during an inspection, and FDA is training inspectors regarding those concerns. Those records requirements are only for foods for which an adequate analytical method to verify the compliance of a nutrient declaration is not available. The records will allow us to verify the declared amount of each such nutrient and that such amount is truthful and not misleading. Thus, the records requirements will help in the efficient enforcement of the Federal Food, Drug, and Cosmetic Act. On January 5, 2017, FDA announced the availability of draft guidance with a request for comment, entitled Questions and Answers on the Nutrition and Supplement Facts Labels Related to the Compliance Date, Added Sugars, and Declaration of Quantitative Amounts of Vitamins and Minerals. Among other things, that guidance, when final, will provide further guidance to industry on the types of records required and how the relevant information can be acquired.

The recordkeeping requirements in the May 2016 final rule are intended to be flexible in that they do not require a specific document to be retained, nor do they require information on proprietary recipes or overall formulations. Instead, the records requirements seek specific content information only for certain nutrients for which no analytical method is available, and this information could be provided in various forms by the manufacturer. Thus, the records required to verify the accuracy of the declared amount of these specific nutrients can include records that do not include proprietary information.

Furthermore, even if a manufacturer's records contained confidential commercial information or trade secret information, or a manufacturer believed that certain information should be protected from public disclosure, there are safeguards to protect against public disclosure of that information and mechanisms that a manufacturer can use to assert that certain information should be protected from disclosure. FDA protects confidential information from disclosure, consistent with applicable statutes and regulations, including 5 U.S.C. 552(b)(4), 18 U.S.C. 1905, and 21 CFR part 20. For example, our regulations pertaining to disclosure of public

information, at 21 CFR part 20, include provisions that protect trade secrets and commercial or financial information which is privileged or confidential. If a manufacturer provides proprietary recipe information to show compliance with the nutrition label regulation, the manufacturer should mark the information as such before providing any requested records to FDA.

38. Seafood Advisory

The Committee directs the FDA ensure that pregnant women receive final guidance on nutrition advice for what seafood is safe and healthy to consume that is consistent, understandable, and based on the FDA's latest scientific review of the net effects of seafood consumption.

FDA Response:

On January 18, 2017, FDA and EPA jointly issued final advice regarding fish consumption. This advice is geared toward helping women who are pregnant or may become pregnant – as well as breastfeeding mothers and parents of young children – make informed choices when it comes to fish that are healthy and safe to eat. (The advice refers to fish and shellfish collectively as “fish.”)

To help these consumers more easily understand the types of fish to select, the agencies have created an easy-to-use reference chart that sorts 62 types of fish into three categories:

- “Best choices” (eat two to three servings a week)
- “Good choices” (eat one serving a week)
- “Fish to avoid”

Fish in the “best choices” category make up nearly 90 percent of fish eaten in the United States.

An FDA analysis of fish consumption data found that 50 percent of pregnant women surveyed ate fewer than 2 ounces a week, far less than the amount recommended. Because the nutritional benefits of eating fish are important for growth and development during pregnancy and early childhood, the agencies are advising and promoting a minimum level of fish consumption for these groups. The advice recommends 2-3 servings of lower-mercury fish per week, or 8 to 12 ounces. However, all fish contain at least traces of mercury, which can be harmful to the brain and nervous system if a person is exposed to too much of it over time. The maximum level of consumption recommended in the final advice is consistent with the previous recommended level of 12 ounces per week. The new advice is consistent with the 2015 - 2020 Dietary Guidelines for Americans.

When updating the advice, the agencies took a cautious and highly protective approach to allow consumers to enjoy the benefits of fish while avoiding those with higher levels of mercury, which is especially important during pregnancy and early childhood. The average mercury content of each type of fish was calculated based on FDA data and information from other sources. The updated advice cautions parents of young children and certain women to avoid seven types of fish that typically have higher mercury levels: tilefish from the Gulf of Mexico; shark; swordfish; orange roughy; bigeye tuna; marlin; and king mackerel.

For fish caught recreationally, consumers are urged to check for local advisories where they are fishing and gauge their fish consumption based on any local and state advisories for those waters. If no information on fishing advisories is available, eat just one fish meal a week from local waters and also, avoid other fish that week. Consumers should clean and trim the fish they catch of fat and skin, since locally-caught fish may contain contaminants besides mercury that can be reduced by proper trimming and cooking, (e.g. broiling instead of frying can reduce some contaminants by letting fat drip away from the fish).

All retailers, grocers and others are urged to post this new advice, including the reference chart listing fish to choose, prominently in their stores so consumers can make informed decisions when and where they purchase fish. The agencies will be implementing a consumer education campaign working with a wide array of public and private partners featuring the new advice.

39. Shrimp Imports

The Committee is concerned the FDA continues to detect an alarming amount of imported shrimp raised with hormones, antibiotics, or other drugs not approved for use in the United States. Therefore, the Committee directs the FDA to work with Customs and Border Protection [CBP] to establish a 2-year pilot program to better track shrimp imports and inspections by port of entry, in order to increase enforcement and improve food safety. In addition, the Committee directs the FDA to assist CBP to provide details on opportunities for enhancing FDA and CBP coordination on improving the safety of shrimp imports into the U.S., initial, both for a briefing required of CBP within 180 days and for the overall pilot program report.

FDA Response:

FDA has a variety of tools to help monitor and determine compliance with seafood safety requirements and has the ability to track import information, import activities, and inspections related to products, including shrimp, offered for import into the U.S. through existing data systems, some of which are directly linked to CBP data systems. FDA screens all import entries

electronically prior to a product entering U.S. commerce. As part of the Agency's surveillance activities at the border, a subset of those entries are physically examined by FDA investigators and may subsequently be sampled and analyzed depending on the potential risk associated with each shipment. If deficiencies are found with a product offered for import, the Agency can issue an Import Alert. Additionally, FDA may conduct sampling of an imported product during the course of a domestic inspection.

FDA also conducts inspections of foreign processing facilities for compliance with FDA regulations and requirements including those concerning seafood HACCP. During an inspection, FDA investigators may also follow up on previous issues of concern or other information that the Agency has obtained through a variety of means, including data entered on commodities offered for import into the U.S.

