DEPARTMENT of HEALTH and HUMAN SERVICES

Fiscal Year

2019

Food and Drug Administration

Justification of
Estimates for
Appropriations Committees

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LETTER FROM THE COMMISSIONER

FDA has responsibilities to protect and promote public health by ensuring the safety, effectiveness, and security of human and animal drugs, biological products, and medical devices; the safety of our nation's food supply, cosmetics, and radiation-emitting products; and regulating tobacco products. Our work helps Americans improve their health and welfare, protects families and children, and enables consumers to have safe and healthy product and food choices. 2017 was a historic year of advances in medicine and public health for FDA. That progress reflects FDA's ongoing efforts to advance science in the areas that we oversee.

Notable accomplishments include:

- Record Product Approvals – FDA approved record numbers of generic drugs, and novel devices, drugs and biologics; including the first-ever gene therapy products for forms of blindness and cancer.
- Increasing Drug Competition – FDA launched the Drug Competition Action Plan to foster increased generic drug development with the goal of reducing barriers to generic drug entry and helping Americans have more affordable medicines through increased choice and competition.
- Confronting Addiction – FDA established an Opioids Policy Steering Committee to advance new policies to confront the epidemic of opioid addiction. We took steps to reduce the rate of new addiction through steps to rationalize prescribing, and measures to expand treatment options for those suffering from opioid use disorder. We also issued a comprehensive plan for tobacco regulation that puts nicotine at the center of our efforts to better protect kids from tobacco products and significantly reduce tobacco-related disease and death.
- Advancing Food Safety – FDA is implementing the FDA Food Safety Modernization Act to empower farmers and producers and help keep the American public safe from food-related illness through preventative steps aimed at controlling risk. We've taken new steps to promote healthier diets and beneficial innovations in new food products.
- Hurricane Response and Recovery – FDA sustained round-the-clock efforts to ensure the safety of food and medical products, and mitigate the risk of drug shortages, after the devastation caused by Hurricanes Harvey, Maria, and Irma.

The FY 2019 Budget provides FDA with the resources to continue to fund our current programs at consistent levels. The request will allow the agency to continue to support our core public health mission, including protecting the safety of the foods we eat. It also includes additional funding to further promote innovation and competition and advance the health and safety of American families, including:

- $400 million in medical product innovation initiatives that will result in improved treatment and diagnostic options for patients; increased competition and medical product efficiencies that can help lower healthcare costs; the development of new industries that will lead to U.S.-based jobs; and manufacturing advances that are more reliable, lower cost and high quality;
- $50 million for 21st Century Cures Act activities;
- $10 million as part of an Administration opioid initiative to support development of tools to stem the misuses and abuses of opioids and development of medication assisted treatments (MATs);
- $10 million for the review of growing numbers of pioneer and generic new animal drugs;
- $22 million in proposed user fees to implement meaningful reforms to the regulation of over the-counter (OTC) monograph drug products to foster OTC innovation and expand consumer choice;
- $21 million to ensure that FDA's offices and labs across the country are modern and efficient, to help FDA carry out its mission and respond to food safety and medical product emergencies.

Our work at the FDA is taking place during an inflection point in both science and policy. There has perhaps never been a better moment in the history to be engaged in public health, and to be leveraging the capabilities of the FDA to support new investment and product innovation.

The U.S. life sciences sector represents one of our nation's great modern achievements. It's a source of rich intellectual property, high-paying jobs and products that are improving the lives of people around the world. We have more opportunity to deliver on the promises of science than at any time before and use new tools and medical advances to alter the trajectory of disease.

We are grateful for the Administration's support of these initiatives and believe these new investments in innovation, entrepreneurship, and the mission of FDA will ultimately lead both to better health outcomes for American families and to greater U.S. economic development.

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

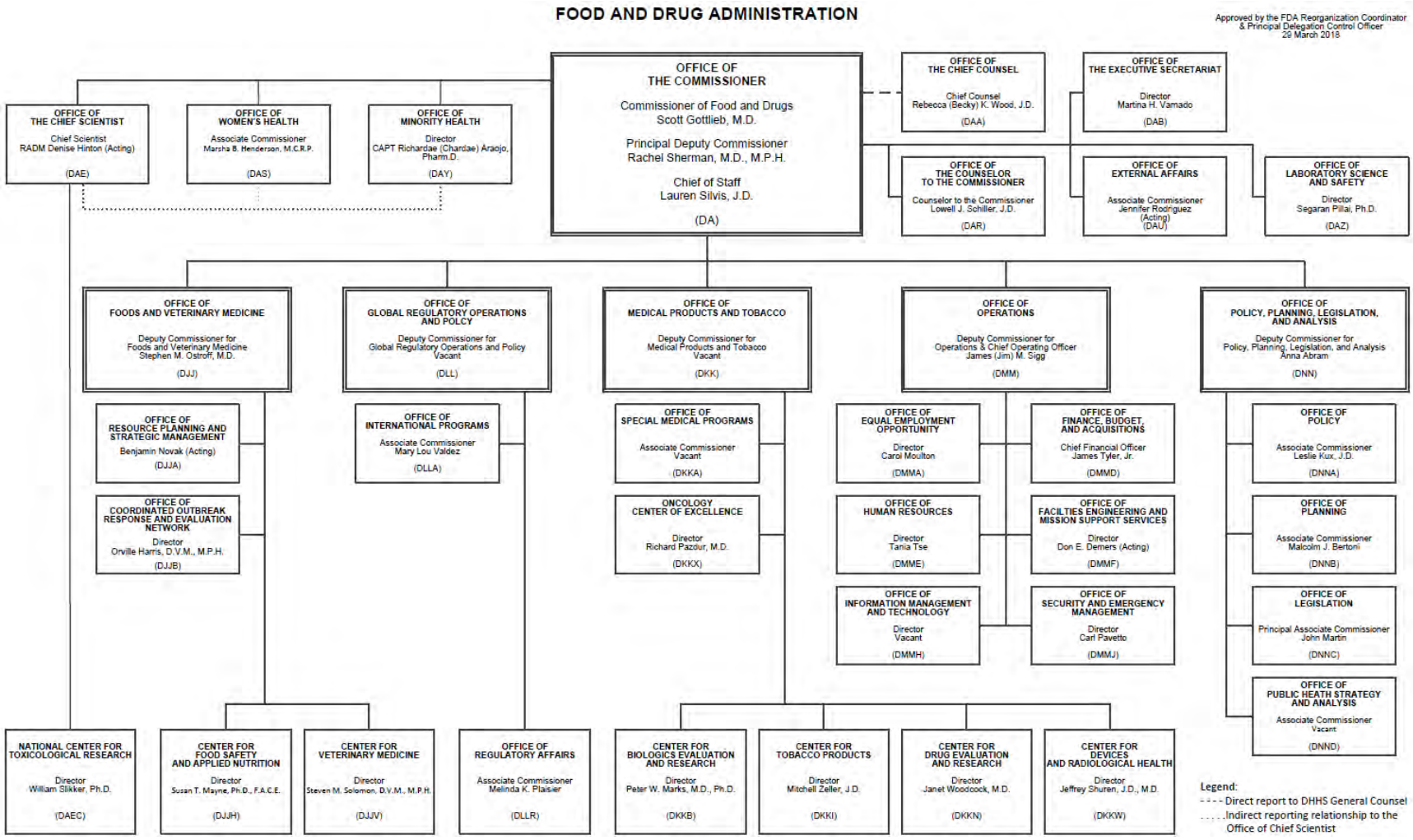
TABLE OF CONTENTS

SIGNIFICANT ITEMS

FDA SPECIFIC ITEMS

GLOSSARY

ORGANIZATION CHART



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EXECUTIVE SUMMARY

This Executive Summary describes the fiscal year (FY) 2019 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.

New Steps to Confront the Opioid Crisis

FDA is addressing the opioid crisis facing the nation, including through the establishment of the Opioids Policy Steering Committee in 2017.

FDA took immediate action where needed, which included the agency's first-of-its-kind request to remove a currently marketed opioid pain medication from sale due to the public health consequences associated with the product's abuse and misuse. FDA identified the following ways to decrease exposure to opioids, prevent new addiction, and support the treatment of those with opioid use disorder:

- development of new Risk Evaluation and Mitigation Strategy requirements for makers of immediate-release opioids
- labeling changes with clarifying information on the use of medication-assisted treatments for patients suffering from opioid use disorder
- creative approaches to packaging, storage, and disposal of opioid medications.

Record Medical Product Approvals

Calendar year 2017 saw groundbreaking medical products brought to market, a record number of generic drug approvals to promote competition, and advancing policies to promote innovation and improve people's lives. For example, FDA coordinated the approval of a novel diagnostic device that can detect hundreds of genetic mutations in a single test to coincide with the Centers for Medicare & Medicaid Services' proposed coverage of the device, thereby facilitating earlier access to the innovative medical technology for Medicare beneficiaries.

In August 2017, FDA also saw a whole new way to treat disease with the approval of the first gene therapy in the United States – with two more approved since then. Innovations like these are creating a turning point in the treatment of serious illnesses with more potential to cure intractable and inherited diseases

FDA approved a record number of novel drugs and biologics in 2017, including 46 new molecular entities; and more than two-thirds were approved using one or more of our expedited review programs. FDA also had a record number of drugs with orphan indications approved and eliminated the entire backlog of pending orphan drug designation requests.

FDA broke records with the highest number of generic drugs approved in a single month, multiple times in 2017 and recorded the highest annual total of generic drug approvals in the agency's history with 1,027 approvals.

In calendar year 2017, the agency approved a record number of new devices, 95 – more than four times the number of novel devices that received market approval in 2009.

Regulatory Efficiency

FDA faces the challenge of regulating new areas of science like gene therapy, targeted medicine, and digital health where traditional approaches to product regulation may not be well suited. To meet these challenges, FDA is taking a fresh look at how to adapt our approaches to make sure that we are enabling beneficial new technology to develop, while maintaining FDA's gold standard for product review and consumer protection. Accomplishments in 2017 included:

- a novel pathway for review of precision-medicine based diagnostic tests by accredited third-parties to reduce the burden on test developers and streamline regulatory assessment
- a pilot program exploring a new way of regulating digital health devices
- a suite of guidances to clarify how FDA will regulate digital health technologies to encourage innovation.

FDA also helped manufacturers of low- to moderate-risk medical devices by reducing unnecessary submissions to the FDA for changes that could not significantly affect device safety or effectiveness, so patients can benefit from upgraded products more quickly.

Other accomplishments in 2017 included:

- developing comprehensive policy framework on regenerative medicine to spur safe and effective innovation
- issuing draft guidance for manufacturers of 3D printed medical devices
- launching a new searchable database to better inform patients and health care professionals of adverse events reported with drug and biologic products
- facilitating faster patient access to needed compounded medicines, while protecting the public from poorly compounded drugs.

FDA continues to promote and encourage work that will enable us to utilize real world data in our regulatory decision making.

FDA took the following actions in 2017 to alert the public and raise awareness of potential safety concerns and violations:

- took action against stem cell clinics marketing products without FDA approval, putting patients at risk
- warned companies making false claims that their unapproved products can treat or cure life-threatening diseases
- advanced a new framework for regulating homeopathic products based on consumer risk
- alerted the public to the dangers of unproven and untested products.

Drug Competition

FDA plays a pivotal role in fostering drug competition through the approval of safe, effective, and lower-cost generic drugs.

FDA is finding innovative ways to help foster competition and provide patients with more access to affordable medications. In May 2017, FDA announced various actions as part of the agency's Drug Competition Action Plan to increase competition in the market for prescription drugs and facilitate entry of lower-cost alternatives.[1]

To encourage generic drug development, FDA has:

- prioritized review of generic drug applications
- issued guidance to enhance regulatory certainty for generic drug development and review
- made significant progress on the massive generic drug review backlog to facilitate enhanced generic drug choices.

FDA also approved a record number of generic drugs in 2017 with 1,027 approvals.

Emergency Response, Recovery, and Medical Countermeasures

FDA has wide-ranging responsibilities to protect the public when the nation is faced with public health threats, whether naturally-occurring, or man-made. The devastation caused by Hurricanes Harvey, Maria, and Irma brought to light the critical work the agency does in overseeing the safety of the food and medical supply in this country. FDA worked around the clock to ensure farmers in Texas and Florida could safely handle their crops affected by flooding. FDA remains committed to the recovery in Puerto Rico and that island's long-term success, and worked closely with drug and medical device manufacturers in Puerto Rico to take steps to address potential and apparent shortages of medical products that resulted from the devastation left by Hurricane Maria. FDA's work and commitment to hurricane victims and patients in need of critical medical products will continue into 2018.

In addition, over the past two years, 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 authorizing 20 diagnostics for emergency use
- support development of vaccines and therapies.

Zika response efforts are part of the FDA'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

Efforts to improve food safety require partnerships to achieve our public health goals. In FY 2017, FDA awarded approximately $31 million to 43 state government organizations to help implement the produce safety rule through training and compliance activities, following up on nearly $22 million in funds made available to states in FY 2016.

In August 2017, in order to help businesses meet the requirements of the FDA's Final Rule for Preventive Controls for Human Food, FDA released a new software tool to help owners and

[1] Association for Accessible Medicines, 2017 Generic Drug Access and Saving Report in the U.S. (2017). Available at https://accessiblemedsorg/resources/blog/2017-generic-drug-access-and-savings-us-report

operators of food facilities create a food safety plan specific to their facilities. The Food Safety Plan Builder is a free software application that businesses can download from the FDA's website to guide them, step-by-step, through the creation of a food safety plan. The development of a food safety plan is one requirement of the new law. While the software tool was primarily developed with small businesses in mind, it can be used by manufacturers of any size.

In May 2017, FDA extended the compliance date for menu labeling by a year, and in November 2017, FDA announced additional draft guidance on the menu labeling requirements. Menu labeling regulations require the disclosure of certain nutritional information for standard menu items in chain restaurants and similar retail food establishments. The draft guidance addresses concerns that were raised about challenges establishments faced in understanding how to meet their obligations under the new regulations. These new policy steps should allow covered establishments to implement the requirements by the May 2018 compliance date.

Tobacco Regulation

On July 28, 2017, FDA announced a new comprehensive plan for tobacco and nicotine regulation that will serve as a multi-year roadmap to better protect kids and significantly reduce tobacco-related disease and death. The approach places nicotine, and the issue of addiction, at the center of the agency's tobacco regulation efforts. The goal is to ensure that the FDA has the proper scientific and regulatory foundation to efficiently and effectively implement the Family Smoking Prevention and Tobacco Control Act.

FDA has begun a public dialogue about lowering nicotine levels in combustible cigarettes to minimally or non-addictive levels through achievable product standards. On March 16, 2018, FDA published an Advance Notice of Proposed Rulemaking (ANPRM) to seek input on the potential public health benefits and any possible adverse effects of limiting nicotine in cigarettes to minimally or non-addictive levels.

Further, FDA indicated that it is seeking public input on several other issues to help ensure that the Agency has the proper science-based policies in place to meaningfully reduce the harms caused by tobacco use. On March 21, 2018, FDA published an ANPRM to seek public comment on the role that flavors in tobacco products—including menthol—play in attracting youth, as well as the role some flavors may play in helping some smokers switch to potentially less harmful forms of nicotine delivery. FDA also announced on March 23, 2018an ANPRM to solicit additional comments and scientific data related to the patterns of use and resulting public health impacts from premium cigars.

To encourage innovations that have the potential to make a notable public health difference and to put foundational rules in place to provide increased clarity and efficiency for industry, the Agency extended the premarket application deadlines described in the May 2016 final rule for certain products. Specifically, the FDA is deferring enforcement of deadlines to submit tobacco product review applications for newly regulated tobacco products that were on the market as of August 8, 2016. Under these revised timelines, applications for newly regulated combustible products, such as cigars, pipe tobacco, and hookah tobacco, would be submitted by August 8, 2021, and applications for non-combustible products such as electronic nicotine delivery systems (ENDS) would be submitted by August 8, 2022.

On November 29, 2017, FDA announced the formation of a new Nicotine Steering Committee, which will be a forum for developing and implementing nicotine policy to address the public

health effects of tobacco usage in this country. The primary focus will be on nicotine replacement therapy (NRT) products for combustible tobacco product cessation. The formation of this group reflects the need to critically examine the evolving science behind the FDA's evaluation of the safety and efficacy of NRT products.

OVERVIEW OF THE BUDGET REQUEST

The FY 2019 Budget Request is $5.8 billion – an overall increase of 11 percent or $662.9 million compared to the FY 2018 Annualized CR level.[2] The request includes $3.2 billion for budget authority – an increase of 14 percent or $432.9 million compared to the FY 2018 Annualized Continuing Resolution (CR) level. The request includes $2.5 billion for user fees – an increase of 7 percent or $189.9 million compared to the FY 2018 Annualized Continuing Resolution level. FDA will also begin implementation of a working capital fund in FY 2019, consistent with the authority requested in the President's Budget.

(Dollars in Thousands)	FY 2018 Annualized CR			FY 2019 President's Budget			FY 2019 President's Budget +/- FY 2018 Annualized CR		
	Food Safety	Medical Safety and Availability	Total	Food Safety	Medical Safety and Availability	Total	Food Safety	Medical Safety and Availability	Total
Programs	$000	$000	$000	$000	$000	$000	$000	$000	$000
Budget Authority:									
Foods	1,022,211	---	1,022,211	1,029,863	---	1,029,863	7,652	---	7,652
Human Drugs	---	488,264	488,264	---	686,364	686,364	---	198,100	198,100
Biologics	---	213,854	213,854	---	251,854	251,854	---	38,000	38,000
Animal Drugs and Feeds	124,951	36,779	161,729	125,806	54,479	180,284	855	17,700	18,555
Devices and Radiological Health	---	327,442	327,442	---	455,442	455,442	---	128,000	128,000
National Center for Toxicological Research	10,164	52,737	62,901	10,233	54,967	65,200	69	2,230	2,299
FDA Headquarters	73,016	89,352	180,980	73,540	115,352	198,565	524	26,000	17,585
FDA White Oak Consolidation	---	---	42,752	---	---	49,430	---	---	6,678
Other Rent and Rent Related	36,053	35,401	71,454	36,300	50,197	86,497	247	14,796	15,043
GSA Rental Payments	78,937	90,115	169,052	79,477	88,944	168,421	540	-1,171	-631
SUBTOTAL, BA Salaries and Expenses	1,345,331	1,333,944	2,740,639	1,355,218	1,757,599	3,171,920	9,887	423,655	431,281
21st Century Cures		19,864	19,864	---	70,000	70,000	---	50,136	50,136
MCMi		9,932	9,932	---	---	---	---	-9,932	-9,932
Building and Facilities	---	---	11,708	---	---	11,788	---	---	80
Total BA	1,345,331	1,363,740	2,782,143	1,355,218	1,827,599	3,253,708	9,887	463,859	471,565
Total User Fees	15,863	1,698,281	2,354,957	15,863	1,806,922	2,544,847	---	108,641	189,890
Total Program Level, Pre-Transfer	1,361,194	3,062,021	5,137,100	1,371,081	3,634,521	5,798,555	9,887	572,500	661,455
Additional Opioids Allocation (non-add)					10,000	10,000		10,000	10,000

Budget Structure and Strategic Plan Framework

The Budget is 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 accurately labeled, and that 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., including medical countermeasures - the drugs, vaccines, and diagnostic tests to counter chemical, biological, radiological, nuclear, and emerging infectious disease threats.
- **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.