FDA already utilizes data to coordinate Agency surveillance and enforcement activities and identify trends that may be occurring in the imported shrimp industry. To help prevent adulterated fishery products from entering domestic commerce, FDA has a monitoring program that also includes testing for residues of unapproved antibiotic chemicals and drugs. Upon discovering any use of an unapproved drug through the testing program or evidence developed during an FDA foreign inspection, FDA typically employs several tools, including Import Alerts, communication to the foreign government's competent authority, increased surveillance by FDA of the potentially adulterated products, and other actions such as seizure.

In addition, it is important to note that FDA is already working closely with CBP on imported seafood activities through mutual involvement with the Presidential Task Force on Combating Illegal, Unreported, and Unregulated (IUU) Fishing and Seafood Fraud. These activities are coordinated, in part, through FDA's presence at the Commercial Targeting and Analysis Center (CTAC) as well as interaction at ports of entry. Based on an IUU recommendation, there already is a pilot program regarding seafood fraud, and imported shrimp is a major commodity to be targeted.

In light of these activities already underway, we do not feel there is a need for an additional pilot program as described in the report language at this time, but would be happy to further discuss this with the Committee.

40. Sodium Guidance

The Committee is aware that the FDA is considering issuing guidance to food manufacturers in order to reduce sodium in various food categories. It is imperative that any guidance be issued using the latest sound science. The Centers for Disease Control and Prevention and the IOM are

working together to update the Dietary Reference Intake [DRI] report on sodium. The FDA is encouraged to issue any voluntary or mandatory guidance based upon an updated DRI report.

FDA Response:

In June 2016, FDA issued draft guidance for public comment for voluntary sodium reduction goals in commercially processed and prepared food, both in the short-term and over the long-term (81 FR 35363). This draft guidance was based on the latest scientific evidence available, and reflects recommendations in the most recent Dietary Reference Intakes (DRI)¹⁰⁷ for sodium, as well as the recently issued 2015-2020 *Dietary Guidelines for Americans* (which involved expert review of the current body of research by the Dietary Guidelines Advisory Committee). FDA's draft voluntary short-term (two-year) targets are aimed at reducing average sodium consumption from 3,400 to 3,000 mg/day, and the voluntary long-term (ten-year) targets are aimed at reducing average sodium consumption to 2,300 mg/day, which is consistent with current federal recommendations. FDA also strongly supports efforts by the National Academies of Science, Engineering and Medicine (National Academies) to formally review the sodium DRI, and FDA is collaborating with CDC, NIH, and USDA to update the DRI for sodium as expeditiously as possible.

The majority of Americans are trying to take action to reduce their sodium (CDC, 2015), and the weight of the scientific evidence supports reducing sodium in the food supply in order to reduce current average sodium consumption levels from 3,400 mg/day—well above the current recommended limit of 2,300 mg/day—thereby reducing the risks associated with increased blood pressure and cardiovascular disease (CVD). Three quarters of sodium intake comes from processed or prepared food – before it is added at the table, or during cooking. Supporting options for food products lower in sodium therefore increases choices for American consumers. Several major food manufacturers are supportive of FDA's efforts in their recently submitted comments on the draft voluntary sodium reduction targets.

Given the scientific evidence in support of reducing sodium intake from current levels to reduce blood pressure, subsequent CVD, and associated health care costs, as well as recent industry feedback on the targets, the Agency believes that it is reasonable to continue work on voluntary sodium reduction targets, even as the DRI is updated. Once the DRI report is finalized (anticipated to be in 2019), FDA is committed to making any needed adjustments to the long-term targets to align them with the findings of the National Academies Committee.

¹⁰⁷ The Dietary Reference Intakes (DRIs) are nutrient reference values developed by the Institute of Medicine of The National Academies of Sciences, Engineering, and Medicine.

Furthermore, FDA will continue extensive outreach with industry and public health groups on our draft voluntary targets to ensure that they are well understood.

41. Sunscreen Ingredients

The Committee is significantly concerned that despite the increase in incidence of skin cancer in the United States, and the January 2016 Presidential Memorandum creating the White House Cancer Moonshot Task Force to prevent and cure cancer, FDA has still not approved a new over-the-counter sunscreen ingredient through the process created by the Sunscreen Innovation Act [SIA]. The Committee has, for multiple years, directed the FDA to clear the sunscreen backlog, and the agency has failed to do so. Therefore, the Committee directs the FDA to include in its report to Congress required by section 4(c) of the SIA by May 26, 2016, an update on how the agency plans to work with stakeholders to resolve the science-based concerns raised in public comments and describe how the agency is appropriately balancing the benefit of additional skin cancer prevention tools versus the hypothetical risk of OTC sunscreens that have been used around the world for decades. FDA is further directed to work with stakeholders to come to an agreement on an appropriate, science-based testing regimen by June 20, 2016. The Committee recommendation maintains the funding increase provided in fiscal year 2016 to address this public health threat. In addition, the Committee directs the FDA to finalize a rule limiting the maximum Sun Protection Factor [SPF] to “50” or “50+”, which was first proposed in 2011, within 90 days of enactment of this Act, and to issue a proposed rule to establish testing and labeling standards for sunscreen sprays within 90 days of enactment of this act.

FDA Response:

FDA transmitted the report entitled “Report to the Committee on Appropriations: Sunscreen Ingredients” to the committee on May 16th, 2016.

FDA has carefully considered what information is needed to ensure that a particular sunscreen active ingredient is safe and effective for use in OTC sunscreen products. FDA’s recommended studies reflect the Agency’s scientific expertise, existing technical guidance, experience from reviewing safety and efficacy data submitted for a generally recognized as safe and effective (GRASE) review of sunscreen active ingredients seeking to be added to the OTC Review for Sunscreens under current OTC drug regulations, and input from outside scientific experts (<http://www.fda.gov/AdvisoryCommittees/Calendar/ucm407137.htm>). The recommended studies are not novel and are consistent with FDA’s standard data requirements for both nonprescription and prescription topical drugs intended for chronic use.

Information on FDA's recommendations and expectations for the safety data needed to show that an active ingredient is GRASE for use in nonprescription sunscreen products has been publicly shared with industry and other interested parties on multiple occasions, including a public advisory committee meeting held in September 2014, proposed sunscreen orders published in 2014 and early 2015 for the eight sunscreen active ingredients that were under evaluation by FDA when the SIA was enacted, sponsor-requested meetings on the proposed sunscreen orders, and an SIA-required draft guidance for industry published in November 2015 which the FDA finalized in November, 2016.

To date FDA has met all statutorily mandated SIA deadlines and remains committed to achieving that goal in the future. As required by the SIA, the FDA is working to finalize OTC monograph regulations for sunscreens by November 26, 2019. The agency anticipates including provisions related to the effectiveness of various SPF levels and dosage forms for sunscreens. The FDA also intends to publish a proposed rulemaking on sunscreens prior to this date in order to provide the opportunity for public comment.

42. Vibrio

The Committee is aware of the public health challenge related to the naturally occurring bacteria called *Vibrio parahaemolyticus* that can accumulate in shellfish and believes that more scientific research is necessary to develop proper controls that will reduce the risk to consumers and sustain a healthy domestic shellfish industry. The Committee encourages the Food and Drug Administration [FDA] to increase funding for research into *Vibrio* illnesses associated with the consumption of raw molluscan shellfish, improve risk assessment models, and develop improved rapid detection methods for virulent *Vibrio* strains.

FDA Response:

FDA shares your concern regarding the public health challenge posed by *Vibrio parahaemolyticus* in shellfish. We are aware of, and actively engaged in activities aimed at reducing the risk that *Vibrio parahaemolyticus* (V.p.) poses to consumers of raw oysters and clams. FDA actively participates with federal, state and industry partners in the Interstate Shellfish Sanitation Conference (ISSC), which plays a key role in the development of the National Shellfish Sanitation Program (NSSP) Model Ordinance. The NSSP contains the standards and controls for implementation by state health authorities and the shellfish industry for controlling the safety of raw molluscan shellfish. FDA works directly with the ISSC *Vibrio*

Management Committee and the CDC to examine the incidence of V.p. illness and to engage the ISSC to adopt improved controls into the NSSP.

FDA has participated in a number of other collaborative efforts with state health authorities and the shellfish industry. For example, FDA works with state shellfish industry members to develop and implement shipboard controls to reduce risk through rapid onboard cooling techniques. Through this effort, FDA has seen a number of industry members implement controls that exceed those currently established in the NSSP and which have achieved significant additional illness reduction.

With respect to research funding, FDA has awarded the ISSC grants aimed at helping to ensure that, in the U.S., the safety net for molluscan shellfish is consistently and uniformly managed at the state and industry level with administrative oversight from FDA, as well as ISSC efforts to examine the science of V.p. and develop control measures aimed at reducing the risk of V.p. FDA also has awarded additional funding to the ISSC to support independent studies conducted by state shellfish authorities, including studies by three states (WA, NJ, CT) aimed at defining science-based industry practices to reduce the risk of V.p. in raw molluscan shellfish. In further support of this effort, FDA again awarded funding to the ISSC in 2015 to support continued research intended to enhance our understanding of V.p. and how current and innovative industry practices impact and may reduce risk.

FDA has also established a Workgroup on Ecological Forecasting for Vibrio. The goal for establishing the workgroup is to coordinate, plan, prioritize, and communicate ecological forecasting activities related to Vibrio within and beyond FDA. Specifically, FDA has collaborated with NOAA under their Ecological Forecasting Roadmap to develop experimental Vibrio forecast products (among others) using FDA's risk models and NOAA's environmental data and hydrodynamic models.

Additionally, FDA has offered a program to extend research and technical assistance on Vibrio to states and industry through the Vibrio Assessment Review Board (VARB). States and industry submit to FDA's VARB requests for research and technical assistance aimed at improving the science and control of Vibrio in molluscan shellfish. Through the VARB, FDA offers, as resources allow, assistance such as laboratory support, technical expertise, and statistical application to aid states and industry as they undertake independent Vibrio projects.

43. White Oak Expansion

The Committee is aware of the need for FDA facilities to accommodate an anticipated expanded workforce due to broader missions related to food safety and other mandates in

legislation over the last few years. Due to the challenging fiscal environment, the Committee encourages the FDA and GSA to consider innovative financing options to allow for the space allocation required. In particular, the Committee directs the FDA and GSA to consider partnership opportunities with non-Federal Government entities that provide reasonable cost options that will enable the FDA to maintain very close proximity to its campus headquarters in White Oak, including space contiguous to the White Oak campus.

FDA Response:

FDA appreciates the recognition of its expanding mission and workforce, the challenging fiscal environment that currently prevents expansion on the White Oak Campus, and the importance of housing FDA staff that exceed the current capacity of the White Oak Campus in very close proximity to the Campus. In FY 2017, FDA began working with GSA to develop a housing strategy to establish the housing demand for staff and continue geographically consolidating FDA's headquarters activities. In Q4 FY 2017, a GSA housing strategy deliverable will establish the requirements for campus-proximate space. GSA will use these requirements to determine the methods to fulfill FDA's space needs. GSA has been in contact with non-Federal Government entities that have indicated they can provide options that will enable FDA to expand into space contiguous with the White Oak Campus. FDA has met with GSA and the aforementioned entities, and is open to potential opportunities that allow for critically needed office space to accommodate FDA's expanding workforce that will further FDA's geographic consolidation.

JOINT EXPLANATORY STATEMENT SIGNIFICANT ITEMS

1. Organizational Chart

The agreement directs the Office of Budget and Program Analysis (OBPA) of the U.S. Department of Agriculture (USDA) to provide an organizational chart for each agency funded by this Act to the division and subdivision level, as appropriate, by June 1, 2017. The agreement also directs the Food and Drug Administration (FDA) and the Farm Credit Administration (FCA) to provide an organizational chart of each agency respectively to the division and subdivision level, as appropriate, by June 1, 2017.

FDA Response:

FDA will provide the requested charts.

2. Food Safety Modernization Act (FSMA)

As part of the increases, the agreement provides an additional \$35,675,000 to support the implementation of the Food Safety Modernization Act (FSMA). Of this amount, \$18,672,000 is provided for the National Integrated Food Safety System and \$16,913,000 is provided for Import Safety. Funds for import safety should help FDA ensure an even playing field in the application

Of FSMA regulations as it relates to both domestic and imported producers, processors, and manufacturers of food and animal feed. The agreement notes that FSMA implementation places additional requirements on state governments and private stakeholders, and therefore urges the

FDA to provide sufficient resources to State education and inspection programs to address these needs. The agreement continues to require quarterly reports to the Committees with a breakdown on funding allocations, as well as projections for future needs.