[2] Includes reductions to Foreign High Risk Inspections and HHS OIG Transfer. See FDA HQ narrative for details.

- **Infrastructure: Facilities and Rent Investments** – ensures FDA staff have optimally functioning offices and labs across the country to execute the agency's food safety and medical product safety mission.

The Budget is structured around four core mission goals: enhancing oversight of FDA-regulated products, improving and safeguarding access to FDA-regulated products to benefit health, promoting better informed decisions about the use of FDA-regulated products, and strengthening organizational excellence and accountability. FDA has also published *Healthy Innovation, Safer Families: FDA's 2018 Strategic Policy Roadmap*, which provides an overview of some of the key priorities the Agency is pursuing to advance FDA's public health mission.[3]

FOOD SAFETY

The FY 2019 Budget provides $1.4 billion for food safety, an increase of $9.9 million compared to the FY 2018 Annualized CR. The request includes $1.3 billion for budget authority – an increase of $9.9 million compared to the FY 2018 Annualized CR, and $15.9 million for user fees – flat with the FY 2018 Annualized CR. This request aligns to FDA's Strategic Policy Roadmap priorities to strengthen food safety and empower consumers to make better and more informed decisions about their diets and health.

Food Safety (+$10 million)

The FY 2019 funding level restores the FY 2018 Annualized CR rescission to the food safety program and maintains current FY 2017 activities. In FY 2019, FDA will continue its statutory mission of promoting and protecting public health by ensuring that the food supply is safe, sanitary, wholesome, and properly labeled. The FY 2019 level will also allow FDA to continue its critical FDA Food Safety Modernization Act (FSMA) implementation activities.

MEDICAL PRODUCT SAFETY AND AVAILABILITY

The FY 2019 Budget Request for medical product safety and availability is $3.6 billion, an increase of $572.5 million above the FY 2018 Annualized CR. The request includes $1.8 billion for budget authority – an increase of $463.9 million compared to the FY 2018 Annualized CR – and $1.8 billion for user fees – an increase of $108.6 million compared to the FY 2018 Annualized CR. As part of this user fee funding level, the FY 2019 Budget proposes to reauthorize the expiring Animal Drug and Animal Generic Drug User Fee programs, as well as reforms to the Over-the-Counter Monograph program supported by new fees. The proposed legislation authorizes the collection and spending of these fees subject to appropriations.

The FY 2019 Budget level for medical product safety aligns to FDA's Strategic Policy Roadmap priorities to reduce the burden of the addiction crises that are threatening American families and leverage innovation and competition to improve healthcare, broaden access, and advance public health goals.

Innovation Initiatives (+$400M)

New scientific opportunities, as well as advances in manufacturing and commerce, give FDA new ways to advance our mission to protect and promote public health. Leveraging these opportunities requires us to make investments in regulatory science that can reduce uncertainty

[3] https://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/ucm591993.htm

for innovators, spur investment in new industries and provide principles for the safe and effective development of new technologies. These same advances also give us new ways to support greater availability and use of generic drugs as a way to promote price competition and patient access. The FY 2019 Budget includes $400 million for initiatives aimed at supporting new and ongoing efforts to foster more investment and innovation in the development of therapeutics and diagnostics that target unmet medical needs; advance drug and device competition; stand up new domestic industries – such as pharmacy outsourcing facilities; and create more modern, domestically-based manufacturing, including continuous manufacturing of drugs and biological products, including vaccines. These manufacturing platforms can bring more businesses back to the U.S., help lower drug and device development costs and reduce the risk of shortages. Investing in these initiatives will help the FDA advance goals that we all share: improved treatment and diagnostic options for patients; lower healthcare costs; the development of new industries that will lead to U.S.-based jobs; and manufacturing advances that are more reliable, lower cost and high quality.

Promote Domestic Manufacturing: Advancing Modern Drug and Biological Product Manufacturing Technologies, Through the Development of Efficient Regulatory Pathways (+$58M)

The FY 2019 Budget Request for FDA includes $58.2M to promote domestic manufacturing. These technologies have great potential to accelerate new, more targeted therapies, enhance product quality and bolster stability in the U.S. drug supply to meet domestic and global needs. These new manufacturing platforms may be especially important in the development of personalized medicines and innovations in cell- and gene-based therapies and vaccines. With these resources, FDA will help reduce the cost and uncertainty of adopting new manufacturing technologies by developing a science-based framework that includes the regulatory tools and guidance for how products will be evaluated, and by funding research, development and testing of these technologies.

Advance a New Domestic Drug Industry and Promote Access by Establishing the Outsourcing Facility Sector as a Robust and Reliable Source of Compounded Products (+$25M)

The FY 2019 Budget includes $25 million to create a "Center of Excellence on Compounding for Outsourcing Facilities." With these resources, FDA will expand engagement with outsourcing facilities and states to help the pharmacy outsourcing industry grow to meet its intended function and adhere to higher quality standards to protect patient health. The Center of Excellence will identify and propose solutions to market barriers to lower the cost for pharmacies to become outsourcing facilities. The Center will provide much-needed education and training to improve product quality, safety, and purchaser confidence, and help the FDA adjust its regulatory oversight to better match the scope of production of an individual compounding pharmacy. FDA will work with industry to improve manufacturing practices, create new programs relating to requested review of method design and stability study protocols, and work with state partners to reduce challenges associated with state regulatory diversity and support state-based oversight of pharmacies.

Bring MedTech Manufacturing Home: Advance Medical Device Manufacturing and Quality (+$12M)

The FY 2019 Budget includes $12 million to establish a voluntary program for device manufacturers to receive certification for meeting objective manufacturing and product quality criteria. As medical devices become more complex – and given the frequent modifications made to devices – spurring advanced manufacturing and creating a competitive marketplace for device quality is critical for both driving technological innovations and assuring patient safety. FDA is already working collaboratively with industry, patients, providers, and payers through the Medical Device Innovation Consortium to develop the parameters of the program. As part of this approach, the FDA will recognize third-party certifiers and offer regulatory incentives for those manufacturers who receive certification demonstrating their quality capability. These actions will increase manufacturing innovation, accelerate availability of high-quality devices to patients and foster a competitive marketplace around device quality similar to other industries, such as automotive and aerospace, that will advance device innovations, reduce manufacturing costs, and improve the quality and safety of medical devices.

Create a New Medical Data Enterprise: Advance the Use of Real-World Evidence to Improve Human and Animal Health and Support Pre-Market Evaluation and Post-Market Safety (+$100M)

The FY 2019 Budget includes $100 million to advance the use of real-world experience to better inform patient care and provide more efficient, robust, and potentially lower-cost ways to develop clinical data that can inform product review and promote innovation. The effort will cover a broad range of medical products, including drugs, biologics, and medical devices. FDA will establish a new capability, including the development of data and analytical tools, to conduct near-real-time evidence evaluation down to the level of individual electronic health records for at least 10 million individuals in a broad range of U.S. healthcare settings. In the case of transcatheter heart valves, leveraging real-world evidence has already resulted in a greater than 400 percent cost savings for industry, improved post-market surveillance and moved the United States from 42nd to, in some cases, first-in-the-world approvals for life-saving technologies. Expanding FDA's capacity to utilize real-world evidence to evaluate the pre- and post-market safety and effectiveness of medical products will generate processes that could improve the efficiency of the regulatory process, better inform patients and providers about pre- and post-market safety, reduce some of the burdens that drive up the time and cost required to bring beneficial innovations to the market and address barriers that can make certain important safety and effectiveness information around the real-world use of products hard to collect and evaluate.

Facilitate Growth and Spur Transformation of the Digital Health Technology Industry by Shifting Regulation to an Efficient and Novel Framework for Reliable Post-Market Oversight (+$70M)

The FY 2019 Budget includes $70 million for FDA to work collaboratively with industry, patients, and providers to establish a new paradigm for digital health technologies. This paradigm will allow companies to market lower-risk products without FDA premarket review and market higher-risk products following a streamlined FDA premarket review. FDA will further reduce the time and cost of market entry of digital health technologies while assuring appropriate patient safeguards by relying on post-market collection of real-world data to support

new and evolving product functions. FDA will also create a Center of Excellence on Digital Health to establish the regulatory paradigm, build new capacity to evaluate and recognize third-party certifiers, and support a cybersecurity unit to complement the advances in software-based devices. Implementing these regulatory innovations and information technology improvements are essential for advancing software-based technologies to improve the health and quality of life of patients while assuring critical safeguards as the current regulatory framework is not well-suited for driving the development of safer, more effective software-based devices, including the use of machine learning and artificial intelligence.

Create a New Platform for How the Agency More Efficiently Develops and Validates Modern Science-Based Principles for New Drug Development (+$78M)

The FY 2019 Budget Request for FDA includes $77.5 million for investments in CDER and FDA HQ to keep pace with rapidly advancing science in drug development.

Applying Cutting Edge Science to Advance Drug Development and Review: Drug Innovation Platform

The FY 2019 budget includes $57.5 million to build a knowledge management system and portal to existing and developing information on drug development and previous regulatory decisions. Rapidly advancing science in drug development requires FDA to have up-to-date scientific standards and assessment tools, as well as evolving technologies, methods, and approaches. Without these tools, the Agency's ability to support innovation and review applications will lag behind the latest science and inhibit innovation. Currently, FDA has a number of drug development guidances where updates to assure new scientific information and new approaches to drug development are incorporated. In addition, guidances are needed in a number of disease areas where there is no existing guidance and therefore no articulated pathway to market for new treatments.

FY 2019 funding for a content management platform will enable the FDA to build on evolving information and decisions and identify gaps in regulatory policies and pathways. FDA's decision-making rests on the regulatory and statutory framework, and on the scientific expertise of its staff, but would be supported and facilitated by a comprehensive knowledge management system that provides access to and analysis of prior regulatory decisions and previously submitted clinical trials information and other relevant datasets. This investment will enable rapid, consistent responses to regulatory questions and prevent delays in response to innovations in drug development.

Oncology Center of Excellence

As part of this initiative to support new drug development, the FY 2019 Budget includes $20 million for the Oncology Center of Excellence (OCE) to stand up a new model for team-based product review that fosters collaboration across FDA's medical product centers, improves review efficiency, and expedites the development of novel science that can improve the lives of patients with cancer. Section 3073 of the 21st Century Cures Act required FDA to establish one or more intercenter institute(s) to help develop and implement processes for coordination of activities in major disease areas between the drug, biologics, and device centers. FDA has established the OCE to create a unified policy approach and clinical review for all drugs, biologics, and devices used in medical oncology.

With these resources, the FDA OCE will leverage the combined talents and skills of all FDA regulatory scientists and reviewers who work in medical oncology product review. OCE will also serve as a single point of contact for external stakeholders for FDA's work in cancer, including professional societies and patient advocacy groups. FDA medical and professional staff will coordinate review of oncology product applications across the medical product centers, policy development, and collaboration with external stakeholders. This Center of Excellence will help expedite the development of oncology and hematology medical products and support an integrated approach in the clinical evaluation of drugs, biologics, and devices for the treatment of cancer.

Stimulate Investment In, and Innovation of, Medical Products Targeted to Rare Diseases (+$20M)

The FY 2019 Budget Request for FDA includes $20 million[4] to foster investment and innovation in, and medical product development for, rare diseases. FDA will develop clinical trial networks to create an understanding of the natural history (such as individual patient experiences and progression of symptoms) and clinical outcomes of rare diseases. FDA will leverage this novel framework when promising medical products have been identified for patients. The initial focus will be on rare and ultra-rare diseases, where product development can be challenging because of the difficulty of recruiting clinical trials. FDA will stimulate medical product development for rare diseases by expanding and enhancing the understanding of rare diseases and the research and drug development processes in this space.

Modernize Generic Drug Development and Review to Enable Increased Competition, Promote Generic Drug Substitution, and Provide Affordable Options for American Patients (+$38M)

The FY 2019 Budget Request includes $37.6 million to create a new review platform that will significantly modernize generic drug review from a text-based to a data-based assessment with structured submissions and FDA assessments. This more automated system will improve clarity for generic sponsors, making initial reviews more efficient and decreasing the risk of refuse-to-file letters, increasing the rate of first-cycle approvals, and greatly increasing overall efficiency. This investment also will support efforts to update generic drug labeling, with an initial focus on oncology products, as part of the agency's efforts to ensure that patients and their providers have access to up-to-date information to inform clinical decisions. If more generic drugs had up-to-date product labels reflecting the latest treatment information, it would encourage wider adoption of generic medicines.

Animal Drug Review (+$10 million)

The FY 2019 Budget includes $9.7 million to support FDA's animal drug review activities. This increase enables the Animal Drugs and Feeds Program to review pioneer and generic new animal drugs within agreed-upon performance targets, meeting statutory timeframes, despite the continually increasing workload, and ensures the long-term stability of both programs moving forward. Additionally, with this funding increase, the Program will meet the statutory conditions required by the FD&C Act to collect and spend user fees. User fees are increased on a yearly basis to cover their portion of any additional workload, but FDA's direct budget authority has not correspondingly increase to keep up with the additional workload. These programs have

[4] $10 million will support activities in CDER and $10 million will support policy related activities in FDA HQ.

had a significant impact on human and animal health, reducing review timeframes, promoting the development of safe and effective drugs to reach the market sooner.

21st Century Cures - FDA Innovation Account (+$50 million)

The 21st Century Cures Act (Cures Act) enacted into law on December 13, 2016, 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.[5] For FY 2019, the Cures Act authorized $70 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.

Over-the-Counter Drug Monograph Reform (+$22 million)

The FY 2019 Budget includes $22 million in proposed user fees for oversight of Over-the-Counter Drug Monograph products. FDA strongly supports implementing meaningful reforms to the regulation of over the-counter (OTC) monograph drug products to promote innovation and to reduce regulatory burden supported by an OTC monograph user fee program. On June 7, 2017, Secretary Price transmitted the User Fee Goals document and FDA's technical assistance to OTC monograph reform and user fee legislation to Congress. This user fee program is essential for supporting the modernization of OTC monograph activities, as these resources will support improving the timeliness of review activities, facilitating innovation on behalf of consumers, and enabling the agency to better respond to urgent safety issues. The recommendations submitted by the Administration are based on public input as well as negotiations with industry, and for the first 5 years, 100 percent of user fee revenue is targeted to come from facility fees. The goals of the OTC Monograph User Fee program are to:

- Build basic infrastructure to meet the goals of monograph reform (hiring, training and information technology)
- Enable industry-initiated innovation (innovation order requests, confidential development meetings, timelines, and performance goals
- Enable streamlining of industry and FDA safety efforts
- Enable efficient completion of Category III final GRASE (Generally Recognized as Safe and Effective) determinations requested by industry or initiated by the FDA
- Develop measures to track success and agency accountability.

Opioids (+$10 million)

As part of the FY 2019 Budget, the Administration is also requesting mandatory resources to address the opioid addiction crisis, including $10 million for FDA activities.[6] These resources

[5] 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.

[6] These funds are presented as a non-add in FDA's budget tables.

would support, among other things, investment in FDA regulatory science in development of tools to stem the misuse and abuses of opioids and for FDA to provide technical assistance related to clinical study design related to MATs (medication-assisted treatments). FDA proposes applying funds to develop algorithm-driven diagnostics to support the opioid use disorder treatment workforce. The goal is to enable evidence-based treatment to allow clinicians to more optimally prescribe MATs. Additionally, to accelerate the development of generic versions of opioid drug products with abuse deterrent formulations (ADF), FDA will use the resources to fund studies to identify additional tools and methodologies that can be used to evaluate whether differences in formulations impact abuse deterrence. FDA anticipates that identification of such tools and methodologies will help generic drug applicants streamline the testing necessary to support approval, resulting in increased competition. FDA welcomes the opportunity to make a meaningful impact on this crisis through these scientific projects that will promote the development of opioids that are harder to manipulate and abuse and concurrently increase access to MATs.

Export Certification (+$4 million)

The FY 2019 Budget includes 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 fully recover its costs in implementing this program.

Generics Spur Access and Competition (Legislative Proposal)

The Federal Food, Drug, and Cosmetic Act provides an incentive to generic drug applicants by granting a 180-day period of exclusivity to the applicant that is first to file a substantially complete application to FDA. Increasing the availability of generic drugs helps to create competition in the marketplace, which then helps to make treatment more affordable and increases access to health care for more patients.

Some "first filers" can block subsequent generic competitors from receiving approval under this exclusivity provision. Similarly, first filers that receive tentative approval but then intentionally delay seeking final approval can block subsequent competitors. As a result, first filers can "park" their exclusivity, and consumers are denied access to generic products and must keep paying brand price.

The FY 2019 Budget includes a legislative proposal to address this problem. The proposal makes the tentative approval of a subsequent generic drug applicant that is blocked solely by a first applicant's 180-day exclusivity, where the first applicant has not yet received final approval, a trigger of the first applicant's 180-day exclusivity. This means the period of exclusivity would immediately begin for the first filer. This proposal will enhance competition and facilitate more timely access to generic drugs. This proposal is estimated to create $1.8 billion in Medicare savings over 10 years.

INFRASTRUCTURE: FACILITIES AND RENT INVESTMENTS

The FY 2019 Budget provides an increase of $28 million over the FY 2018 Annualized CR level to ensure 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. This level supports increased FTE levels associated with medical product user fees, increased facility costs related to real estate taxes, rental rates, maintenance, and utilities, and White Oak campus utility infrastructure capacity and reliability improvements, security infrastructure, and the campus safety program.

The FY 2019 Budget also attempts to sustain the current condition of FDA's owned buildings at its six mission-critical sites, as FDA's owned buildings continue to age and equipment and systems failures occur, leading to more demands for repairs and non-standard maintenance requests.

OVERVIEW OF PERFORMANCE

FDA accomplishes its core mission through activities that can be grouped under the following four goals, which apply to all of FDA's major program areas:

- Enhance oversight of FDA-regulated products
- Improve and safeguard access to FDA-regulated products to benefit health
- Promote better informed decisions about the use of FDA-regulated products
- Strengthen organizational excellence and accountability.

FDA's FY 2019 Budget is structured around these goals, as discussed in the Overview of the Budget Request.

TRANSPARENCY AND ACCOUNTABILITY

FDA-TRACK is the Agency's performance management program that collects, monitors, analyzes and reports key performance data and projects from FDA's program offices and cross-cutting initiatives. Each quarter, the FDA-TRACK team reviews results from each office and meets with office representatives to discuss accomplishments and any projected shortfalls in performance. If necessary, the discussion is raised to the FDA executive leadership level where the office directors would present and explain their performance results. Performance data and projects are then posted onto the FDA-TRACK website and a monthly newsletter is sent to the approximately 50,000 email subscribers.

FDA-TRACK provides insights into the activities of key program offices and facilitates discussion, best practices, decision-making and ultimately, performance improvement. Since the inception of FDA-TRACK, FDA has seen significant performance improvement in areas such as:

- Elimination of generic new animal drug applications backlog
- Increase in hospital participation in the MedSun program
- Efficiency in the 510(k) review procedures
- Reduction of FOIA backlog

Today, the FDA-TRACK website provides the public insights into the daily operations of the Agency, and how our day-to-day work impacts and is reflected in our mission. The public can better understand how Agency initiatives are progressing, including the current implementation of the 21st Century Cures Act (Cures-TRACK) and our ongoing efforts to implement legislation and policy through rulemaking (UnifiedAgenda-TRACK).

ALL PURPOSE TABLE

(Dollars in Thousands)	FY 2017 Final		FY 2017 Actuals		FY 2018 Annualized CR		FY 2019 President's Budget		FY 2019 President's Budget +/- FY 2018 Annualized CR	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Foods	**3,935**	**1,040,761**	**3,905**	**1,025,503**	**3,939**	**1,033,082**	**3,939**	**1,040,734**	**---**	**7,652**
Budget Authority	***3,935***	***1,029,175***	***3,905***	***1,025,503***	***3,895***	***1,022,211***	***3,895***	***1,029,863***	**---**	***7,652***
User Fees	---	***11,586***	---	---	***44***	***10,871***	***44***	***10,871***	---	---
Center	1,118	315,356	1,088	310,994	1,081	313,526	1,081	316,326	---	2,800
Budget Authority	1,118	314,806	1,088	310,994	1,078	312,694	1,078	315,494	---	2,800
User Fees	---	550	---	---	3	832	3	832	---	---
Food and Feed Recall	---	*243*	---	---	*1*	*243*	1	243	---	---
Voluntary Qualified Importer Program	---	*243*	---	---	*1*	*243*	1	243	---	---
Third Party Auditor Program	---	*64*	---	---	*1*	*346*	1	346	---	---
Field	2,817	725,405	2,817	714,509	2,858	719,556	2,858	724,408	---	4,852
Budget Authority	2,817	714,369	2,817	714,509	2,817	709,517	2,817	714,369	---	4,852
User Fees	---	11,036	---	---	41	10,039	41	10,039	---	---
Food and Feed Recall	---	1,000	---	---	*4*	*1,000*	4	1,000	---	---
Food Reinspection	---	4,575	---	---	*19*	*4,575*	19	4,575	---	---
Voluntary Qualified Importer Program	---	4,320	---	---	*18*	*4,320*	18	4,320	---	---
Third Party Auditor Program	---	1,141	---	---	---	*144*	---	144	---	---
Human Drugs	**6,030**	**1,329,631**	**6,033**	**1,549,170**	**6,361**	**1,611,475**	**6,407**	**1,852,776**	**46**	**241,301**
Budget Authority	***2,117***	***491,607***	***2,120***	***488,626***	***2,117***	***488,264***	***2,163***	***686,364***	***46***	***198,100***
User Fees	***3,913***	***838,024***	***3,913***	***1,060,544***	***4,244***	***1,123,211***	***4,244***	***1,166,412***	**---**	***43,201***
Center	4,986	1,124,853	4,989	1,370,578	5,286	1,413,615	5,322	1,650,865	36	237,250
Budget Authority	1,317	355,438	1,320	352,419	1,317	353,020	1,353	548,388	36	195,368
User Fees	3,669	769,415	3,669	1,018,159	3,969	1,060,595	3,969	1,102,477	---	41,882
Prescription Drug (PDUFA)	*2,514*	533,134	*2,514*	678,553	*2,443*	*654,835*	2,443	690,203	---	35,368
Generic Drug (GDUFA)	*1,046*	219,018	*1,046*	309,435	*1,313*	*369,065*	1,313	374,894	---	5,829
Biosimilars (BsUFA)	*104*	16,706	*104*	29,435	*211*	*36,116*	211	36,752	---	636
Outsourcing Facility	*5*	557	*5*	736	*2*	*579*	2	628	---	49
Field	1,044	204,778	1,044	178,592	1,075	197,860	1,085	201,911	10	4,051
Budget Authority	800	136,169	800	136,207	800	135,244	810	137,976	10	2,732
User Fees	244	68,609	244	42,385	275	62,616	275	63,935	---	1,319
Prescription Drug (PDUFA)	52	10,878	52	8,593	*41*	*8,038*	41	8,472	---	434
Generic Drug (GDUFA)	189	55,973	189	33,185	*226*	*53,104*	226	53,943	---	839
Biosimilars (BsUFA)	---	1,416	---	213	*7*	*1,120*	7	1,140	---	20
Outsourcing Facility	3	342	3	394	*1*	*354*	1	380	---	26
Biologics	**1,414**	**339,492**	**1,414**	**340,016**	**1,375**	**358,025**	**1,383**	**403,268**	**8**	**45,243**
Budget Authority	***852***	***215,317***	***852***	***215,443***	***852***	***213,854***	***860***	***251,854***	***8***	***38,000***
User Fees	***562***	***124,175***	***562***	***124,573***	***523***	***144,171***	***523***	***151,414***	**---**	***7,243***
Center	1,177	296,066	1,177	296,923	1,135	315,328	1,143	360,492	8	45,164
Budget Authority	620	173,937	620	174,052	620	172,755	628	210,755	8	38,000
User Fees	557	122,129	557	122,871	515	142,573	515	149,737	---	7,164
Prescription Drug (PDUFA)	*507*	*109,704*	*507*	*111,173*	*458*	*127,961*	458	134,872	---	6,911
Medical Device (MDUFA)	*50*	*10,508*	*50*	*10,826*	*51*	*13,405*	51	13,639	---	234
Generic Drug (GDUFA)	---	*1,088*	---	*872*	*5*	*1,032*	5	1,048	---	16
Biosimilars (BsUFA)	---	*829*	---	---	*1*	*175*	1	178	---	3
Field	237	43,426	237	43,093	240	42,697	240	42,776	---	79
Budget Authority	232	41,380	232	41,391	232	41,099	232	41,099	---	---
User Fees	5	2,046	5	1,702	8	1,598	8	1,677	---	79
Prescription Drug (PDUFA)	*5*	*1,847*	*5*	*1,517*	*7*	*1,397*	7	1,472	---	75
Medical Device (MDUFA)	---	*199*	---	*185*	*1*	*201*	1	205	---	4
Animal Drugs and Feed	**942**	**195,042**	**942**	**190,879**	**959**	**187,348**	**1,043**	**225,065**	**84**	**37,717**
Budget Authority	***808***	***162,835***	***808***	***162,852***	***808***	***161,729***	***844***	***180,284***	***36***	***18,555***
User Fees	***134***	***32,207***	***134***	***28,027***	***151***	***25,619***	***199***	***44,781***	***48***	***19,162***
Center	615	128,876	615	126,217	626	121,808	710	158,894	84	37,086
Budget Authority	481	98,205	481	98,205	481	97,538	517	115,673	36	18,135
User Fees	134	30,671	134	28,012	145	24,270	193	43,221	48	18,951
Animal Drug (ADUFA)	*81*	*20,879*	*81*	*17,977*	*94*	*15,890*	112	26,971	18	11,081
Animal Generic Drug (AGDUFA)	*53*	*9,792*	*53*	*10,035*	*51*	*8,268*	81	16,138	30	7,870
Third Party Auditor Program					---	*112*	---	112	---	---
Field	327	66,166	327	64,662	333	65,540	333	66,171	---	631
Budget Authority	327	64,630	327	64,647	327	64,191	327	64,611	---	420
User Fees	---	1,536	---	15	6	1,349	6	1,560	---	211
Animal Drug (ADUFA)	---	*427*	---	*15*	*2*	*307*	2	427	---	120
Animal Generic Drug (AGDUFA)	---	*302*	---	---	*1*	*235*	1	326	---	91
Food Reinspection	---	*807*	---	---	*3*	*807*	3	807	---	---
Third Party Auditor Program					---	---	---	---	---	---

(Dollars in Thousands)	FY 2017 Final		FY 2017 Actuals		FY 2018 Annualized CR		FY 2019 President's Budget		FY 2019 President's Budget +/- FY 2018 Annualized CR	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Devices and Radiological Health	**2,215**	**448,114**	**2,215**	**450,799**	**2,394**	**504,844**	**2,416**	**635,635**	**22**	**130,791**
Budget Authority	***1,663***	***329,681***	***1,663***	***329,764***	***1,663***	***327,442***	***1,685***	***455,442***	***22***	***128,000***
User Fees	***552***	***118,433***	***552***	***121,035***	***731***	***177,402***	***731***	***180,193***	---	***2,791***
Center	1,682	348,788	1,682	354,520	1,863	406,021	1,885	536,776	22	130,755
Budget Authority	1,150	246,261	1,150	246,319	1,150	244,588	1,172	372,588	22	128,000
User Fees	532	102,527	532	108,201	713	161,433	713	164,188	---	2,755
Prescription Drug (PDUFA)	---	---	---	---	*5*	*1,237*	5	1,305	---	68
Medical Device (MDUFA)	*503*	*96,150*	*503*	*102,451*	*676*	*153,819*	676	156,506	---	2,687
Mammography Quality Standards Act (MQSA)	*29*	*6,377*	*29*	*5,750*	*32*	*6,377*	32	6,377	---	---
Field	533	99,326	533	96,279	531	98,822	531	98,858	---	36
Budget Authority	513	83,420	513	83,445	513	82,853	513	82,853	---	---
User Fees	20	15,906	20	12,834	18	15,969	18	16,005	---	36
Medical Device (MDUFA)	*11*	*2,014*	*11*	*1,873*	*10*	*2,077*	*10*	*2,113*	---	36
Mammography Quality Standards Act (MQSA)	*9*	*13,892*	*9*	*10,961*	*8*	*13,892*	*8*	*13,892*	---	---
National Center for Toxicological Research (BA Only)	**314**	**63,331**	**314**	**63,331**	314	62,901	*314*	*65,200*	---	2,299
Family Smoking Prevention and Tobacco Control Act	**886**	**596,338**	**886**	**754,076**	**886**	**592,288**	**982**	**662,043**	**96**	**69,755**
Center (UF Only)	843	581,438	843	742,641	843	577,489	*932*	*647,493*	89	70,004
Field (UF Only)	43	14,900	43	11,435	43	14,799	*50*	*14,550*	7	-249
FDA Headquarters	**1,168**	**282,678**	**1,195**	**302,146**	**1,268**	**315,546**	**1,298**	**347,240**	**30**	**31,694**
Budget Authority	***742***	***182,237***	***769***	***187,063***	742	180,980	759	198,565	17	17,585
User Fees	***426***	***100,441***	***426***	***115,083***	***526***	***134,566***	***539***	***148,675***	***13***	***14,109***
Prescription Drug (PDUFA)	*219*	*46,202*	*219*	*53,970*	*252*	*56,236*	*252*	*59,272*	---	3,036
Medical Device (MDUFA)	*31*	*5,732*	*31*	*8,118*	*43*	*10,373*	*43*	*10,554*	---	181
Generic Drug (GDUFA)	*101*	*25,050*	*101*	*30,587*	*148*	*44,859*	*148*	*45,568*	---	709
Biosimilars (BsUFA)	*9*	*1,388*	*9*	*1,976*	*8*	*1,659*	*8*	*1,688*	---	29
Animal Drug (ADUFA)	*1*	*947*	*1*	*874*	*4*	*654*	*5*	*1,208*	1	554
Animal Generic Drug (AGDUFA)	---	*453*	---	*212*	*1*	*267*	*3*	*971*	2	704
Family Smoking Prevention and Tobacco Control Act	*63*	*19,132*	*63*	*19,072*	64	19,002	*74*	*27,870*	10	8,868
Mammography Quality Standards Act (MQSA)	*2*	*253*	*2*	*274*	*2*	*253*	*2*	*253*	---	---
Food and Feed Recall	---	*75*	---	---	---	*75*	---	*75*	---	---
Food Reinspection	---	*480*	---	---	*2*	*480*	*2*	*480*	---	---
Voluntary Qualified Importer Program	---	*277*	---	---	*1*	*277*	*1*	*277*	---	---
Third Party Auditor Program	---	*73*	---	---	---	*39*	---	*39*	---	---
Outsourcing Facility	---	*379*	---	---	*1*	*392*	*1*	*420*	---	28
FDA White Oak Consolidation	**---**	**46,856**	**---**	**46,856**	**---**	**46,349**	**---**	**57,373**	**---**	**11,024**
Budget Authority	---	***43,044***	---	43,044	---	42,752	---	*49,430*	---	6,678
User Fees	---	***3,812***	---	***3,812***	---	***3,597***	---	***7,943***	---	***4,346***
Prescription Drug (PDUFA)	---	3,812	---	3,812	---	*3,597*	---	*3,792*	---	195
Medical Device (MDUFA)	---	---	---	---	---	---	---	---	---	---
Generic Drug (GDUFA)	---	---	---	---	---	---	---	---	---	---
Biosimilars (BsUFA)	---	---	---	---	---	---	---	---	---	---
Animal Drug (ADUFA)	---	---	---	---	---	---	---	---	---	---
Animal Generic Drug (AGDUFA)	---	---	---	---	---	---	---	---	---	---
Family Smoking Prevention and Tobacco Control Act	---	---	---	---	---	---	---	*4,151*	---	4,151

(Dollars in Thousands)	FY 2017 Final		FY 2017 Actuals		FY 2018 Annualized CR		FY 2019 President's Budget		FY 2019 President's Budget +/- FY 2018 Annualized CR	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Other Rent and Rent Related	---	**117,147**	---	**116,653**	---	**122,740**	---	**138,793**	---	**16,053**
Budget Authority	---	***71,943***	---	71,943	---	71,454	---	*86,497*	---	15,043
User Fees	---	***45,204***	---	***44,710***	---	***51,286***	---	***52,296***	---	***1,010***
Prescription Drug (PDUFA)	---	26,340	---	25,047	---	*24,672*	---	*26,005*	---	1,333
Medical Device (MDUFA)	---	4,174	---	4,174	---	*5,187*	---	*5,278*	---	91
Generic Drug (GDUFA)	---	6,962	---	6,962	---	*12,946*	---	*13,150*	---	204
Biosimilars (BsUFA)	---	633	---	633	---	*805*	---	*819*	---	14
Animal Drug (ADUFA)	---	236	---	236	---	*720*	---	*1,000*	---	280
Animal Generic Drug (AGDUFA)	---	113	---	113	---	*273*	---	*379*	---	106
Family Smoking Prevention and Tobacco Control Act	---	*6,250*	---	7,545	---	6,208	---	*5,190*	---	-1,018
Food and Feed Recall	---	43	---	---	---	*43*	---	*43*	---	---
Food Reinspection	---	204	---	---	---	*204*	---	*204*	---	---
Voluntary Qualified Importer Program	---	170	---	---	---	*170*	---	*170*	---	---
Third Party Auditor Program	---	45	---	---	---	*24*	---	*24*	---	---
Outsourcing Facility	---	34	---	---	---	*34*	---	*34*	---	---
GSA Rental Payments	---	**232,139**	---	**220,653**	---	**238,491**	---	**239,916**	---	**1,425**
Budget Authority	---	***170,208***	---	170,208	---	169,052	---	*168,421*	---	-631
User Fees	---	***61,931***	---	***50,445***	---	***69,439***	---	***71,495***	---	***2,056***
Prescription Drug (PDUFA)	---	*22,607*	---	*22,607*	---	*33,373*	---	*35,175*	---	1,802
Medical Device (MDUFA)	---	*7,306*	---	*6,106*	---	*8,229*	---	*8,373*	---	144
Generic Drug (GDUFA)	---	*14,920*	---	*12,471*	---	*12,594*	---	*12,793*	---	199
Biosimilars (BsUFA)	---	*1,107*	---	*461*	---	*339*	---	*345*	---	6
Animal Drug (ADUFA)	---	*1,184*	---	---	---	*522*	---	*725*	---	203
Animal Generic Drug (AGDUFA)	---	*681*	---	---	---	*376*	---	*522*	---	146
Family Smoking Prevention and Tobacco Control Act	---	*13,280*	---	*8,800*	---	13,190	---	*12,746*	---	-444
Food and Feed Recall	---	*73*	---	---	---	*73*	---	*73*	---	---
Food Reinspection	---	*348*	---	---	---	*348*	---	*348*	---	---
Voluntary Qualified Importer Program	---	*290*	---	---	---	*290*	---	*290*	---	---
Third Party Auditor Program	---	*77*	---	---	---	*47*	---	*47*	---	---
Outsourcing Facility	---	*58*	---	---	---	*58*	---	*58*	---	---
Color Certification	**40**	**9,682**	**40**	**9,545**	**37**	**10,125**	***37***	***10,062***	**---**	**-63**
Export Certification	**24**	**4,696**	**24**	**4,546**	**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	**24**	**7,686**	**24**	**4,934**	**---**	**7,686**	**---**	***7,686***	**---**	**---**
Over the Counter Monograph (Proposed)	**---**	**---**	**---**	**---**	**---**	**---**	**---**	***22,000***	**---**	**22,000**
Food and Drug Safety -- No Year (P.L. 113-6)	**---**	**---**	**---**	**1,972**	**---**	**---**	**---**	**---**	**---**	**---**
Food Safety	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**
Drug Safety	**---**	**---**	**---**	**1,972**	**---**	**---**	**---**	**---**	**---**	**---**
21st Century Cures (BA Only)	**26**	**20,000**	**26**	**12,441**	**26**	**19,864**	***26***	***70,000***	**---**	**50,136**
MCMi -- No Year	**4**	**10,000**	**4**	**1,817**	**---**	**9,932**	**---**	**---**	**---**	**-9,932**
Subtotal, Salaries and Expenses	**17,022**	**4,743,593**	**17,022**	**5,095,337**	**17,585**	**5,125,392**	**17,871**	**5,786,767**	**286**	**661,375**
Buildings and Facilities (Budget Authority)	**---**	**11,788**	**---**	**9,243**	**---**	**11,708**	**---**	**11,788**	**---**	**80**
Total Program Level	**17,022**	**4,755,381**	**17,022**	**5,104,580**	**17,585**	**5,137,100**	**17,871**	**5,798,555**	**286**	**661,455**