FDA Response:

FDA will provide the requested reports.

3. Foreign High-Risk Inspections

The \$2,500,000 increase above the amount provided in fiscal year 2016 for foreign high-risk inspections will allow FDA's Office of the Global Regulatory Operations Policy to continue efforts to develop and utilize a targeted, risk-based, and efficient inspection model that incorporates commercially available information on high-risk establishments for onsite verifications. FDA is directed to provide the Committees with an update on these efforts, including estimated efficiencies and concerns, and plans to continue or expand this effort in the future.

FDA Response:

FDA will provide the requested update.

4. Employee Conduct

Employees charged with implementing federal programs are expected to carry out their duties in a legal and ethical manner, free from conflicts of interest, without seeking private gain or advancing a private agenda, and without giving preferential treatment to any outside organization or individual. The agency is reminded of its responsibility to ensure that federal employees handle information, including information received from the employees, offices, or Committees of the Congress, in a professional and confidential manner according to the federal government's code of conduct, standards, regulations, and statutes.

FDA Response:

The agency continues to strengthen its ethics and integrity program to help employees avoid conflicts of interest. The agency is committed to preventive activities, such as continuing awareness campaigns of ethics standards for employees and in depth training to supervisors and managers to avoid conflicts. Additionally, the agency has established recommended actions when behavior in violation of these principles has been confirmed.

5. Laboratory Developed Tests

The agreement strongly urges the FDA to continue to work with Congress to address the issues and concerns regarding the regulation of Laboratory Developed Tests.

FDA Response:

FDA will work with Congress to address any issues or concerns related to Laboratory Developed Tests.

6. Compounding

The agreement remains concerned with the draft MOU that the FDA proposed under Section 503A of the FDCA. Section 503A distinguishes between "distribution" and "dispensing" for the purposes of the MOU. In the DQSA, Congress only allowed the FDA to regulate "distribution." The MOU appears to exceed the authority granted in the statute by redefining "distribution" in a manner that includes dispensing. Congress did not intend to include dispensing of compounded drugs over state lines within the scope of the MOU. The MOU should not address dispensing of compounded drugs to a patient over state lines if all other requirements of 503A are met.

FDA Response:

Section 503A of the FD&C Act describes the conditions that must be satisfied for a drug compounded by a licensed pharmacist in a State licensed pharmacy or Federal facility, or by a licensed physician, to qualify for exemptions from section 505 (concerning pre-market approval requirements), section 502(f)(1) (concerning labeling with adequate directions for use), and section 501(a)(2)(B)(concerning current good manufacturing practice requirements).

When Congress enacted the DQSA, it left intact as one of the conditions necessary to qualify for the exemptions listed in section 503A of the FD&C Act that:

(1) the drug product is compounded in a State that has entered into an MOU with FDA that addresses the distribution of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounded drug products distributed outside such State

(2) if the drug product is compounded in a State that has not entered into such an MOU, the licensed pharmacist, pharmacy, or physician does not distribute, or cause to be distributed, compounded drug products out of the State in which they are compounded in quantities that exceed 5 percent of the total prescription orders dispensed or distributed by such pharmacy or physician (see section 503A(b)(3)(B)(i) and (b)(3)(B)(ii) of the FD&C Act).

Even though the statute did not direct FDA to obtain public input on the draft standard MOU, other than the consultation with the National Association of Boards of Pharmacy (NABP), FDA has engaged in a public process to obtain comments on the draft standard MOU. FDA has

solicited public input from the public generally through written comments to the docket, and has also discussed the proposed MOU with representatives from the 50 states.

FDA discussed the concepts it was considering for the MOU at an Intergovernmental Working Meeting with representatives of the 50 States and NABP in March, 2014. After the draft standard MOU was published for comment, FDA discussed the published draft at Intergovernmental Working Meetings with representatives of the 50 States in March, 2015, and again in November, 2015, after the comment period closed. FDA received over 3,000 comments to the docket on the draft MOU. FDA is considering all of the comments, including comments on the definition of “distribution,” as we work to finalize the MOU.

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HIV/AIDS FUNCTIONAL TABLE

HIV/AIDS Resource Funding

(Dollars in Thousands)

Program	FY 2016 Actual	FY 2017 Estimate	FY 2018 Estimate
Human Drugs	\$30,412	\$30,412	\$30,412
Biologics	\$31,899	\$31,838	\$30,976
Medical Devices	\$342	\$342	\$342
Field Activity	\$32,500	\$33,125	\$33,750
Toxicological	---	\$139	\$51
Other Activities	\$3,977	\$3,977	\$3,977
Total HIV/AIDS	\$99,130	\$99,833	\$99,508

CROSSCUTS

<i>(dollars in thousands)</i>	FY 2016 Estimate	FY 2017 Estimate	FY 2018 Estimate
AIDS/HIV	99,130	99,833	99,508
Antimicrobial Resistance	43,491	43,993	41,424
Behavioral Health	33,201	36,056	37,417
Global Health	166,031	170,080	180,820
Immunization	26,222	27,062	29,727
Medical Countermeasures Initiative (MCMi)	24,552	24,552	24,552
Pandemic Influenza	33,967	37,579	34,095
Patient Safety	398,630	380,683	405,378
Pediatric Drugs	12,113	13,001	13,349
Precision Medicine	2,392	2,392	2,392
Prescription Drug Abuse	11,256	12,539	12,537
Prevention	4,256,031	4,207,520	4,581,067
Quality Improvement	24,033	25,576	25,988
Tobacco	599,000	635,000	672,000

CHARGES AND ASSESSMENTS

Food and Drug Administration Department of Health and Human Services Charges and Assessments Fiscal Year 2016 Actuals

Assessments:	\$872,042
NIH eRA Grants Management System	\$169,638
Pilot phase to support migration of FDA Grants Data into the Department's consolidated eRA Grants Management System	
Department Ethics Program	\$700,000
The Office of General Counsel provides legal and related support services to FDA	
Federal Audit Clearinghouse	\$2,404
Fee For Service:	\$45,924,743
Program Support Center/ Office of the Secretary	\$10,732,477
Provides various services to the FDA, including some Information and Systems Management Services	
Financial Management Portfolio (FMP)	\$730,483
Procurement Management Portfolio (PMP)	\$0
Administrative Operations Portfolio (AOP)	\$6,817,398
Includes costs for security, building operations, shredding, storage, graphics, property disposal, trans-share, mail	
Real Estate and Logistics Portfolio	\$3,184,596
Includes building operations, shredding, storage, property disposal,	
Federal Occupational Health (FOH):	\$2,930,519
FDA agency health units and services	
Information & System Management Services	\$24,205,476
Freedom of Information (FOIA)	\$369,139
Unified Financial Management Systems (UFMS)	\$6,496,000
The Program Support Center delivers and manages O&M Services for UFMS by supporting daily operations.	
HCAS Operations and Maintenance	\$2,229,000
HCAS O&M services provide support for daily operations of the HCAS application.	
Information Technology Infrastructure & Operations (ITIO)	\$3,335,553
Telecommunications team offers expertise on Network / Telecommunications / Security. Trusted Internet Connections and IT Security.	
Department IT Management	\$3,463,137
Office of Enterprise Application Development (OEAD)	\$5,903,000
Services include activities for HHS' civilian employees and Commissioned Corps Officers, and maintenance and operation of the systems housing current and historical pay and leave records	
Office of Information Security (OIS)	\$2,409,647
Includes computer security incident response center	
Office of Human Resource Services	\$8,056,271
Includes HR Center services tier I, payroll liaison, systems planning and implementation	
Jointly Funded Projects:	\$3,445,524
Enterprise Information Management	\$0
FDA's contribution to the HHS Enterprise Infrastructure Fund. Funds are used for Enterprise Information Technology programs/projects outlined in the Enterprise Information Technology Strategic Plan or benefitting the corporate enterprise, such as enterprise buys/licenses.	
International Health Bilateral Agreement	\$1,231,159
Agreement to provide funding in support of the bilateral-multilateral activities performed on behalf of the Public Service by the Office of Global Health Affairs	

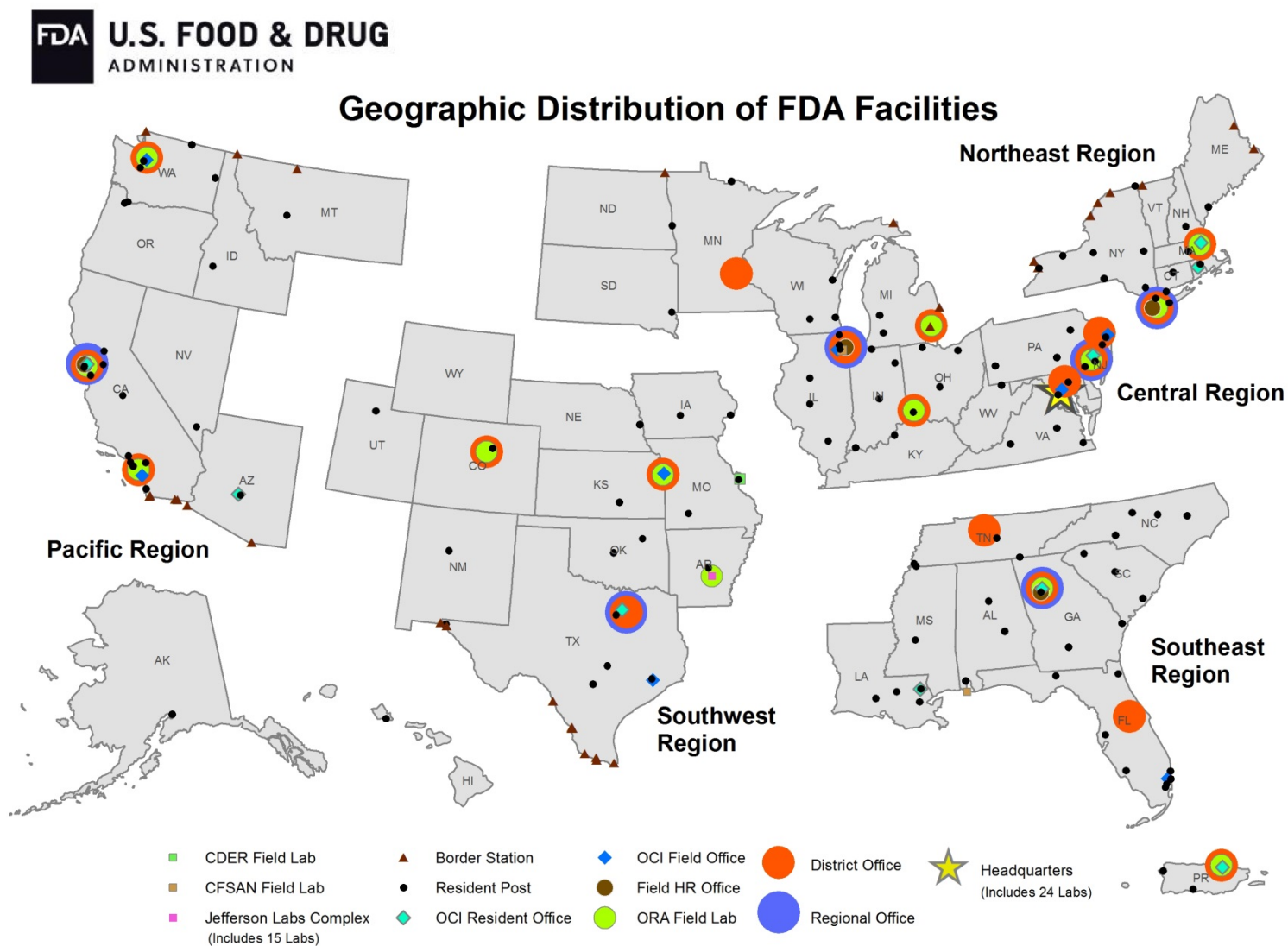
Other Jointly Funded Projects	\$2,214,365
CFO Audit of Financial Statements Audit services to be performed at the FDA in support of the fiscal year 2010 financial statement audit of the Department of Health and Human Services (DHHS) contracted and monitored by Office of the Inspector General (OIG) and its components, and related services.	\$434,693
Office of Public Health/Blood Safety Agreement to provide funding for the advisory committee on Blood Safety	\$300,000
Regional Health Administrators IAG with OS/Office of Public Health & Science to support ten Regional Health Administrators. Their core mission is to promote understanding of and control functions within their respective regions improvements in public health and to conduct specific management.	\$308,010
President's Council on Bioethics TAP to fund the council which advises the President of Bioethical issues related to the advances in biomedical science and technology	\$294,000
Media Monitoring Provides Agency leadership and staff with the latest analysis of what the media is reporting about Department-wide and Agency-specific priorities, initiatives, and programs	\$157,124
Intra-department Council on Native American Affairs IAG with DHHS, Administration on Children and Families, for staff and administrative support for the Interdepartmental Council for Native American Affairs Committee meetings and assignments.(ICNAA), to conduct semi-annual Council meetings, Executive	\$15,909
National Science Advisory Board for Biosecurity Agreement with NIH to develop improved biosecurity measures for classes of legitimate biological research that could be misused to threaten public health or national security	\$325,000
NIH Negotiation of Indirect Cost Rates (New) Agreement with NIH/OD to support costs associated with the negotiation of indirect cost rates with commercial organizations	\$18,000
HHS Broadcast Studio (New) It is a communication tool used for departmental messaging, both to internal and external audiences and is key to the government-wide open government initiative.	\$16,979
OPM USAJOBS Fees charged by OPM to Federal Agencies to cover the cost of providing Federal Employment Information and services. OPM assesses an annual per-capita-fee based on each OPDIV percentage of the Departments total FTE on all paid employees with access to USAJOBS. The cost is distributed within HHS based on each OPDIV percentage of the Departments total FTE.	\$92,331
President's Advisory Committee on Combating Antibiotic-Resistant Bacteria Combating Antibiotic Resistant Bacteria, directs that "the Federal Government will work domestically and internationally to detect, prevent, and control illness and death related to antibiotic-resistant infections by implementing measures that reduce the emergence and spread of antibiotic-resistant bacteria and help ensure the continued availability of effective therapeutics for the treatment of bacterial infections"	\$175,000
National Science Advisory Board for Biosecurity This will support the administrative management of the Council in efforts to coordinate and collaborate on biosafety and biosecurity issues within HHS.	\$77,319