(Dollars in Thousands)	FY 2017 Final		FY 2017 Actuals		FY 2018 Annualized CR		FY 2019 President's Budget		FY 2019 President's Budget +/- FY 2018 Annualized CR	
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Non-Field Activities	*11,991*	*3,163,450*	*11,991*	*3,586,375*	*12,479*	*3,548,742*	*12,748*	*4,110,011*	*269*	*561,269*
Field Activities	*5,001*	*1,154,001*	*5,001*	*1,108,570*	*5,080*	*1,139,274*	*5,097*	*1,148,674*	*17*	*9,400*
White Oak, Rent Activities, and B&F	---	*407,930*	---	*393,405*	---	*419,288*	---	*447,870*	---	*28,582*
Food and Drug Safety -- No Year	---	---	---	*1,972*	---	---	---	---	---	---
21st Century Cures	*26*	*20,000*	*26*	*12,441*	*26*	*19,864*	*26*	*70,000*	---	*50,136*
MCMi -- No Year	*4*	*10,000*	*4*	*1,817*	---	*9,932*	---	---	---	*-9,932*
User Fees:										
Current Law										
Prescription Drug (PDUFA)	*3,297*	*754,524*	*3,297*	*905,272*	*3,206*	*911,346*	*3,206*	*960,568*	---	*49,222*
Medical Device (MDUFA)	*595*	*126,083*	*595*	*133,733*	*781*	*193,291*	*781*	*196,668*	---	*3,377*
Generic Drug (GDUFA)	*1,336*	*323,011*	*1,336*	*393,512*	*1,692*	*493,600*	*1,692*	*501,396*	---	*7,796*
Biosimilars (BsUFA)	*113*	*22,079*	*113*	*32,718*	*227*	*40,214*	*227*	*40,922*	---	*708*
Animal Drug (ADUFA)	*82*	*23,673*	*82*	*19,102*	*100*	*18,093*	*119*	*30,331*	*19*	*12,238*
Animal Generic Drug (AGDUFA)	*53*	*11,341*	*53*	*10,360*	*53*	*9,419*	*85*	*18,336*	*32*	*8,917*
Family Smoking Prevention and Tobacco Control Act	*949*	*635,000*	*949*	*789,493*	*950*	*630,688*	*1,056*	*712,000*	*106*	*81,312*
Subtotal, Current Law	**6,425**	**1,895,711**	**6,425**	**2,284,190**	**7,009**	**2,296,651**	**7,166**	**2,460,221**	**157**	**163,570**
Indefinite										
Mammography Quality Standards Act (MQSA)	*40*	*20,522*	*40*	*16,985*	*42*	*20,522*	*42*	*20,522*	---	---
Color Certification	*40*	*9,682*	*40*	*9,545*	*37*	*10,125*	*37*	*10,062*	---	*-63*
Export Certification	*24*	*4,696*	*24*	*4,546*	*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	*24*	*7,686*	*24*	*4,934*	---	*7,686*	---	*7,686*	---	---
Food and Feed Recall	---	*1,434*	---	---	*5*	*1,434*	*5*	*1,434*	---	---
Food Reinspection	---	*6,414*	---	---	*24*	*6,414*	*24*	*6,414*	---	---
Voluntary Qualified Importer Program	---	*5,300*	---	---	*20*	*5,300*	*20*	*5,300*	---	---
Third Party Auditor Program	---	*1,400*	---	---	*1*	*712*	*1*	*712*	---	---
Outsourcing Facility	*8*	*1,370*	*8*	*1,130*	*4*	*1,417*	*4*	*1,520*	---	*103*
Over the Counter Monograph (Proposed)	---	---	---	---	---	---	---	*22,000*	---	*22,000*
Subtotal, Indefinite	**136**	**58,504**	**136**	**37,140**	**159**	**58,306**	**159**	**84,626**	**---**	**26,320**
Total User Fees	**6,561**	**1,954,215**	**6,561**	**2,321,330**	**7,168**	**2,354,957**	**7,325**	**2,544,847**	**157**	**189,890**
Total Budget Authority, Pre-Transfer	**10,461**	**2,801,166**	**10,461**	**2,783,250**	**10,417**	**2,782,143**	**10,546**	**3,253,708**	**129**	**471,565**
BA, S&E	*10,431*	*2,759,378*	*10,431*	*2,759,749*	*10,391*	*2,740,639*	*10,520*	*3,171,920*	*129*	*431,281*
BA, B&F	---	*11,788*	---	*9,243*	---	*11,708*	---	*11,788*	---	*80*
Total Mandatory Resources - Directed Transfer	---	---	---	---	---	---	---	---	---	---
21st Century Cures	*26*	*20,000*	*26*	*12,441*	*26*	*19,864*	*26*	*70,000*	---	*50,136*
MCMi -- No Year	*4*	*10,000*	*4*	*1,817*	---	*9,932*	---	---	---	*-9,932*
Total Program Level, Pre-Transfer	**17,022**	**4,755,381**	**17,022**	**5,104,580**	**17,585**	**5,137,100**	**17,871**	**5,798,555**	**286**	**661,455**
HHS OIG transfer (BA Only)	**---**	**-1,500**	**---**	**---**	**---**	**-1,490**	**---**	**---**	**---**	**1,490**
Total Budget Authority, Post-Transfer	**10,461**	**2,799,666**	**10,461**	**2,783,250**	**10,417**	**2,780,653**	**10,546**	**3,253,708**	**129**	**473,055**
Total User Fees	***6,561***	***1,954,215***	***6,561***	***2,321,330***	***7,168***	***2,354,957***	***7,325***	***2,544,847***	***157***	***189,890***
Total Program Level, Post-Transfer	**17,022**	**4,753,881**	**17,022**	**5,104,580**	**17,585**	**5,135,610**	**17,871**	**5,798,555**	**286**	**662,945**
Additional Opioids Allocation (non-add)	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**10,000**	**---**	**10,000**

*For FY 2017 and 2018, 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 2019, FDA proposes to discontinue the transfer.

** FTE figures do not include an estimated 79 reimbursable, 2 CRADA, 2 FOIA, 26 PEPFAR, and 3 Zika

***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.

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

*****The FY 2017, FY 2018, and 2019 columns reflect reallocated funding across the programs addressing reorganizations impacting food and veterinary medicine activities 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 no companies have announced planned use of the voucher.

MAJOR ACTIVITIES TABLE

(Dollars in Thousands)	FY 2017 Final						FY 2018 Annualized CR						FY 2019 President's Budget						FY 2019 President's Budget +/- FY 2018 Annualized 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	
Programs	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000
Budget Authority:																								
Foods	**3,935**	**1,029,175**	**---**	**---**	**3,935**	**1,029,175**	**3,895**	**1,022,211**	**---**	**---**	**3,895**	**1,022,211**	**3,895**	**1,029,863**	**---**	**---**	**3,895**	**1,029,863**	**---**	**7,652**	**---**	**---**	**---**	**7,652**
Center	1,118	314,806	---	---	1,118	314,806	1,078	312,694	---	---	1,078	312,694	1,078	315,494	---	---	1,078	315,494	---	**2,800**	---	---	---	**2,800**
Field	2,817	714,369	---	---	2,817	714,369	2,817	709,517	---	---	2,817	709,517	2,817	714,369	---	---	2,817	714,369	---	**4,852**	---	---	---	**4,852**
Human Drugs	**---**	**---**	**2,117**	**491,607**	**2,117**	**491,607**	**---**	**---**	**2,117**	**488,264**	**2,117**	**488,264**	**---**	**---**	**2,163**	**686,364**	**2,163**	**686,364**	**---**	**---**	**46**	**198,100**	**46**	**198,100**
Center	---	---	1,317	355,438	1,317	355,438	---	---	1,317	353,020	1,317	353,020	---	---	1,353	548,388	1,353	548,388	---	---	**36**	**195,368**	**36**	**195,368**
Field	---	---	800	136,169	800	136,169	---	---	800	135,244	800	135,244	---	---	810	137,976	810	137,976	---	---	**10**	**2,732**	**10**	**2,732**
Biologics	**---**	**---**	**852**	**215,317**	**852**	**215,317**	**---**	**---**	**852**	**213,854**	**852**	**213,854**	**---**	**---**	**860**	**251,854**	**860**	**251,854**	**---**	**---**	**8**	**38,000**	**8**	**38,000**
Center	---	---	620	173,937	620	173,937	---	---	620	172,755	620	172,755	---	---	628	210,755	628	210,755	---	---	**8**	**38,000**	**8**	**38,000**
Field	---	---	232	41,380	232	41,380	---	---	232	41,099	232	41,099	---	---	232	41,099	232	41,099	---	---	---	---	---	---
Animal Drugs and Feeds	**628**	**125,805**	**180**	**37,030**	**808**	**162,835**	**628**	**124,951**	**180**	**36,779**	**808**	**161,729**	**628**	**125,806**	**216**	**54,479**	**844**	**180,284**	**---**	**855**	**36**	**17,700**	**36**	**18,555**
Center	316	64,049	165	34,156	481	98,205	316	63,614.04	165.00	33,924.05	481	97,538	316	64,049	201	51,624	517	115,673	---	**435**	**36**	**17,700**	**36**	**18,135**
Field	312	61,756	15	2,874	327	64,630	312	61,336.50	15.00	2,854.48	327	64,191	312	61,756	15	2,854	327	64,611	---	**420**	---		---	**420**
Devices and Radiological Health	**---**	**---**	**1,663**	**329,681**	**1,663**	**329,681**	**---**	**---**	**1,663**	**327,442**	**1,663**	**327,442**	**---**	**---**	**1,685**	**455,442**	**1,685**	**455,442**	**---**	**---**	**22**	**128,000**	**22**	**128,000**
Center	---	---	1,150	246,261	1,150	246,261	---	---	1,150	244,588	1,150	244,588	---	---	1,172	372,588	1,172	372,588	---	---	**22**	**128,000**	**22**	**128,000**
Field	---	---	513	83,420	513	83,420	---	---	513	82,853	513	82,853	---	---	513	82,853	513	82,853	---	---	---	---	---	---
National Center for Toxicological Research	**52**	**10,233**	**262**	**53,098**	**314**	**63,331**	**52**	**10,164**	**262**	**52,737**	**314**	**62,901**	**52**	**10,233**	**262**	**54,967**	**314**	**65,200**	**---**	**69**	**---**	**2,230**	**---**	**2,299**
FDA Headquarters	**311**	**73,540**	**431**	**89,958**	**742**	**182,237**	**311**	**73,016**	**431**	**89,352**	**742**	**180,980**	**311**	**73,540**	**448**	**115,352**	**759**	**198,565**	**---**	**524**	**17**	**26,000**	**17**	**17,585**
FDA White Oak Consolidation	**---**	**---**	**---**	**---**	**---**	**43,044**	**---**	**---**	**---**	**---**	**---**	**42,752**	**---**	**---**	**---**	**---**	**---**	**49,430**	**---**	**---**	**---**	**---**	**---**	**6,678**
Other Rent and Rent Related	**---**	**36,300**	**---**	**35,643**	**---**	**71,943**	**---**	**36,053**	**---**	**35,401**	**---**	**71,454**	**---**	**36,300**	**---**	**50,197**	**---**	**86,497**	**---**	**247**	**---**	**14,796**	**---**	**15,043**
GSA Rental Payments	**---**	**79,477**	**---**	**90,731**	**---**	**170,208**	**---**	**78,937**	**---**	**90,115**	**---**	**169,052**	**---**	**79,477**	**---**	**88,944**	**---**	**168,421**	**---**	**540**	**---**	**-1,171**	**---**	**-631**
SUBTOTAL, BA Salaries and Expenses	**4,926**	**1,354,530**	**5,505**	**1,343,065**	**10,431**	**2,759,378**	**4,886**	**1,345,331**	**5,505**	**1,333,944**	**10,391**	**2,740,639**	**4,886**	**1,355,218**	**5,634**	**1,757,599**	**10,520**	**3,171,920**	**---**	**9,887**	**129**	**423,655**	**129**	**431,281**
21st Century Cures			**26**	**20,000**	**26**	**20,000**			**26**	**19,864**	**26**	**19,864**	**---**	**---**	**---**	**70,000**	**---**	**70,000**	**---**	**---**	**-26**	**50,136**	**-26**	**50,136**
MCMi			**4**	**10,000**	**4**	**10,000**			**---**	**9,932**		**9,932**	**---**	**---**	**---**		**---**	**---**	**---**	**---**	**---**	**-9,932**	**---**	**-9,932**
Building and Facilities	**---**	**---**	**---**	**---**	**---**	**11,788**	**---**	**---**	**---**	**---**	**---**	**11,708**	**---**	**---**	**---**	**---**	**---**	**11,788**	**---**	**---**	**---**	**---**	**---**	**80**
Non-Field Activities	**1,797**	**462,628**	**3,945**	**952,848**	**5,742**	**1,434,215**	**1,757**	**459,487**	**3,945**	**946,378**	**5,702**	**1,424,477**	**1,757**	**463,315**	**4,064**	**1,353,676**	**5,821**	**1,826,664**	**---**	**3,828**	**119**	**407,298**	**119**	**402,187**
Field Activities	**3,129**	**776,125**	**1,560**	**263,843**	**4,689**	**1,039,968**	**3,129**	**770,853**	**1,560**	**262,051**	**4,689**	**1,032,904**	**3,129**	**776,125**	**1,570**	**264,783**	**4,699**	**1,040,908**	**---**	**5,272**	**10**	**2,732**	**10**	**8,004**
White Oak, Rent Activities, and B&F	**---**	**115,777**	**---**	**126,374**	**---**	**296,983**	**---**	**114,991**	**---**	**125,516**	**---**	**294,966**	**---**	**115,778**	**---**	**139,141**	**---**	**316,136**	**---**	**787**	**---**	**13,625**	**---**	**21,170**
21st Century Cures	**---**	**---**	**26**	**20,000**	**26**	**20,000**	**---**	**---**	**26**	**19,864**	**26**	**19,864**	**---**	**---**	**26**	**70,000**	**26**	**70,000**	**---**	**---**	**---**	**50,136**	**---**	**50,136**
MCMi	**---**	**---**	**4**	**10,000**	**4**	**10,000**	**---**	**---**	**---**	**9,932**	**---**	**9,932**	**---**	**---**	**---**		**---**	**---**	**---**	**---**	**---**	**-9,932**	**---**	**-9,932**
Total BA	**4,926**	**1,354,530**	**5,535**	**1,373,065**	**10,461**	**2,801,166**	**4,886**	**1,345,331**	**5,531**	**1,363,740**	**10,417**	**2,782,143**	**4,886**	**1,355,218**	**5,660**	**1,827,599**	**10,546**	**3,253,708**	**---**	**9,887**	**129**	**463,859**	**129**	**471,565**
Total BA, Pre-Transfer	**4,926**	**1,354,530**	**5,535**	**1,373,065**	**10,461**	**2,801,166**	**4,886**	**1,345,331**	**5,531**	**1,363,740**	**10,417**	**2,782,143**	**4,886**	**1,355,218**	**5,660**	**1,827,599**	**10,546**	**3,253,708**	**---**	**9,887**	**129**	**463,859**	**129**	**471,565**