Activity	FY 2016 Actual	FY 2017 Estimate	FY 2018 Estimate
Assessments.....	\$ 872,042	\$ 1,038,602	\$ 1,238,722
Fee for Service.....	\$ 45,924,743	\$ 51,162,231	\$ 51,162,231
Program Support Center/OS.....	\$ 10,732,477	\$ 15,795,461	\$ 15,795,461
Federal Occupational Health.....	\$ 2,930,519	\$ 3,309,175	\$ 3,309,175
Information System Management Service.....	\$ 24,205,476	\$ 23,869,450	\$ 23,869,450
Human Resource Center – Rockville, Maryland.....	\$ 8,056,271	\$ 8,188,145	\$ 8,188,145
Jointly Funded Services.....	\$ 3,445,524	\$ 3,516,627	\$ 3,542,645
International Health - Bilateral Agreement.....	\$ 1,231,159	\$ 1,231,159	\$ 1,231,159
Other Jointly Funded Projects	\$ 2,214,365	\$ 2,285,468	\$ 2,311,486
Total.....	\$ 50,242,309	\$ 55,717,460	\$ 55,943,598

CENTRAL ACCOUNT

Program (dollars in thousands)	FY 2016 Actuals		FY 2017 Estimates		FY 2018 Estimates	
	BA	UF	BA	UF	BA	UF
Foods.....	16,892	-	17,082	-	17,082	-
Center.....	5,425	-	5,425	-	5,425	-
Field.....	11,466	-	11,657	-	11,657	-
Human Drugs.....	18,070	56,434	17,996	58,631	17,996	58,631
Center.....	14,821	53,672	14,827	55,819	14,827	55,819
Field.....	3,249	2,763	3,169	2,812	3,169	2,812
Biologics	5,411	7,450	5,389	7,585	5,389	7,585
Center.....	4,455	6,589	4,455	6,709	4,455	6,709
Field.....	956	861	934	876	934	876
Animal Drugs and Feeds.....	3,386	1,678	3,479	1,825	3,479	1,825
Center	2,048	1,646	2,099	1,792	2,099	1,792
Field.....	1,338	32	1,380	33	1,380	33
Devices and Radiological Health.....	7,800	7,610	7,768	8,348	7,768	8,348
Center.....	5,698	7,488	5,714	8,223	5,714	8,223
Field.....	2,102	122	2,054	125	2,054	125
National Center for Toxicological Research....	852	-	852	-	852	-
FDA Headquarters	12,493	6,680	12,714	6,801	12,714	6,801
Total	64,903	79,851	65,280	83,189	65,280	83,189

GEOGRAPHICAL DISTRIBUTION OF FDA FACILITIES



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GLOSSARY OF ACRONYMS

3D	3-Dimensional
ACOMS	Advisory Committee Oversight and Management Staff
ACSI	American Customer Satisfaction Index
ADE	Adverse Drug Experience
ADEPT	Autonomous Diagnostics to Enable Prevention and Therapeutics
ADHD	Attention-Deficit / Hyperactivity Disorder
ADUFA	Animal Drug User Fee Act
AGDUFA	Animal Generic Drug User Fee Act
AMP	Real Property Asset Management Plan
ANDA	Abbreviated New Drug Application
ANPRM	Advance Notice of Proposed Rulemaking
APEC	American Customer Satisfaction Index
ARL	Arkansas Regional Laboratory
ARS	Agriculture Research Service
ARS	Acute Radiation Syndrome
B&F	Buildings and Facilities
BA	Budget Authority
BACPAK	Bacterial Pathogen Knowledge Base
BARDA	Biomedical Advanced Research and Development Authority
BIMO	Bioresearch Monitoring
BLA	Biologic License Application
BMAR	Backlog of Maintenance and Repairs