(Dollars in Thousands)	FY 2017 Final						FY 2018 Annualized CR						FY 2019 President's Budget						FY 2019 President's Budget +/- FY 2018 Annualized 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	
Programs	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**	**FTE**	**$000**
Total User Fees	**---**	**16,551**	**5,572**	**1,292,982**	**6,561**	**1,954,215**	**50**	**15,863**	**6,131**	**1,698,281**	**7,168**	**2,354,957**	**50**	**15,863**	**6,182**	**1,806,922**	**7,325**	**2,544,847**	**---**	**---**	**51**	**108,641**	**157**	**189,890**
Current Law																			**---**	**---**	**---**	**---**	**---**	**---**
Prescription Drug (PDUFA)	---	---	3,297	754,524	3,297	754,524	---	---	3,206	911,346	3,206	911,346	---	---	3,206	960,568	3,206	960,568	**---**	**---**	**---**	**49,222**	**---**	**49,222**
Medical Device (MDUFA)	---	---	595	126,083	595	126,083	---	---	781	193,291	781	193,291	---	---	781	196,668	781	196,668	**---**	**---**	**---**	**3,377**	**---**	**3,377**
Generic Drug (GDUFA)	---	---	1,336	323,011	1,336	323,011	---	---	1,692	493,600	1,692	493,600	---	---	1,692	501,396	1,692	501,396	**---**	**---**	**---**	**7,796**	**---**	**7,796**
Biosimilars (BsUFA)	---	---	113	22,079	113	22,079	---	---	227	40,214	227	40,214	---	---	227	40,922	227	40,922	**---**	**---**	**---**	**708**	**---**	**708**
Animal Drug (ADUFA)	---	---	82	23,673	82	23,673	---	---	100	18,093	100	18,093	---	---	119	30,331	119	30,331	**---**	**---**	**19**	**12,238**	**19**	**12,238**
Animal Generic Drug (AGDUFA)	---	---	53	11,341	53	11,341	---	---	53	9,419	53	9,419	---	---	85	18,336	85	18,336	**---**	**---**	**32**	**8,917**	**32**	**8,917**
Family Smoking Prevention and Tobacco Control Act	---	---	---	---	949	635,000	---	---	---	---	950	630,688	---	---	---	---	1,056	712,000	**---**	**---**	**---**	**---**	**106**	**81,312**
Mammography Quality Standards Act (MQSA)	---	---	40	20,522	40	20,522	---	---	42	20,522	42	20,522	---	---	42	20,522	42	20,522	**---**	**---**	**---**	**---**	**---**	**---**
Color Certification	---	---	---	---	40	9,682	---	---	---	---	37	10,125	---	---	---	---	37	10,062	**---**	**---**	**---**	**---**	**---**	**-63**
Export Certification	---	2,003	24	2,693	24	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**	**---**	**4,280**
Priority Review Vouchers (PRV) Tropical Disease	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**---**	**---**	**---**	**---**	**---**	**---**
Priority Review Vouchers (PRV) Pediatric Disease	---	---	24	7,686	24	7,686	---	---	---	7,686	---	7,686	---	---	---	7,686	---	7,686	**---**	**---**	**---**	**---**	**---**	**---**
Food and Feed Recall	---	1,434	---	---	---	1,434	5	1,434	---	---	5	1,434	5	1,434	---	---	5	1,434	**---**	**---**	**---**	**---**	**---**	**---**
Food Reinspection	---	6,414	---	---	---	6,414	24	6,414	---	---	24	6,414	24	6,414	---	---	24	6,414	**---**	**---**	**---**	**---**	**---**	**---**
Voluntary Qualified Importer Program	---	5,300	---	---	---	5,300	20	5,300	---	---	20	5,300	20	5,300	---	---	20	5,300	**---**	**---**	**---**	**---**	**---**	**---**
Third Party Auditor Program	---	1,400	---	---	---	1,400	1	712	---	---	1	712	1	712	---	---	1	712	**---**	**---**	**---**	**---**	**---**	**---**
Outsourcing Facility	---	---	8	1,370	8	1,370	---	---	4	1,417	4	1,417	---	---	4	1,520	4	1,520	**---**	**---**	**---**	**103**	**---**	**103**
Over the Counter Monograph (Proposed)															---	22,000	---	22,000	**---**	**---**	**---**	**22,000**	**---**	**22,000**
Total Program Level, Pre-Transfer	**4,926**	**1,371,081**	**11,107**	**2,666,047**	**17,022**	**4,755,381**	**4,936**	**1,361,194**	**11,662**	**3,062,021**	**17,585**	**5,137,100**	**4,936**	**1,371,081**	**11,842**	**3,634,521**	**17,871**	**5,798,555**	**---**	**9,887**	**180**	**572,500**	**286**	**661,455**
HHS OIG transfer					**---**	**-1,500**					**---**	**-1,490**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**---**	**1,490**
Total BA, Post-Transfer	**4,926**	**1,354,530**	**5,535**	**1,373,065**	**10,461**	**2,799,666**	**4,886**	**1,345,331**	**5,531**	**1,363,740**	**10,417**	**2,780,653**	**4,886**	**1,355,218**	**5,660**	**1,827,599**	**10,546**	**3,253,708**	**---**	**9,887**	**129**	**463,859**	**129**	**473,055**
Total Program Level, Post-Transfer	**4,926**	**1,371,081**	**11,107**	**2,666,047**	**17,022**	**4,753,881**	**4,936**	**1,361,194**	**11,662**	**3,062,021**	**17,585**	**5,135,610**	**4,936**	**1,371,081**	**11,842**	**3,634,521**	**17,871**	**5,798,555**	**---**	**9,887**	**180**	**572,500**	**286**	**662,945**
Additional Opioids Allocation (non-add)															**---**	**10,000**	**---**	**10,000**	**---**	**---**	**---**	**10,000**	**---**	**10,000**

* Total Budget Authority includes ~$10 million for the China Initiative for FY 2017, FY 2018, and FY 2019, and $7.5 million for FY 2017 and FY 2018 for Foreign High Risk Inspections. 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 2017 and 2018, 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 2019, FDA proposes to discontinue the transfer.

***The FY 2017, FY 2018, and 2019 columns reflect reallocated funding across the programs addressing reorganizations impacting food and veterinary medicine activities 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 no companies have announced planned use of the voucher.

BUDGET AUTHORITY CROSSWALK

(Dollars in Thousands)	FY 2017 Final		FY 2018 Annualized CR		Reductions		Food Safety		Medical Product Safety																				White Oak	FY 2019 President's Budget	
									21st Century Cures Act and other no-year funding		Animal Drug Review		Promote Domestic Manufacturing		New Domestic Drug Industry		MedTech Manufacturing		New Medical Data Enterprise		Transformation of Digital Health Technology		New Platform for Drug Development		Generic Drug Development and Review		Investment and Innovation for Rare Diseases		Infrastructure	Total Medical Product Safety			
	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000	FTE	$000			FTE	$000	FTE	$000	$000	FTE	$000	$000	FTE	$000
Salaries and Expenses Account:																																		
Foods	**3,935**	**1,029,175**	**3,895**	**1,022,211**	---	---	---	**7,652**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**3,895**	**1,029,863**
Center	1,118	314,806	1,078	312,694	---	---	---	2,800	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	1,078	315,494
Field	2,817	714,369	2,817	709,517	---	---	---	4,852	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	2,817	714,369
Human Drugs	**2,117**	**491,607**	**2,117**	**488,264**	---	---	---	---	---	---	---	---	**2**	**35,000**	**27**	**25,000**	---	---	**2**	**23,000**	---	---	**5**	**57,500**	**5**	**37,600**	**5**	**20,000**	---	**46**	**198,100**	---	**2,163**	**686,364**
Center	1,317	355,438	1,317	353,020	---	---	---	---	---	---	---	---	2	35,000	17	22,268	---	---	2	23,000	---	---	5	57,500	5	37,600	5	20,000	---	36	195,368	---	1,353	548,388
Field	800	136,169	800	135,244	---	---	---	---	---	---	---	---	---	---	10	2,732	---	---	---	---	---	---	---	---	---	---	---	---	---	10	2,732	---	810	137,976
Biologics	**852**	**215,317**	**852**	**213,854**	---	---	---	---	---	---	---	---	**4**	**15,000**	---	---	---	---	**4**	**23,000**	---	---	---	---	---	---	---	---	---	**8**	**38,000**	---	**860**	**251,854**
Center	620	173,937	620	172,755	---	---	---	---	---	---	---	---	4	15,000	---	---	---	---	4	23,000	---	---	---	---	---	---	---	---	---	8	38,000	---	628	210,755
Field	232	41,380	232	41,099	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	232	41,099
Animal Drugs and Feeds	**808**	**162,835**	**808**	**161,729**	---	---	---	**855**	---	---	**32**	**9,700**	---	---	---	---	---	---	**4**	**8,000**	---	---	---	---	---	---	---	---	---	**36**	**17,700**	---	**844**	**180,284**
Center	481	98,205	481	97,538	---	---	---	435	---	---	32	9,700	---	---	---	---	---	---	4	8,000	---	---	---	---	---	---	---	---	---	36	17,700	---	517	115,673
Field	327	64,630	327	64,191	---	---	---	420	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	327	64,611
Devices and Radiological Health	**1,663**	**329,681**	**1,663**	**327,442**	---	---	---	---	---	---	---	---	---	---	---	---	**4**	**12,000**	**5**	**46,000**	**13**	**70,000**	---	---	---	---	---	---	---	**22**	**128,000**	---	**1,685**	**455,442**
Center	1,150	246,261	1,150	244,588	---	---	---	---	---	---	---	---	---	---	---	---	4	12,000	5	46,000	13	70,000	---	---	---	---	---	---	---	22	128,000	---	1,172	372,588
Field	513	83,420	513	82,853	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	513	82,853
National Center for Toxicological Research	**314**	**63,331**	**314**	**62,901**	---	---	---	**69**	---	---	---	---	---	**2,230**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	2,230	---	314	65,200
FDA Headquarters	**742**	**182,237**	**742**	**180,980**	---	**-8,939**	---	**524**	---	---	---	---	**4**	**6,000**	---	---	---	---	---	---	---	---	**13**	**20,000**	---	---	---	---	---	17	26,000	---	759	198,565
FDA White Oak Consolidation	---	**43,044**	---	**42,752**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**6,678**	---	49,430
Other Rent and Rent Related	---	**71,943**	---	**71,454**	---	---	---	**247**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**14,796**	---	14,796	---	---	86,497
GSA Rental Payments	---	**170,208**	---	**169,052**	---	---	---	**540**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**-1,171**	---	-1,171	---	---	168,421
Subtotal, Salaries and Expenses Account	**10,431**	**2,759,378**	**10,391**	**2,740,639**	---	**-8,939**	---	**9,887**	---	---	**32**	**9,700**	**10**	**58,230**	**27**	**25,000**	**4**	**12,000**	**15**	**100,000**	**13**	**70,000**	**18**	**77,500**	**5**	**37,600**	**5**	**20,000**	**13,625**	**129**	**423,655**	**6,678**	**10,520**	**3,171,920**
Buildings and Facilities Account	---	**11,788**	---	**11,708**	---		---																								---	**80**	---	11,788
Total Budget Authority, Pre-Transfer	**10,431**	**2,771,166**	**10,391**	**2,752,347**	---	**-8,939**	---	**9,887**	---	---	**32**	**9,700**	**10**	**58,230**	**27**	**25,000**	**4**	**12,000**	**15**	**100,000**	**13**	**70,000**	**18**	**77,500**	**5**	**37,600**	**5**	**20,000**	**13,625**	**129**	**423,655**	**6,758**	**10,520**	**3,183,708**
Non-Field Activities	**5,742**	**1,434,215**	**5,702**	**1,424,477**	---	**-8,939**	---	**3,828**	---	---	**32**	**9,700**	**10**	**58,230**	**17**	**22,268**	**4**	**12,000**	**15**	**100,000**	**13**	**70,000**	**18**	**77,500**	**5**	**37,600**	**5**	**20,000**	---	**119**	**407,298**	---	**5,821**	**1,826,664**
Field Activities	**4,689**	**1,039,968**	**4,689**	**1,032,904**	---	---	---	**5,272**	---	---	---	---	---	---	**10**	**2,732**	---	---	---	---	---	---	---	---	---	---	---	---	---	**10**	**2,732**	---	**4,699**	**1,040,908**
Rent Activities, B&F, and White Oak	---	**296,983**	---	**294,966**	---	---	---	**787**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	**13,625**	---	**13,625**	**6,758**	---	**316,136**
21st Century Cures	**26**	**20,000**	**26**	**19,864**	---	---	---	---	---	**50,136**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---		---	**50,136**	---	**26**	**70,000**
MCMi	**4**	**10,000**	---	**9,932**	---	---	---	---	---	**-9,932**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---		---	**-9,932**	---	---	---
Total Budget Authority with 21st Century Cures	**10,461**	**2,801,166**	**10,417**	**2,782,143**	---	**-8,939**	---	**9,887**	---	**40,204**	**32**	**9,700**	**10**	**58,230**	**27**	**25,000**	**4**	**12,000**	**15**	**100,000**	**13**	**70,000**	**18**	**77,500**	**5**	**37,600**	**5**	**20,000**	**13,625**	**129**	**463,859**	**6,758**	**10,546**	**3,253,708**
HHS OIG transfer	---	**-1,500**	---	**-1,490**	---	**1,490**	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---
Total Budget Authority, Post-Transfer	**10,461**	**2,799,666**	**10,417**	**2,780,653**	---	**-7,449**	---	**9,887**	---	**40,204**	**32**	**9,700**	**10**	**58,230**	**27**	**25,000**	**4**	**12,000**	**15**	**100,000**	**13**	**70,000**	**18**	**77,500**	**5**	**37,600**	**5**	**20,000**	**13,625**	**129**	**463,859**	**6,758**	**10,546**	**3,253,708**

*For FY 2017 and 2018, 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 2019, FDA proposes to discontinue the transfer.

**The FY 2017, FY 2018, and 2019 columns reflect reallocated funding across the programs addressing reorganizations impacting food and veterinary medicine activities as well as to better align the funding structure to services related to intergovernmental affairs.

***Of the funding for the Rare Diseases initiative, $10M will support policy related activities in FDA Headquarters.

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 2019 Budget, since the location of programs may have changed in prior years or be proposed for change in FY 2019. This approach allows increases and decreases in this book to reflect true funding changes.

FY 2019 REALLOCATIONS

(Dollars in Thousands)	OFVM Reorganization		IGA Staff		Total	
	FTE	$000	FTE	$000	FTE	$000
Salaries and Expenses Account:						
Foods	**30**	**3,812**	**---**	**-140**	**30**	**3,672**
Center	30	3,812	---	---	30	3,812
Field	---	---	---	-140	---	-140
Human Drugs	**---**	**---**	**-3**	**-596**	**-3**	**-596**
Center	---	---	-3	-558	-3	-558
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	**-30**	**-3,812**	**3**	**962**	**-27**	**-2,850**
FDA White Oak Consolidation	**---**	**---**	**---**	**---**	**---**	**---**
Other Rent and Rent Related	**---**	**---**	**---**	**---**	**---**	**---**
GSA Rental Payments	**---**	**---**	**---**	**---**	**---**	**---**
Subtotal, Salaries and Expenses Account	**---**	**---**	**---**	**---**	**---**	**---**
Buildings and Facilities Account	**---**	**---**	**---**	**---**	**---**	**---**
Total Budget Authority, Pre-Transfer	**---**	**---**	**---**	**---**	**---**	**---**
Non-Field Activities	**---**	**---**	**---**	**231**	**---**	**231**
Field Activities	**---**	**---**	**---**	**-231**	**---**	**-231**
Rent Activities, B&F, and White Oak	**---**	**---**	**---**	**---**	**---**	**---**

*Reflect reallocated funding across the programs addressing reorganizations impacting food and veterinary medicine activities as well as to better align the funding structure to services related to intergovernmental affairs.

** FDA has notified the Congress and is in the process of implementing the OFVM Reorganization.

BUDGET EXHIBITS

APPROPRIATION 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; $5,583,474,000: Provided, That of the amount provided under this heading, $960,568,000 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; $196,668,000 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; $501,396,000 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; $40,922,000 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; $712,000,000 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, and biosimilar biological product user fees that exceed the respective fiscal year 2019 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, and biosimilar biological product assessments for fiscal year 2019, including any such fees collected prior to fiscal year 2019 but credited for fiscal year 2019, shall be subject to the fiscal year 2019 limitations: Provided further, That the Secretary may accept payment during fiscal year 2019 of user fees specified under this heading and authorized for fiscal year 2020, prior to the due date for such fees, and that amounts of such fees assessed for fiscal year 2020 for which the Secretary accepts payment in fiscal year 2019 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 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 funds may be transferred from one specified activity to another with the prior 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), third-party logistics provider licensing and inspection fees authorized by 21 U.S.C. 360eee-3(c)(1), 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, to remain available until expended.

Salaries and Expenses (Legislative Proposal)

Contingent upon the enactment of authorizing legislation, the Secretary shall charge a fee for animal drug review, animal generic drug review activities, and over-the-counter monograph drug activities: Provided, That fees of $30,331,000, for animal drug reviews, shall be credited to this account and remain available until expended; $18,336,000 for animal generic drug reviews, shall be credited to this account and remain available until expended; $22,000,000 for over-the-counter monograph drug activities, 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 animal drug, animal generic drug, and over-the-counter monograph drug user fees that exceed the respective fiscal year 2019 limitations are appropriated and shall be credited to this account and remain available until expended: Provided further, That fees derived from animal drug, animal generic drug, and over-the-counter monograph drug reviews for fiscal year 2019 received during fiscal year 2019, including any such fees assessed prior to fiscal year 2019 but credited for fiscal year 2019, shall be subject to the fiscal year 2019 limitations: Provided further, That the Secretary may accept payment during fiscal year 2019 of user fees specified in this paragraph and authorized for fiscal year 2020, prior to the due date for such fees, and that amounts of such fees assessed for fiscal year 2020 for which the Secretary accepts payment in fiscal year 2019 shall not be included in amounts in this paragraph.

FDA Innovation, Cures Act

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", $70,000,000, 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.

FY 2019 PROPOSED GENERAL PROVISIONS

SEC. 714. None of the funds made available by this Act may be used to notify a sponsor or otherwise acknowledge receipt of a submission for an exemption for investigational use of a drug or biological product under section 505(i) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)) or section 351(a)(3) of the Public Health Service Act (42 U.S.C. 262(a)(3)) in research in which a human embryo is intentionally created or modified to include a heritable genetic modification. Any such submission shall be deemed to have not been received by the Secretary, and the exemption may not go into effect.

SEC. 725. (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 2019 for "Department of Health and Human Services - Food and Drug Administration - Salaries and Expenses", not to exceed $5,000,000 of available amounts 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. 715. No partially hydrogenated oils as defined in the order published by the Food and Drug Administration in the Federal Register on June 17, 2015 (80 Fed. Reg. 34650 et seq.) shall be deemed unsafe within the meaning of section 409(a) and no food that is introduced or delivered for introduction into interstate commerce that bears or contains a partially hydrogenated oil shall be deemed adulterated under sections 402(a)(1) or 402(a)(2)(C)(i) by virtue of bearing or containing a partially hydrogenated oil until the compliance date as specified in such order (June 18, 2018).

Sec. 724. INCREASE IN EXPORT CERTIFICATION FEES.— Section 801(e)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 381(e)(4)) is amended— (a) in subparagraph (B) by striking "but shall not exceed $175 for each certification" and inserting "in an amount specified in subparagraph (E)"; and (b) by adding at the end the following new subparagraphs: "(E) 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 section738(c)(2)(C), applied without regard to the limitation in clause (ii)(II) of such subparagraph. (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.".

APPROPRIATION LANGUAGE ANALYSIS

Language Provision	Explanation
Animal Drug User Fee	The Administration will propose legislation to allow FDA to collect fees for animal drugs. The additional resources are estimated at $30,331,000. 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 $18,336,000. 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.
Over the Counter Monograph	The Administration will propose legislation to allow FDA to collect fees for over the counter monograph. The additional resources are estimated at $22,000,000. This will support implementing meaningful reforms to the regulation of over the-counter (OTC) monograph drug products to promote innovation and to reduce regulatory burden supported by an OTC monograph user fee program.

AMOUNTS AVAILABLE FOR OBLIGATION

(dollars in thousands)	FY 2017 Final	FY 2018 Annualized CR	FY 2019 President's Budget
General Fund Discretionary Appropriation:			
Appropriation	2,799,666	2,780,653	3,253,708
Total Discretionary Appropriation	**2,799,666**	**2,780,653**	**3,253,708**
Mandatory Appropriation:			
CRADA	2,000	2,000	2,000
Total Mandatory Appropriation	**2,000**	**2,000**	**2,000**
Offsetting Collections:			
Non-Federal Sources:	1,954,215	2,354,957	2,544,847
Total Offsetting Collections	**1,954,215**	**2,354,957**	**2,544,847**
Total Obligations	**4,755,881**	**5,137,610**	**5,800,555**

*For FY 2017 and FY 2018, 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 2019, FDA proposes to discontinue the transfer.

SUMMARY OF CHANGES

(dollars in thousands)	Budget Authority	User Fees	Program Level	FTE
FY 2018 Annualized CR	**2,780,653**	**2,354,957**	**5,135,610**	**17,585**
FY 2019 Program Changes				
Budget Authority Changes				
Reductions	-7,449	---	-7,449	---
Food Safety	9,887	---	9,887	---
21st Century Cures Act and Other No-year Funding	40,204	---	40,204	---
Animal Drug Review	9,700	---	9,700	32
Promote Domestic Manufacturing	58,230	---	58,230	10
New Domestic Drug Industry	25,000	---	25,000	27
MedTech Manufacturing	12,000	---	12,000	4
New Medical Data Enterprise	100,000	---	100,000	15
Growth and Transformation of Digital Health Technology Industry	70,000	---	70,000	13
New Platform for Drug Development	77,500	---	77,500	18
Modernizing Generic Drug Development and Review	37,600	---	37,600	5
Investment and Innovation for Rare Diseases	20,000	---	20,000	5
Infrastructure	13,625	---	13,625	---
White Oak	6,758	---	6,758	---
Total Budget Authority Changes	**473,055**	**---**	**473,055**	**129**
User Fee Changes				
Current Law				
Prescription Drug (PDUFA)	---	49,222	49,222	---
Medical Device (MDUFA)	---	3,377	3,377	---
Generic Drug (GDUFA)	---	7,796	7,796	---
Biosimilars (BsUFA)	---	708	708	---
Animal Drug (ADUFA)	---	12,238	12,238	19
Animal Generic Drug (AGDUFA)	---	8,917	8,917	32
Family Smoking Prevention and Tobacco Control Act	---	81,312	81,312	106
Indefinite				
Mammography Quality Standards Act (MQSA)	---	---	---	---
Color Certification	---	-63	-63	---
Export Certification	---	4,280	4,280	---
Priority Review Vouchers (PRV) Tropical Disease	---	---	---	---
Priority Review Vouchers (PRV) Pediatric Disease	---	---	---	---
Food and Feed Recall	---	---	---	---
Food Reinspection	---	---	---	---
Voluntary Qualified Importer Program	---	---	---	---
Third Party Auditor Program	---	---	---	---
Outsourcing Facility	---	103	103	---
Over the Counter Monograph (Proposed)	---	22,000	22,000	---
Subtotal, Current Law	**---**	**189,890**	**189,890**	**157**
Net Program Changes	**473,055**	**189,890**	**662,945**	**286**
Total FDA Request for FY 2018	**3,253,708**	**2,544,847**	**5,798,555**	**17,871**

*For FY 2017 and FY 2018, 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 2019, FDA proposes to discontinue the transfer.

** FTE figures do not include an estimated 79 reimbursable, 2 CRADA, 2 FOIA, 26 PEPFAR and 3 Zika.

BUDGET AUTHORITY BY ACTIVITY

(dollars in thousands)	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
Salaries and Expenses Account:			
Foods	**1,025,503**	**1,022,211**	**1,029,863**
Center	310,994	312,694	315,494
Field	714,509	709,517	714,369
Human Drugs	**488,626**	**488,264**	**686,364**
Center	352,419	353,020	548,388
Field	136,207	135,244	137,976
Biologics	**215,443**	**213,854**	**251,854**
Center	174,052	172,755	210,755
Field	41,391	41,099	41,099
Animal Drugs and Feeds	**162,852**	**161,729**	**180,284**
Center	98,205	97,538	115,673
Field	64,647	64,191	64,611
Devices and Radiological Health	**329,764**	**327,442**	**455,442**
Center	246,319	244,588	372,588
Field	83,445	82,853	82,853
National Center for Toxicological Research	**63,331**	**62,901**	**65,200**
FDA Headquarters	**187,063**	**180,980**	**198,565**
FDA White Oak Consolidation	**43,044**	**42,752**	**49,430**
Other Rent and Rent Related	**71,943**	**71,454**	**86,497**
GSA Rental Payments	**170,208**	**169,052**	**168,421**
Subtotal, Salaries and Expenses Account	**2,757,777**	**2,740,639**	**3,171,920**
21st Century Cures	**12,441**	**19,864**	**70,000**
MCMi - No Year	**1,817**	**9,932**	**---**
Buildings and Facilities Account	**9,243**	**11,708**	**11,788**
Total Budget Authority	**2,783,250**	**2,782,143**	**3,253,708**
FTE	**10,461**	**10,417**	**10,546**

*For FY 2017 and FY 2018 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 2019, FDA proposes to discontinue the transfer.
** FTE figures do not include an estimated 79 reimbursable, 2 CRADA, 2 FOIA, 26 PEPFAR, 4 MCMi and 3 Zika

APPROPRIATIONS HISTORY

(dollars)	Budget Estimate to Congress	House Allowance	Senate Allowance	Appropriation
General Fund Appropriation*:				
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 1/	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 2/	4,953,946,000	4,649,566,000	4,655,869,000	4,685,089,000
FY 2018	5,044,110,000	5,095,301,000	5,098,341,000	
FY 2019	5,702,141,000			

* Excludes Indefinite user fees.

1/ 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.

2/ The FY 2017 Omnibus Appropriation includes $10 million in no-year funding to address Emerging Public Health Threats.

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NARRATIVE BY ACTIVITY

FOODS

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
Foods	**1,040,761**	**1,025,503**	**1,033,082**	**1,040,734**	**7,652**
Budget Authority	***1,029,175***	***1,025,503***	***1,022,211***	***1,029,863***	***7,652***
User Fees	***11,586***	---	***10,871***	***10,871***	---
Center	315,356	310,994	313,526	316,326	2,800
Budget Authority	314,806	310,994	312,694	315,494	2,800
User Fees	550	---	832	832	---
Food And Feed Recall	*243*	---	*243*	*243*	---
Voluntary Qualified Importer Program	*243*	---	*243*	*243*	---
Third Party Auditor Program	*64*	---	*346*	*346*	---
Field	725,405	714,509	719,556	724,408	4,852
Budget Authority	714,369	714,509	709,517	714,369	4,852
User Fees	11,036	---	10,039	10,039	---
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*	---	*144*	*144*	---
FTE	**3,935**	**3,905**	**3,939**	**3,939**	**---**

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.[7]

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 FVM Strategic Plan goals.

Enhance Oversight

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

- An estimated 48 million foodborne illnesses occur every year[8]
- An estimated 128,000 hospitalizations and 3,000 deaths result[9]
- Foodborne illnesses cost an average of $3,630 per case[10]
- More than $36 billion per year in medical costs, lost productivity, and other burdens to society.[11]

The FVM Strategic Plan[12] 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.

[7] 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.

[8] 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.

[9] 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.

[10] 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

[11] 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

[12] https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofFoods/UCM507379.pdf

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.[13]

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

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. 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.

[13] 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.

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.[14] In 2017, FDA launched a new web page on fda.gov which compiles compliance dates for all of the foundational FSMA rules into a single graphic.

FSMA recognizes that FDA had previously-established regulations that are specific to seafood, juice, and Low-Acid Canned Foods (LACF) and, therefore, some exemptions were made in the FSMA rules for these products. However, there are still some requirements in the FSMA regulations that apply to processors of these products. To help producers of low-acid canned foods, juice, and seafood products understand which parts of the FSMA rules apply to them and how the FSMA rules may affect their operations, in 2017 FDA published three guidance documents: Low-Acid Canned Foods and FSMA, Juice HACCP and FSMA, and Seafood HACCP and FSMA.

FSMA heralded a new era of enhanced collaboration between FDA and its counterparts in state governments across the country. State officials were instrumental in providing comments to help FDA create regulations that take into account the complexities of food production and are designed to be flexible and practical while meeting the agency's public health goals.

In September 2017, FDA awarded 43 states a total of $30.85 million in cooperative agreements to develop produce safety programs that will enable them to deliver education and technical assistance to farmers and create infrastructure to provide inspection, compliance, and oversight.

Since the inception of FSMA, leaders of FDA's Foods Program have made stakeholder engagement a top priority. This robust commitment to engagement was particularly evident as the foundational rules implementing the FSMA took shape. FDA was involved in more than 600 engagements between FSMA's enactment in 2011 and the finalization of the rules in 2015-16.

Selected Rules Published in 2017

Below is the FSMA-related rule published by the Foods Program in the last calendar year.

Date	#	Title	Description
Sep 2017	FDA-2011-N-0921	FSMA Proposed Rule: Standards for the Growing, Harvesting, Packing, and Holding of Produce for Human Consumption; Extension of Compliance Dates for Subpart E	Proposes to extend, for covered produce other than sprouts, the dates for compliance with the agricultural water provisions in the Standards for the Growing, Harvesting, Packing, and Holding of Produce for Human Consumption rule.

In July 2017, FDA released a proposed rule to extend, for covered produce other than sprouts, the dates for compliance with the agricultural water provisions in the Standards for the Growing, Harvesting, Packing, and Holding of Produce for Human Consumption rule (FSMA Produce

[14] http://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm253380.htm

rule). FDA is proposing to extend the compliance dates to address questions about the practical implementation of compliance with certain provisions and to consider how we might further reduce the regulatory burden or increase flexibility while continuing to achieve our regulatory objectives, in keeping with the Administration's policies. The FSMA Produce rule establishes, for the first time, science-based minimum standards for the safe growing, harvesting, packing, and holding of fruits and vegetables grown for human consumption.

In 2017, FDA released an online food safety training module for carriers engaged in the transportation of food by rail or motor vehicle in the United States. FDA is offering this training free of charge to help carriers meet the requirements of the FDA's Sanitary Transportation of Human and Animal Food Rule (Sanitary Transportation Rule). The Sanitary Transportation Rule requires rail and motor vehicle carriers covered by the rule to provide food safety training to their personnel engaged in transportation operations. The training must provide personnel with an awareness of 1) potential food safety problems, 2) basic sanitary practices, and 3) carrier responsibilities. The carrier training requirement applies when the shipper and carrier have agreed, in a written contract, that the carrier is responsible, in whole or part, for sanitary conditions during transportation operations. A carrier may wish to offer this FDA module to their operations personnel as a means of satisfying the training requirements of the Sanitary Transportation Rule or to complement other training offered by the carrier.

In August 2017, FDA announced the availability of a Small Entity Compliance Guide (SECG) to help small businesses comply with the Final Rule on Mitigation Strategies to Protect Food Against Intentional Adulteration (or Intentional Adulteration Rule), one of the seven foundational rules mandated by FSMA. It provides nonbinding recommendations on such topics as developing a food defense plan and records management. The compliance date for small businesses under the Intentional Adulteration Rule is July 27, 2020. Very small businesses are exempt from the rule, except for a documentation requirement described in the SECG, which has a compliance date of July 26, 2020.

Launched Food Safety Plan Builder

In August 2017, to help businesses meet the requirements of the FSMA Final Rule for Preventive Controls for Human Food, FDA released a new software tool for owners and operators of food facilities to use to create a food safety plan specific to their facilities. The Food Safety Plan Builder (FSPB) is a free software application developed by FDA that businesses can download from the FDA's website to guide them, step-by-step, through the creation of a food safety plan, as required by FSMA. The user is taken through a series of sections (tabs) in the application that prompt the user to answer questions and/or fill in information specific to their business and facility. Once all the tabs have been completed, the file may be saved or printed, and the firm will have a food safety plan to use in its operations and to provide when FDA conducts an inspection. While the Food Safety Plan Builder was primarily designed for use by small manufacturers which may have limited resources, any size manufacturer can opt to use it. To assist users, FDA has also developed an overview video about the application, as well as individual videos that demonstrate how to navigate the various tabs.

Updated Guidance for Foreign Supplier Verification Programs (FSVP) Rule

In FY 2017, FDA updated FDA.gov to include revised fact sheets and new guidance as a resource for importers subject to the FSVP rule. The first major compliance date for importers covered by the FSVP rule was May 30, 2017. FSVP is another one of the seven foundational

FSMA rules. A central tenet of that law is that the same preventive food safety standards apply to food consumed in the U.S., regardless of where the food is produced. FSVP achieves this by requiring importers to verify that their foreign suppliers of food for human and animal consumption meet applicable FDA safety standards.

Launched Accredited Third-Party Certification Site

The Accredited Third-Party Certification program is a voluntary program established by FSMA to expand FDA's oversight of imported foods. In FY 2017, FDA launched the website through which organizations can apply to be recognized as a Third-Party accreditation body.

Accreditation bodies recognized by FDA will have the ability to accredit third-party certification bodies, also known as third-party auditors. These accredited certification bodies will conduct food safety audits of foreign food entities and, based on their audit findings, may issue certifications of those entities and the foods for humans and animals that they produce. Such certifications may be used to help establish eligibility for participation in the Voluntary Qualified Importer Program (VQIP), which was also established by FSMA. VQIP offers expedited review and entry of food for eligible participants. In addition, FDA can require that an imported product be certified in specific circumstances to prevent a potentially harmful food from entering the U.S.

Foreign governments and agencies or private third-parties may apply to be recognized as an accreditation body. The process includes a web-based application and a user fee.

Hurricane Response

The recent hurricanes (Harvey, Irma, and Maria), have resulted in numerous challenges for the residents of affected regions, for farmers, and for manufacturers of FDA-regulated products. CFSAN has provided technical assistance and support in the following areas:

- the safety of crops and other foods potentially exposed to flood-waters (these three hurricanes struck a large number of states/territories with agricultural activities)
- food safety issues involving products that may not have been stored safely due to factors such as limited power/refrigeration
- the procurement and safety of food and bottled water to meet the needs of the residents of Puerto Rico
- doing our part to support the dairy industry in Puerto Rico, which was experiencing challenges in purchasing and distributing feed to herds.

FDA performs extensive preliminary work in advance of storms to help prepare for the potential impacts. For example, FDA uses storm protection data, Geographic Information Systems (GIS), and firm registration databases to prepare maps to identify FDA-regulated firms, including those that manufacture critical products that could be damaged by the storms.

Often the most significant role that FDA plays comes after the storm, as facilities come back on line and may need remediation, and farmers seek to put crops or farmland that were damaged back into commercial use. For example, since Hurricane Harvey devastated the rice fields around Houston, FDA has been working with local producers and states to help determine which crops can be used commercially. FDA has been supporting farmers and food producers impacted by these storms, and disseminating information about the proper handling of crops exposed to floodwaters, and when these products can be safely diverted into animal feed uses.

The direct discussions FDA is having with state officials and with farmers are aimed at providing our most up-to-date, science-based information on which crops can enter commerce without creating risks to consumers or animals. FDA has experts in the affected regions who can help provide direct assistance and we are taking additional steps to support recovery efforts. FDA incident management group (IMG) continues to work through the numerous challenges posed, in concert with our state, local, and other federal partners.

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 joined the program and several are working towards ISO accreditation.

Improved Pathogen Detection and Traceability

Figure 1 GenomeTrakr

FDA operates the national network of whole genome sequencers (WGS) – GenomeTrakr, the first integrated network of State and Federal laboratories to use whole genome sequencing to track foodborne pathogens to improve outbreak response and effective monitoring of preventive controls. Whole genome sequencing reveals the complete DNA make-up of an organism. This technology points investigators to specific food products potentially related to an outbreak, and provides insight into the origin of the contaminated food. This capability is particularly important considering the global nature of the food supply.

The Network is now in its fifth year and has collected more than 170,000 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 with great precision.

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.

The FDA Foods Program applies WGS regularly to trace foodborne outbreaks for Salmonella and Listeria monocytogenes. 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.

In 2017, FDA collected sequences as a regular part of foodborne outbreak investigations and compliance actions. WGS was used to support more than 165 cases of product adulteration and insanitary conditions investigated by the FDA.

For example, in 2017, FDA used the GenomeTrakr to link Listeria monocytogenes to an artisanal cheese manufacturer and creamery that had manufactured soft raw milk cheeses contaminated with this pathogen. The soft cheese was the source of an outbreak that included 6 illnesses and 2 deaths. As in previous cases, the low level and sporadic nature of Listeria contamination associated with this product would have been difficult to identify and associate with clinical cases of illness without WGS, which likely prevented additional consumers failing ill and limited the scope of the FDA investigation to the specific facility producing contaminated product.

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.

In the summer of 2017, FDA also used WGS to augment investigation of a large and widespread Salmonella outbreak associated with imported papaya. The outbreak, caused by several strains of Salmonella extended to more than 26 states and included more than 250 illnesses and two deaths. The application of WGS permitted source tracking back to specific overseas agricultural regions and also allowed for the rapid identification of different serological variants of Salmonella as they emerged from contaminated papaya samples.[15]

Developed and Applied Novel Technologies to Improve Food Safety

Addressing emerging safety concerns as food science technology advances remains a priority for the Foods Program. In FY 2017, FDA scientists further extended its environmental studies of foodborne illness outbreaks associated with Salmonella Newport[16] contaminated vegetables grown on the Delaware/Maryland/Virginia (Delmarva) peninsula. FDA helped to address several important scientific questions raised by the Delmarva Food Safety Taskforce by examining the prevalence of Salmonella in growing regions in Delaware and documenting infiltration and

[15] 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.

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

persistence of Salmonella through the blossoms of tomatoes, cucumbers, and cantaloupes – all high-risk crops cultivated on the Delmarva. Taken together, these data have further strengthened FDA's guidance for safe produce production on the Delmarva and have provided additional important Salmonella isolates to the GenomeTrakr database. It is important to note that we have not had any significant outbreak events associated with Delmarva produce since the Taskforce rolled out its science and communications efforts in 2015.