BPA	Bisphenol A
BPCA	Best Pharmaceuticals for Children Act
BRF	Beltsville Research Facility
BsUFA	Biosimilars User Fee Act
CBER	Center for Biologics Evaluation and Research
CBP	Customs and Border Protection
CBRN	Chemical, Biological, Radiological, and Nuclear
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CERSIs	Centers of Excellence in Regulatory Science and Innovation
CFR	Code of Federal Regulations
CFSAN	Center for Food Safety and Applied Nutrition
cGMP	current Good Manufacturing Practice
CIADM	Centers for Innovation in Advanced Development and Manufacturing
CIO	Chief Information Officer
CMS	Centers for Medicare & Medicaid Services
CMV	Cytomegalovirus
CORE	Coordinated Outbreak Response and Evaluation
CORES	Collaborative Opportunities for Research Excellence in Science
CRADA	Cooperative Research & Development Agreement (CRADA)
CSU	Central Shared Use
CT	Computed Tomography Imaging

CTP	Center for Tobacco Products
CUP	Central Utility Plant
CVM	Center for Veterinary Medicine
CY	Calendar Year
DARPA	Defense Advanced Research Projects Agency
DHRD	Division of Human Resource Development
DHS	Department of Homeland Security
DILI	Drug-Induced Liver Injury
DIO	Division of Import Operations
DNA	DeoxyriboNucleic Acid
DOD	Department of Defense
DSC	Drug Safety Communication
DTC	Direct-To-Consumer
DTRA	Defense Threat Reduction Agency
DxOD	Diagnostics on Demand
EADB	Estrogenic Activity Database
EDKB	Endocrine Disruptor Knowledge Base
EDR	Electronic Data Room
EDSR	Electronic Document Submission and Review
EIR	Entrepreneurs in Residence
EMA	Economically Motivated Adulteration
eMDR	Electronic Medical Device Reporting
E.O.	Executive Order

EON	Emergency Operations Network
EON IMS	Emergency Operations Network Incident Management System
ESPC	Energy Savings Performance Contract
ESRD	End-Stage Renal Disease
ETASU	Elements to Assure Safe Use
EUA	Emergency Use Authorizations
FACA	Federal Advisory Committee Act
FAERS	FDA Adverse Event Reporting System
FAO	Food and Agriculture Organization
FATA	Federal Anti-Tampering Act
FCC	Forensic Chemistry Center
FCI	Facility Condition Index
FCN	Food Contact Substance Notification
FD&C Act	Federal Food, Drug and Cosmetic Act
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act of 2007
FDAMA	Food and Drug Administration Modernization Act
FDASIA	Food and Drug Administration Safety and Innovation Act
FDA-TRACK	FDA-wide performance management system
FDCA	Federal Food, Drug and Cosmetic Act
FEMP	Federal Energy Management Program
FERN	Food Emergency Response Network
FFDM	Full-Field Digital Mammography

FMT	Fecal Microbiota Transplantation
FOI	Freedom of Information Act
FOIA	Freedom of Information Act
FPC	Federal Partners Collaboration
FSIS	Food Safety Inspection Service
FSMA	Food Safety Modernization Act
FSVP	Foreign Supplier Verification Programs
FTE	Full Time Equivalent
FVM	Foods and Veterinary Medicine
FY	Fiscal Year
GDUFA	Generic Drug User Fee Amendments
GFI	Guidance for Industry
GIS	Geographic Information System
GMP	Good Manufacturing Practices
GO	Global Regulatory Operations and Policy Directorate
GSA	General Services Administration
GUDID	Global UDI Database
HDE	Humanitarian Device Exemption
HHS	Department of Health and Human Services
HIV	Human Immunodeficiency Virus
HQ	FDA Headquarters
HRWG	High Risk Working Group
HSP	Human Subject Protection

HUD	Humanitarian Use Device
HVAC	Heating, Ventilation, and Air Conditioning
ICCR	International Cooperation on Cosmetics Regulation
ICH	International Conference on Harmonization
ICOR	International Consortium of Orthopedic Registries
IDE	Investigational Device Exemption
IFT	Institute of Food Technologists
IMDRF	International Medical Device Regulators Forum
IND	Investigational New Drug
IOM	Institute of Medicine
IRB	Institutional Review Board
IT	Information Technology
ITACS	Import Trade Auxiliary Communications System
IVD	In Vitro Diagnostics
JLC	Jefferson Labs Complex
LSBC	Life Sciences-Biodefense Laboratory Complex
MAQC	MicroArray Quality Control
MCM	Medical Countermeasure
MCMi	Medical Countermeasures initiative
MDE	Medical Device Epidemiology
MDIC	Medical Device Innovation Consortium

MDR	Medical Device Reporting
MDSAP	Medical Device Single Audit Program
MDSP	Medical Device Shortages Program
MDUFA	Medical Device User Fee Amendments
MDUFMA	Medical Device User Fee and Modernization Act
MERS	Middle East Respiratory Syndrome
MERS-CoV	Middle East Respiratory Syndrome Coronavirus
MFRPS	Manufactured Food Regulatory Program Standards
microRNA	Micro Ribonucleic Acid
MIT/HST	Massachusetts Institute of Technology/Health Science and Technology
MOD	Module
MQSA	Mammography Quality Standards Act
MRI	Magnetic Resonance Imaging
MRTTP	Modified Risk Tobacco Product
NA	Not Approvable
NADA	New Animal Drug Application
NARMS	National Antimicrobial Resistance Monitoring System
NCBI	National Center for Biotechnology Information
NCTR	National Center for Toxicological Research
NDA	New Drug Application
NGO	Non-governmental Organization
NIH	National Institutes of Health
NIOSH	National Institute for Occupational Safety and Health

NME	New Molecular Entity
NSABB	National Science Advisory Board for Biosecurity
NSAID	Non-Steroidal Anti-Inflammatory Drugs
NSE	Not Substantially Equivalent
NYTS	National Youth Tobacco Survey
OBE	Office of Biostatistics and Epidemiology, CBER
OC	Office of the Commissioner
OCAC	Office of Cosmetics and Colors
OCC	Office of the Chief Counsel
OCE	Office of Compliance and Enforcement
OCET	Office of Counterterrorism and Emerging Threats
OCI	Office of Criminal Investigations
OCM	Office of Crisis Management
OCP	Office of Combination Products
OCS	Office of the Chief Scientist
OCT	Optical Coherence Tomography
OCTC	Office of the Counselor to the Commissioner
OEA	Office of External Affairs
OECD	Organization for Economic Co-Operation and Development
OFVM	Office of Foods and Veterinary Medicine
OGCP	Office of Good Clinical Practice
OGROP	Office of Global Regulatory Operations and Policy
OHCA	Office of Health and Constituent Affairs