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, borne out of whole genome sequencing, 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 allow Salmonella Newport to persist within tomatoes and other produce. These adaptive traits provide potential targets for preventive controls against Salmonella known to invade produce production.[17]

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.

Finally, with the goal of placing cutting edge technologies directly in the hands of frontline food and environmental field inspectors, FDA microbiologists made significant strides in the development of portable and rapid lab-in-a-backpack tools that integrate rapid sampling and diagnostic technologies (i.e., qPCR) with detailed pathogen characterization tools such as whole-genome sequencing. Field tests in environmental regions prone to Salmonella in the wild were highly successful using current mobile technology configurations. Continued development will aim to make existing tools more portable using nanopore-based whole genome sequencing and smart-phone mediated qPCR devices.

Conducted Major Sampling of Produce

In response to recent foodborne illness outbreaks linked to various types of sprouts, FDA conducted a large-scale sampling study as part of its efforts to learn more about potential contamination in these products and how to protect consumers from disease-causing bacteria in sprouts. Sprouts are especially vulnerable to pathogens given the warm, moist, and nutrient-rich conditions needed to grow them. This study was concluded in August 2017. From 1996 to July 2016, there were 46 reported outbreaks of foodborne illness in the United States linked to sprouts. These outbreaks accounted for 2,474 illnesses, 187 hospitalizations, and three deaths. The agency's testing program was designed to estimate the prevalences of Salmonella, Listeria monocytogenes, and Escherichia coli (E. coli) O157:H7 in sprouts, and to identify patterns in hopes of preventing these pathogens from contaminating sprouts. FDA collected 825 samples from 37 states, Puerto Rico, and the District of Columbia, and found that most of the positive samples came from a small number of sprouting operations: A total of 14 positive

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

samples were found at eight of the 94 growers, and ten of these samples came from just four growers. FDA tested samples collected at three points in the production process (seeds, finished product, and spent irrigation water) to gain insights into the sources of contamination in sprouts. The agency found:

- *Salmonella* on 2.35 percent of seed samples
- *Listeria monocytogenes* on 1.28 percent of finished sprouts
- None of the finished sprout or spent irrigation water samples tested positive for *E. coli* O157:H7.

In September 2017, CFSAN issued two largescale surveillance sampling assignments, one focusing on fresh herbs and the other on processed avocados/guacamole. The assignments will be carried out over approximately the next 18 months. The objectives of these assignments are to determine the prevalence of select pathogens in the respective commodities, to identify common factors associated with positive findings (such as origin or variety), and to take regulatory action as warranted to protect consumers. The fresh herbs assignment targets Salmonella and Shiga toxin-producing E. coli on fresh cilantro, parsley, and basil. These herbs are grown low to the ground and are thus susceptible to contamination, such as from irrigation water splashing off the ground. Additionally, they are often eaten without a "kill step," and consumers may be unaware that they are eating fresh herbs when they are included in multi-ingredient dishes. Similarly, processed avocado/guacamole products, including avocado that is fresh cut, refrigerated or frozen, can be packaged and consumed without a "kill-step" applied prior to consumption. Both fresh herbs and processed avocados/guacamole have been associated with recalls and outbreaks of foodborne illness in recent years.

FDA Recognizes Australia as Having a Comparable Food Safety System to the U.S.

In FY 2017, FDA signed an arrangement with the Australian Department of Agriculture and Water Resources recognizing each other's food safety systems as comparable. This is the third time that FDA has recognized a foreign food safety system as comparable, the first being New Zealand in 2012 and Canada in 2016.

By recognizing each other's systems as comparable, FDA and the Australian Department of Agriculture and Water Resources have confidence that they can leverage each other's science-based regulatory systems to help ensure food safety. For example, each partner intends to consider the oversight of the other when prioritizing inspection activities. The benefits go beyond inspection and admissibility. Systems recognition establishes a framework for regulatory cooperation in a variety of areas that range from scientific collaboration to outbreak response.

Systems recognition is voluntary and not required for a country to export foods to the U.S. FDA continues to have inspection authority over food imported from any country with which it has an arrangement and can exercise this authority as needed. Imports from Australia must continue to comply with U.S. statutory and regulatory requirements to ensure safety and proper labeling, including the new standards adopted under FSMA.

Evaluating 'Organ-on-Chips' Technology

FDA has a leading role in advancing revolutionary new testing technology that creates human organ systems in miniature on micro-engineered chips about the size of a AA battery.

On April 11, 2017, FDA announced a multi-year research and development agreement with a company called Emulate Inc. to test the company's "Organs-on-Chips" technology in laboratories at the agency's Center for Food Safety and Applied Nutrition.

Beginning with a liver-chip, FDA scientists will be evaluating the effectiveness of the technology, designed to give researchers a better understanding of the effects of disease-causing bacteria in foods, chemicals, and other potentially harmful materials on the human body.

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.

Figure 2 Seafood Labeling

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.

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, 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.

Encouraged the Safe Production of Dietary Supplements

In FY 2017, FDA field investigators completed inspections of both domestic and foreign firms to enforce dietary supplement regulations, including current Good Manufacturing Practices (cGMPs) and labeling requirements. These inspections resulted in:

- 70 warning letters
- 3 untitled letters
- 69 detentions

- 3 injunctions.

Additionally, FDA initiated several regulatory actions aimed at protecting consumers from fraudulent products that were, in some cases, marketed as dietary supplements. These include products making fraudulent claims about cancer as well as bodybuilding products containing steroids.

Premarket notification of new dietary ingredients (NDIs) is FDA's only opportunity to identify potentially unsafe supplements before they are available to consumers. In FY 2017, FDA received a record number of 101 NDI notifications. Of the notifications submitted, 68 were deemed incomplete or determined to not pertain to an ingredient intended to be used in a dietary supplement. Of the remaining 33 notifications, FDA acknowledged 13 with no objection and raised safety or identity concerns with 20.

FDA emphasizes education and outreach regarding NDI notifications and regularly engages with submitters before and during the notification review process. FDA continues to review stakeholder comments submitted in response to the revised draft NDI guidance issued in August 2016 and engages with stakeholders on issues related to the revised draft guidance. In 2017, FDA also announced and planned a public meeting to discuss development of an authoritative list of pre-DSHEA dietary ingredients, an idea raised in the revised draft guidance on which a number of stakeholders commented favorably.

In FY 2017, FDA received more than 3,500 adverse event reports (AERs) related to dietary supplements. The reports are evaluated by clinical reviewers in the Center for Food Safety and Applied Nutrition (CFSAN) to monitor the safety of consumer products. FDA is undergoing a modernization of the CFSAN Adverse Event Reporting System (CAERS) to track when and how an AER is evaluated. In addition, FDA is working on a solution for linking AER data to data on compliance and other FDA actions through the use of a high-end analytics platform tailored for big data. This platform will merge and link multiple internal and external data sets and will be able to track products and adverse events throughout the signal's lifecycle, including regulatory actions recommended or taken.

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.

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 human food, cosmetic, and dietary supplement products and ensures the removal of violative products from commerce. In FY 2017, FDA classified 367 Class I (most serious), 380 Class II, and 47 Class III recall events for human food, cosmetic, and dietary supplement products.

FDA issues import controls when non-compliant food products are discovered or when food companies manufacture or ship non-compliant products. In FY 2017, FDA issued 1,191 import alert notices (of which 548 were reviewed by CFSAN).

FDA expanded Import Alert # 28-13 covering lead in turmeric to cover all spices because in 2017 sampling by FDA and State Departments of Health revealed additional types of spices and spice products having high levels of lead that may render the products injurious to health. Particularly vulnerable populations susceptible to lead poisoning include infants, small children, pregnant women, and people with underlying kidney disorders.

Additionally, CFSAN worked with the FDA field offices to assist in 769 cases where the district needed CFSAN's technical expertise to determine import admissibility.

FDA also 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 2017, FDA issued five (5) injunctions, one (1) seizure and one (1) suspension related to adulterated or misbranded food.

Selected Guidances Issued in 2016 and 2017

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.[18]

Date	#	Title	Description
Nov 2017	FDA-2011-F-0172	Draft Guidance for Industry: Menu Labeling Supplemental Guidance	Addresses concerns raised by stakeholders regarding the implementation of nutrition labeling required for foods sold in covered establishments, including expanded and new interpretations of policy.
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

[18] For more information on guidance please visit http://www.fda.gov/Food/GuidanceRegulation/

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
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.

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,[19] 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 guidance[20] 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

[19] Guidance for Industry: Labeling of Infant Formula, http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm517113.htm

[20] Substantiation for Structure/Function Claims Made in Infant Formula Labels and Labeling, http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm514640.htm

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

FDA developed a 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.[21] 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).

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 2017, FDA ensured safe access to the food supply by reviewing 9 Food and Color Additive Petitions, 54 GRAS notifications, and 107 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.

[21] Source: Microbiological Surveillance Sampling: FY16 Cucumbers and Hot Peppers, http://www.fda.gov/Food/ComplianceEnforcement/Sampling/ucm473115.htm

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 and requires food labels that bear nutrient content claims and certain health messages to comply with specific requirements.

The Foods Program also 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 initiative.[22]

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 issues.[23]

In FY 2017, Congress appropriated $3 million to fund FDA to work with USDA to provide education and outreach to the public on agricultural biotechnology and food and animal feed ingredients derived from biotechnology. To kick off this work, FDA hosted public meetings in Charlotte, NC, and San Francisco, CA regarding its Agricultural Biotechnology Education and Outreach Initiative. The purpose of these meetings was to provide the public with an opportunity to share information, experiences, and suggestions to help inform the development of this education and outreach initiative.

FDA Proposes to Extend Compliance Dates for Nutrition Facts Label Final Rules

In FY 2017, FDA proposed to extend the compliance dates for the Nutrition Facts and Supplement Facts label final rule and the Serving Size final rule from July 26, 2018, to Jan. 1, 2020, for manufacturers with $10 million or more in annual food sales. Manufacturers with less than $10 million in annual food sales would receive an extra year to comply—until Jan. 1, 2021.

FDA is committed to making sure that consumers have the facts they need to make informed decisions about their diet and the foods they feed their families. The proposed rule only

[22] Food Safety Survey Shows Consumer Knowledge Up, Still Room to Grow, http://www.fda.gov/Food/NewsEvents/ConstituentUpdates/ucm529604.htm

[23] FDA Releases 2014 Health and Diet Survey Findings, http://www.fda.gov/Food/NewsEvents/ConstituentUpdates/ucm499141.htm

addresses the compliance dates. FDA is not proposing any other changes to the Nutrition Facts Label and Serving Size final rules.

The agency is proposing to extend the compliance dates in response to the continued concern that companies and trade associations have shared with us regarding the time needed for implementation of the final rules. These stakeholders expressed concerns about their ability to update all products by the original compliance dates and the importance of obtaining clarification from the FDA on a number of technical issues relating to the final rules.

Pending completion of this rulemaking, FDA intends to exercise enforcement discretion with respect to the current July 26, 2018, and July 26, 2019, compliance dates.

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

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 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 2015 Actual	$903,340,000	$903,340,000	---
FY 2016 Actual	$998,230,000	$998,230,000	---
FY 2017 Actual	$1,025,503,000	$1,025,503,000	---
FY 2018 Annualized CR	$1,033,082,000	$1,022,211,000	$10,871,000
FY 2019 President's Budget	$1,040,734,000	$1,029,863,000	$10,871,000

BUDGET REQUEST

The FY 2019 Budget Request for the Foods Program is $1,040,734,000 of which $1,029,863,000 is budget authority and $10,871,000 is user fees. Budget authority increases by $7,652,000 compared to the FY 2018 Annualized CR level and user fees remain nearly flat. The Center for Food Safety and Applied Nutrition (CFSAN) amount in this request is $316,326,000. The Office of Regulatory Affairs amount is $724,408,000.

The FY 2019 funding level restores the Foods Program to maintain FY 2017 funded activities. In FY 2019, the Foods Program will continue its statutory mission of promoting and protecting

public health by ensuring that the nation's food supply is safe, sanitary, wholesome, and properly labeled, and that cosmetic products are safe and properly labeled. This mission becomes more challenging every year as globalization, advances in science and technology, and shifts in consumer expectations drive change throughout the human and animal food systems. In response to these increasing demands, the Foods Program conducts a variety of activities aimed at providing American consumers with food and cosmetics products that are safe and properly labeled.

One ongoing priority is the implementation of the FDA Food Safety Modernization Act (FSMA), a sweeping modernization of FDA's food safety program based on science and risk-based prevention of food safety problems for both domestic and imported food. FSMA requires:

- comprehensive prevention-oriented food safety standards across the food system
- mandated domestic inspection frequency, based on risk, to ensure high rates of compliance
- a national integrated food safety system based on full partnership with states
- a new import safety system based on food safety accountability for importers, increased foreign presence, and more collaboration with foreign governments.

The Budget also supports the development of state produce safety infrastructure as states prepare for their increased role in conducting inspections on larger farms and continuing outreach and education to small farms as they prepare for their upcoming compliance dates.

In addition to implementing FSMA and promoting a safe and nutritious food supply, other examples of Foods Program priorities funded within base include:

- Enhancing the safety of dietary supplements and food additives
- Improving quick and accurate detection and response to foodborne outbreaks by advancing the use of a new technology known as 'whole genome sequencing' to track outbreaks and contamination through the "GenomeTrakr" network of state and federal laboratories
- Providing consumers with information that is useful and accurate for safe handling of food products.

In FY 2019, FDA will continue work to develop analytical methods to detect and measure:

- food allergens
- naturally-occurring toxins
- industrial chemicals
- food additives
- food adulterants,
- food pathogens.

These analytical methods enhance compliance and surveillance and enable FDA to ensure the safety of the food supply and reduce foodborne sickness. Further, FDA will continue to research, develop, and deploy the most effective methods for identifying, containing, and eliminating hazards in foods, dietary supplements, and cosmetics.

Activities to improve nutritional quality of packaged and restaurant foods will continue in FY 2019 by promoting industry compliance with the updated Nutrition Facts Label and requirements for calorie labeling for menus and vending machines, and educating consumers on how to best

use this information. These labeling rules reflect the latest public health and scientific evidence, including the link between diet and chronic disease such as obesity and heart disease. The new labels will replace out-of-date serving sizes to better align with how much people really eat, and will feature a modern design to highlight key parts of the label such as calories and serving sizes.

The Foods Program will maintain current levels of operational activities to inspect regulated products and manufacturers, conduct sample analyses of regulated products, and review imported products offered for entry into the United States. FDA will continue to work with its state, local, tribal, territorial, and foreign counterparts to make the best use of all available public resources and improve program efficiency and effectiveness.

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 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
213301: Complete review and action on the safety evaluation of direct and indirect food and color additive petitions, within 360 days of receipt. *(Output)*	FY 2017: 100% Target: 80% (Target Exceeded)	80%	80%	Maintain
214101: 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 2017: 812 enrolled Target: 697 enrolled (Target Exceeded)	827	842	+15
212404: Reduce the incidence of infection caused by key pathogens commonly transmitted by food: Campylobacter species. *(Outcome)*	CY 2016: 11.79 cases/100,000 Target: 10.6 cases/100,000 (Target Not Met)	9.7 cases/ 100,000	9.2 cases/ 100,000	- 0.5
212405: Reduce the incidence of infection caused by key pathogens commonly transmitted by food: Shiga toxin-producing *Escherichia coli (STEC)* O157:H7. *(Outcome)*	CY 2015[24]: 0.95 cases/100,000 Target: 0.95 cases/100,000 (Target Met)	0.76 cases/ 100,000	0.68 cases/ 100,000	- 0.08
212407: Reduce the incidence of infection caused by key pathogens commonly transmitted by food: *Salmonella species*. *(Outcome)*	CY 2016: 15.4 cases/100,000 Target: 13.2 cases/100,000 (Target Not Met)	12.4 cases/ 100,000	11.9 cases/ 100,000	- 0.5

[24] 2016 data is not yet available for this specific serotype of STEC O157:H7 in the CDC Morbidity and Mortality Weekly Report (MMWR) https://www.cdc.gov/mmwr/volumes/66/wr/pdfs/mm6615.pdf

Measure	Year and Most Recent Result /Target for Recent Result (Summary of Result)	FY 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
214306: The average number of working days to serotype priority pathogens in food (Screening Only) *(Output)*	FY 2017: 3 working days Target: 3 working days (Target Met)	3 working days	3 working days	Maintain
214212: Percentage of planned import food field exams. (Output)	FY 2017: 94% Target: 99% (Target Not Met)	95%	95%	Maintain
214206: Maintain accreditation for ORA labs. *(Outcome)*	FY 2017: 13 labs Target: 13 labs (Target Met)	13 labs	13 labs	Maintain
214209: As required by the FSMA Legislation, cover all of the High Risk domestic inventory every three years. (Output)	FY 2017: 34.8% Target: 33% (Target Exceeded)	66%	99%	+33%
214305: Increase laboratory surge capacity in the event of terrorist attack on the food supply. (Radiological and chemical samples/week). *(Outcome)*	FY 2017: 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 2017 target of 80% by reviewing and completing 100% of the petitions received within 360 days of receipt, a result consistent with the FY 2016 performance of 100% 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 2017 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 2018 and FY 2019 targets reflect increases in the number of enrollees by 15 above the previous year's actual number of enrollees or target.

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 required to conduct these analyses from 14 days 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 2017, 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 2018 and FY 2019 are three days, maintaining the critically important downward progress in analytical return times achieved in FY 2017.

New ORA Field Performance Measures

ORA has been working to improve the field performance measures to better align with ORA's Program Alignment initiative. In this submission, ORA has completed the process of adjusting the performance goals, so that the FY 2018 and FY 2019 targets now complete a certain percentage of the planned inspections in ORA's annual Workplan. The ORA Workplan is the necessary mechanism that takes into account all the complex variables (geography, commodity, risk, availability, efficiency, etc.) that allows ORA to plan which inspections to do. With these newly formulated performance goals, ORA is committing to complete a certain percentage of the initially planned inspections. This revision strengthens the importance of the Workplan, and allows the flexibility to respond dynamically to changing circumstances during the year to better handle emerging risks and evolving public health priorities such as the heavy hurricane damage this past year. This is a significant departure from the previous performance goals, so FY 2018 will be an important year in resetting the new baselines. Also, since the targets are now based on a planned number of inspections, it is possible to inspect more than what was planned and thus have an actual inspection rate over 100%.