OIM	Office of Information Management
OIP	Office of International Programs
OIR	Office of In Vitro Diagnostics and Radiological Health
OL	Office of Legislation
OMA	Office of Media Affairs
OMB	Office of Management and Budget
OMPT	Office of Medical Products and Tobacco
OO	Office of Operations
OOPD	Office of Orphan Products Development
OPP	Office of Policy and Planning
OPT	Office of Pediatric Therapeutics
ORA	Office of Regulatory Affairs
ORISE	Oak Ridge Institute for Science and Education
ORRR	Other Rent and Rent Related
ORSI	Office of Regulatory Science and Innovation
OSE	Office of Surveillance and Epidemiology, CDER
OSI	Office of Scientific Integrity
OSMP	Office of Special Medical Programs
OSPD	Office of Scientific and Professional Development
OTC	Over-the-counter
PAC	Pediatric Advisory Committee
PAD	Program Activity Data
PAHO	Pan American Health Organization

PAHPRA	Pandemic and All-Hazards Preparedness Reauthorization Act of 2013
PATH	Population Assessment of Tobacco and Health
PB	President's Budget
PC	Preventive Control
PDC	Pediatric Device Consortia
PDMA	Prescription Drug Marketing Act
PDUFA	Prescription Drug User Fee Act
PHEMCE	Public Health and Emergency Countermeasures Enterprise
PIC/S	Pharmaceutical Inspection Convention and Cooperation Scheme
PMA	Premarket Approval Application
PREA	Pediatric Research Equity Act
PREDICT	Predictive Risk-Based Evaluation for Dynamic Import Compliance Targeting
PRISM	Post-Licensure Rapid Immunization Safety Monitoring
PTN	Pediatric Trials Network
QSDAR	Quantitative Spectroscopic Data-Activity Relationships
REMS	Risk Evaluation and Mitigation Strategy
RFCTG	Regulators Forum Cell Therapy Group
RTA	Refusal to Accept
SE	Substantially Equivalent (when used by Device and Biologics Programs)
SEQC	Sequencing Quality Control
SE	Substantial Equivalence
SLEP	Shelf Life Extension Program

SEQC	Sequencing Quality Control
SNS	Strategic National Stockpile
SLEP	Shelf Life Extension Program
SP	Strategic Priority
SRL	Southeast Regional Laboratory
SW	Southwest
TB	Tuberculosis
TCORS	Tobacco Centers of Regulatory Science
TB	Tuberculosis
TIMS	Tobacco Inspection Management System
TPMP	Tobacco Product Manufacturing Practice
TPSAC	Tobacco Product Scientific Advisory Committee
UDI	Unique Device Identification
UESC	Utility Energy Service Contract
UF	User Fee
UESC	Utility Energy Service Contract
UN	United Nations
USAMRIID	United States Army Medical Research Institute for Infectious Diseases
USC	United States Code
USDA	United States Department of Agriculture
USP	U.S. Pharmacopoeia

VAERS	Vaccine Adverse Event Reporting System
VICH	Veterinary International Conference on Harmonization
VKA	Vitamin K Antagonist
WD	Withdrawn
WEAC	Winchester Engineering and Analytical Center
WHO	World Health Organization

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GLOSSARY OF TABLES

All-Purpose Table (APT)	Provides comprehensive financial information on the budget at the program, project, and activity (PPA) levels.
Amounts Available for Obligation	Lists the base appropriations followed by any rescissions, supplemental funding, transfers, and any other adjustments to provide a total obligation level for that Fiscal Year.
Appropriations History	Lists the ten year history of appropriations and estimates for FDA's Salary and Expenses and Building and Facilities appropriations, excluding indefinite user fees.
Budget Authority By Activity	Provides budget authority and FTE for three years: FY 2015, FY 2016, and FY 2017.
Budget Authority Crosswalks	Highlights absorptions, reductions, and increases by program line and major initiative for a given fiscal year – for example Food Safety, Medical Product Safety and Availability, and Rent and Infrastructure – starting from the prior budget year.
Crosscuts	Shows programs that are crosscutting throughout FDA. Each crosscut program line in the table shows a “snapshot” of the funding that is targeted toward a specific area in each fiscal year and provides an indication of resource trends.
Detail of Full-Time Equivalent Employment (FTE)	Provides FTE data by FDA organizational component – such as CFSAN, CDER, CBER, etc. – for each of the three fiscal years included in the CJ (Prior Year, Current Year, and Budget Year) as well as a five-year history of the average General Schedule (GS) grade.
Detail of Positions	Provides information on the number of General Schedule (GS), Executive Level (EX), Executive Service (ES), Commissioned Corps (CC), Administratively Determined (AD), and other positions – including Administrative Law Judges (AL), Wage Grade – across FDA, including a three year history of the average GS levels and salaries.
HIV/AIDS Functional Table	Shows a “snapshot” of the funding in FDA targeted toward HIV/AIDS related programs and activities for five fiscal years and provides a breakout of the funding by program line.

Major Activities Table	Provides an overview of the FDA budget by program and major activities: Food Safety and Medical Product Safety and Availability, including absorptions, reductions, and increases.
Object Classification Tables	Provides information by object class for budget authority, user fees, and total program level – which is a combination of both budget authority and user fees. Object classes are categories that present obligations by the items or services purchased by the Federal Government.
Physicians' Comparability Allowance (PCA)	Provides information on physicians' comparability allowances that are paid to eligible Government physicians (including dentists) in order to recruit and retain them. The PCA is paid only to physicians serving in positions for which there is a significant recruitment and retention problem.
Salaries and Expenses	Breakdowns all salaries and expenses incurred by FDA by object class. The totals for each object class match the object classification tables for budget authority, user fees, and total program level. This table excludes object classes 31.0 to 43.0, when compared to the Object Classification tables.
Summary of Changes	Summarizes the changes in estimates from FY 2016 to FY 2017 and explains those changes on an item-by-item basis by budget authority, user fees, program level, and FTE.