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. The new three-year cycle began again in FY 2017 during which 34.8 percent of the identified inventory was inspected. The FY 2018 and FY 2019 targets are 66% and 99% respectively.

Import Food Field Exams

During FY 2017, ORA accomplished 150,955 out of 160,189 planned import food field label exams. Although this is a high level performance, it falls short of the 99 percent target. Import resource constraints had a significant impact on the ability to meet this target. Additional resources for entry review and shifting the focus in FY 2018 to work plan targets for food exams will help streamline this work, and improve the field's ability to meet this work plan target in FY 2018.

PROGRAM ACTIVITY DATA

Foods Program Activity Data (PAD)

CFSAN Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
Food and Color Additive Petitions			
Petitions Filed [1]	10	10	10
Petitions Reviewed [2]	10	10	10
Premarket Notifications for Food Contact Substances			
Notifications Received	107	130	130
Notifications Reviewed [3]	107	128	128
Infant Formula Notifications			
Notifications Received [4]	15	15	15
Notifications Reviewed [5]	8	11	11
FDA Review Time	90 days	90 days	90 days
New Dietary Ingredient Notifications			
Notifications Received [6]	101	85	85
Notifications Reviewed [7]	101	85	85
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 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	***8,484***	***8,000***	***8,000***
Domestic Food Safety Program Inspections	6,145	**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	195		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	321		
Domestic Fish & Fishery Products (HACCP) Inspections	763		
Import (Seafood Program Including HACCP) Inspections	253		
Juice HACCP Inspection Program (HACCP)	167		
Interstate Travel Sanitation (ITS) Inspections	909		
Domestic Field Exams/Tests	3,541	2,500	2,500
Domestic Laboratory Samples Analyzed	13,548	13,000	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS [1]	***1,548***	***1,400***	***1,400***
All Foreign Inspections	1,548	1,400	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	***10,032***	***9,400***	***9,400***
IMPORTS			
Import Field Exams/Tests	229,129	168,200	168,200
Import Laboratory Samples Analyzed	23,774	35,300	35,300
Import Physical Exam Subtotal	**252,903**	**203,500**	**203,500**
Import Line Decisions	15,251,687	16,014,271	16,814,985
Percent of Import Lines Physically Examined	1.66%	1.27%	1.21%
Prior Notice Security Import Reviews (Bioterrorism Act Mandate)	81,035	80,000	80,000
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	***8,460***	***9,062***	***9,062***
UNIQUE COUNT OF STATE PARTNERSHIPS FOOD ESTABLISHMENT INSPECTIONS	***110***	***100***	***100***
State Contract Food Safety (Non HACCP) Inspections	7,497	8,000	8,000
State Contract Domestic Seafood HACCP Inspections	902	1,000	1,000
State Contract Juice HACCP	61	100	100
State Contract LACF	129	100	100
State Partnership Inspections	110	100	100
State Contract Foods Funding	$12,465,850	$12,839,826	$13,225,020
Number of FERN State Laboratories	19	19	19
Number of Food Safety State Laboratories	15	15	15
Annual FERN State Cooperative Agreements/Operations Funding	$16,436,868	$16,929,974	$17,437,873
Total State & Annual FERN Funding	**$28,902,718**	**$29,769,800**	**$30,662,894**
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	***18,602***	***18,562***	***18,562***

[1] The FY 2017 actual unique count of foreign inspections includes 161 OIP inspections (118 for China, 39 for India, & 4 for Latin America).

Field Cosmetics Program Activity Data (PAD)

Field Cosmetics Program Workload and Outputs	FY 2017 Actuals	FY 2018 Estimate	FY 2019 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***95***	***100***	***100***
Domestic Inspections	95	100	100
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***5***	***0***	***0***
Foreign Inspections	5	0	0
IMPORTS			
Import Field Exams/Tests	10,118	1,600	1,600
Import Laboratory Samples Analyzed	423	400	400
Import Physical Exam Subtotal	**10,541**	**2,000**	**2,000**
Import Line Decisions	2,625,555	2,756,833	2,894,674
Percent of Import Lines Physically Examined	0.40%	0.07%	0.07%
GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS	***100***	***100***	***100***

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HUMAN DRUGS

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
Human Drugs	**1,329,631**	**1,549,170**	**1,611,475**	**1,852,776**	**241,301**
Budget Authority	***491,607***	***488,626***	***488,264***	***686,364***	***198,100***
User Fees	***838,024***	***1,060,544***	***1,123,211***	***1,166,412***	***43,201***
Center	1,124,853	1,370,578	1,413,615	1,650,865	237,250
Budget Authority	355,438	352,419	353,020	548,388	195,368
User Fees	769,415	1,018,159	1,060,595	1,102,477	41,882
Prescription Drug (PDUFA)	*533,134*	*678,553*	*654,835*	*690,203*	*35,368*
Generic Drug (GDUFA)	*219,018*	*309,435*	*369,065*	*374,894*	*5,829*
Biosimilars (BsUFA)	*16,706*	*29,435*	*36,116*	*36,752*	*636*
Outsourcing Facility	*557*	*736*	*579*	*628*	*49*
Field	204,778	178,592	197,860	201,911	4,051
Budget Authority	136,169	136,207	135,244	137,976	2,732
User Fees	68,609	42,385	62,616	63,935	1,319
Prescription Drug (PDUFA)	*10,878*	*8,593*	*8,038*	*8,472*	*434*
Generic Drug (GDUFA)	*55,973*	*33,185*	*53,104*	*53,943*	*839*
Biosimilars (BsUFA)	*1,416*	*213*	*1,120*	*1,140*	*20*
Outsourcing Facility	*342*	*394*	*354*	*380*	*26*
FTE	**6,030**	**6,033**	**6,361**	**6,407**	**46**

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); and Food and Drug Administration Reauthorization Act of 2017 (FDARA) (P.L. 115-52).

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

Office of Regulatory Affairs (ORA) field drugs program comprise 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 uses, meet established quality standards, and 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 in the context of current priorities.

Figure 3 Medicine for a Patient

Improve and Safeguard Access

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 while maintaining the Agency's high standards for safety and efficacy.

In calendar year 2017, CDER approved 46 novel drugs. From 2007 through 2016, CDER has averaged about 30 novel drug approvals per year. Novel drugs are often innovative products that serve previously unmet medical needs or otherwise 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 designations. Early and repeated communications between FDA and sponsors have been helpful strategies for expediting products to market.

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

- Assisting with establishing flexible clinical development designs and accepting such designs when they support the Agency's high standards for demonstrating safety and efficacy;
- Meeting frequently and working closely with industry sponsors throughout the development process to plan efficient clinical trial programs and agree on needed data; and
- Helping create clinical trial networks and "master protocols," where appropriate, to streamline clinical trials, greatly reduce the cost of conducting these trials and reduce the time needed to carry them out while preserving high regulatory standards.

FDARA Implementation

FDA's recent accomplishments include implementing several components of the Food and Drug Administration Reauthorization Act of 2017 (FDARA). This authority reauthorized medical product user fees, ensuring continuity for human drug review programs and certain postmarket oversight activities, which are critical to FDA's mission of protecting and promoting public health.

Drug Shortages

Drug shortages can delay or prevent patients from getting needed care. Drugs in short supply may also lead health care professionals to rely on alternative drug products that may be less effective or associated with higher risks than the drug in shortage. Authorities granted by Congress as part of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) have enabled FDA to coordinate with manufacturers to help prevent or mitigate drug shortages. This included effectively holding industry accountable for early notification of discontinuances or interruptions in manufacturing of covered prescription drugs that are likely to lead to a significant disruption in supply. These requirements have helped FDA 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 23 new shortages in 2016. Specifically, in 2017, multiple hurricanes impacted drug manufacturing in Puerto Rico. FDA has been working with manufacturers to resume production, preventing multiple shortages. However, some shortages – including of IV fluids – worsened due to the hurricane impact in Puerto Rico. FDA has expedited review of new applications and worked with manufacturers to increase supplies of IV fluids to meet patient need in the US. As a result of the early and continued efforts of FDA, these shortages are anticipated to be resolved by early 2018.

User Fees

FDARA provided the second authorizations of the Generic Drug User Fee Amendments (GDUFA II), and the Biosimilars User Fee Act (BsUFA II), as well as the sixth authorization of the Prescription Drug User Fee Act (PDUFA VI). The five-year reauthorization ensured FDA continued to receive consistent funding from FY 2018 through FY 2022 to support program innovation, evaluation, and improvement. GDUFA II, BsUFA II and PDUFA VI continue to deliver tremendous public health benefits by: providing timely access to more affordable generic drugs and biosimilar biological products; providing patients with more affordable treatments; and enhancing FDA's capacity to fulfill its mission of bringing novel drug products to market.

New Drug Review

One of the key programs under PDUFA V has been the creation of a new review program for new molecular entity (NME) new drug applications (NDAs) and original biologics license applications (BLAs) for applications received between 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. To accomplish these goals, the Program provides new opportunities for communication between applicants and the FDA review team, as well as additional time (60 days) for FDA to review these highly complex applications.

Under PDUFA V, FDA achieved its performance goals for the percentage of applications acted on by the goal date for standard and priority reviews. During the PDUFA V timeframe, FDA received 230 applications that were reviewed under this Program, which involves a more interactive review process with applicants. FDA met the goal dates for all FY 2016 Program cohort applications that received actions by September 30, 2017. The FY 2017 Program cohort has received 45 applications to date. While most of these applications are still under review and

within their PDUFA goal date, FDA met the goal dates for all applications that received a first cycle action by September 30, 2017. FDA will continue to focus on these highly innovative products that represent important new medicines for the American people.

PDUFA VI continues to support drug development oversight and marketing application review for the new drugs regulatory program. A few of the important components of the PDUFA VI agreement include resources for the highly successful and resource-intensive Breakthrough Therapy program; commitments regarding FDA's ongoing Patient-Focused Drug Development Initiative; additional postmarket funding for FDA's Sentinel system; and process improvement work related to combination product review. FDA will also continue to apply the Program to the review of all NME NDAs and BLAs, including applications that are resubmitted following a Refuse-to-File decision, received from October 1, 2017 through September 30, 2022.

Generic Drug Review

With increasing healthcare costs, many Americans face challenges in accessing medically necessary drug products. The availability of safe and effective generic drugs can help reduce the cost of medications. As such, 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.

The initial passage of GDUFA brought opportunities for 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 hiring and training many new employees, replacing fragmented information technology systems with a new integrated system, and substantially enhancing review and business processes. The Agency's commitment to GDUFA led to a record number of combined approvals and tentative approvals in FY 2017[25]. FDA achieved these goals by providing greater predictability, transparency, and efficiency, along with improved timeliness, to the human generic drug review process.

GDUFA II was signed into law on August 18, 2017, with the passage of FDARA. Under GDUFA II, FDA will continue modernizing the generic drug program by focusing efforts on improving the efficiency, quality, and predictability of the human generic drug program, thereby ensuring that Americans have timely access to safe, effective, high quality, and lower cost human generic drugs.

Biosimilars

BsUFA supports the review process for biosimilar biological product applications. 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. As of December 14, 2017, over 60 programs were in the BPD Program. CDER has received meeting requests to discuss the development of biosimilar products for 27 different reference products. As of December 14, 2017, FDA has licensed nine

[25] See the Activities Report of the Generic Drug Program (FY 2017) at https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm584749.htm. During FY 2017, OGD approved or tentatively approved 937 ANDAs, 100 of which were approved or tentatively approved in June 2017.

biosimilar products: Zarxio (filgrastim-sndz), which has been determined to be biosimilar to Neupogen; Inflectra (infliximab-dyyb), Renflexis (infliximab-abda) and Ixifi (infliximab-qbtx), which have been determined to be biosimilar to Remicade; Erelzi (etanercept-szzs), which has been determined to be biosimilar to Enbrel; Amjevita (adalimumab-atto) and Cyltezo (adalimumab-adbm), which have been determined to be biosimilar to Humira; Mvasi (bevacizumab-awwb), which has been determined to be biosimilar to Avastin; and Ogivri (trastuzumab-dkst), which has been determined to be biosimilar to Herceptin. These significant accomplishments represent the next step to increasing treatment options for patients.

In addition to guidance issued in 2015 and 2016, 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 of each product. As stated in the final guidance, FDA is continuing to consider the appropriate suffix format for interchangeable products.

FDA is continuing to consider comments on the proposed rule, "Designation of Official Names and Proper Names for Certain Biological Products," which issued in August 2015. This proposed rule would designate nonproprietary names that include a suffix for six previously licensed biological products. Comments under consideration include 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.

On September 21, 2017, the FDA issued a Draft Guidance for Industry: "Statistical Approaches to Evaluate Analytical Similarity." This guidance is intended to provide advice on the evaluation of analytical similarity to sponsors interested in developing biosimilar products for licensure under section 351(k) of the Public Health Service Act (PHS Act). This evaluation is to support the demonstration that a proposed biosimilar product is highly similar to a reference product.

On October 23, 2017, FDA released new educational materials targeted to health care professionals about biosimilar and interchangeable products and updated the FDA Biosimilars website (www.fda.gov/biosimilars). The goal of the educational materials is to increase understanding about these important new types of medication among health care professionals and other stakeholders. FDA also developed tools to help professional societies and stakeholder organizations share information about biosimilars with their colleagues and members, and placed advertisements in health care provider journals and on targeted web sites for health care providers, in addition to releasing an updated Consumer Update on biosimilars.

FDA also held a webinar for Health Care Professionals on December 5, 2017: "Overview of the Regulatory Framework and the Development and Approval of Biosimilar Products in the U.S." This webinar provided an overview of the regulatory framework for biosimilar products,

including a background, information on terminology and the general requirements of the approval pathway for biosimilars, and the approach and scientific concepts used in the development of biosimilar 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, enhance internal and external communications, advance innovative clinical trials through 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 new hiring authorities to improve the Agency's ability to compete with industry and academia in hiring and retaining scientific experts.

In May 2017, FDA published a five-year plan for issuing guidance documents to facilitate the collection and review of patient-focused data for drug development. FDA implemented an approach to record and track the submission and review of patient experience data. In December 2017, the Agency conducted a public workshop, titled "Patient-Focused Drug Development: Guidance 1 - Collecting Comprehensive and Representative Input." FDA held the public workshop to obtain feedback from stakeholders, including patients, caregivers, patients' advocates, academic and medical researchers, expert practitioners, and drug developers.

FDA is establishing a qualification process for drug development tools (DDTs) (i.e., biomarkers, clinical outcome assessments (COAs), and animal models) for proposed contexts of use for drugs and biologics. Once a DDT is qualified under the new process, it can be used for its qualified context of use to support regulatory decisions. In 2017, the first COA from the COA Drug Development Tool Qualification program was accepted for review under these updated provisions —the Symptoms of Major Depressive Disorder Scale—and the Agency expects to act on that submission soon. The Scale is a 16-item, patient-reported outcome instrument intended to capture the patient voice by measuring the symptoms of major depressive disorder that matter most to patients. FDA also held two recent multi-stakeholder collaborations to help inform future guidance by the Agency, discussing the evidentiary criteria to support biomarker qualification efforts.

The Cures Act allows FDA to issue grants to study continuous manufacturing—a technologically advanced and automated manufacturing method. Continuous manufacturing provides a faster, more reliable way to make drugs and biological products and can help reduce drug shortages and recalls related to problems with product or facility quality. In 2017, FDA granted an award to the University of Connecticut to develop and build a continuous manufacturing platform with modular components for complex dosage forms, as well as to create a library based on Graphical User Interfaces. This research is likely to advance the Agency's regulatory science and facilitate production of high-quality, cost-effective complex drug products for the benefit of the public.

The Cures Act supports the Agency's evaluation of the potential use of utility of real world evidence (RWE) to support the approval of new indications of approved medical products or to satisfy post-approval study requirements for marketed products. On June 5, 2017, FDA became the first regulatory body in the world to approve the most recent iteration of the Sapien valve, the Sapien 3, to treat high-risk patients whose surgically-placed aortic or mitral bioprosthetic valves

were old and worn out. This approval was based in part on data from the Transcatheter Valve Therapy (TVT) Registry, a partnership of the American College of Cardiology and the Society of Thoracic Surgeons. Also in June 2017, FDA announced a partnership with CancerLinQ, the American Society of Clinical Oncology's big data initiative. FDA and CancerLinQ will be using real world, aggregate, de-identified patient care data from oncology practices to understand a variety of issues related to the appropriate use of newly approved therapies. FDA is establishing a program to evaluate the potential use of RWE to support regulatory decisions. The draft framework is due in December 2018, but the Agency is already gathering stakeholder input to move this field forward. FDA will continue to partner with a range of stakeholders to address the challenges and realize the opportunities posed by RWE and RWD.

These are a few examples of FDA's implementation of the Cures Act. The continued implementation of the Cures Act will support and enhance FDA's work to make the process for bringing safe, effective, and innovative treatments to patients more efficient. FDA's improvements in transparency, consistency, predictability, and efficiency will benefit industry, healthcare providers, and, most importantly, patients.

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. Addressing the opioid crisis is a top priority at FDA, and the Agency has committed to using its full expertise and resources to combat the epidemic.

We have taken a number of actions at the FDA over the past several years to help reduce the number of people who become addicted, or who ultimately overdose from prescription opioids. We've improved product labeling and removed Opana ER from the market for safety reasons. We've introduced a revised blueprint for prescriber education, and with the establishment of the Opioids Policy Steering Committee, will continue to facilitate appropriate prescribing of opioid analgesics and ensure training is made available to prescribers. We've encouraged the development of abuse-deterrent formulations, having approved 10 products to date with abuse deterrent labelling. In addition, we have approved an additional form of naloxone, nasal narcan, to reverse opioid overdoses, which can be administered by laypersons and are, therefore, better available to save lives. At the same time, we are actively considering ways to expand access to naloxone and facilitate the switch to OTC naloxone while also joining efforts to break the stigma associated with medications used for treatment of addiction.

In February 2016, FDA announced its comprehensive opioids action plan for reducing the impact of opioid misuse and abuse on American families and communities. FDA continues to accomplish goals laid out as part of that plan under the HHS Opioid Strategy, launched in April, 2017. This is a comprehensive, evidence-based strategy that provides the overarching framework to leverage the expertise and resources of Health and Human Services agencies in a strategic and coordinated manner.

To develop and continue efforts under the HHS Opioid Strategy, FDA plans to confront this epidemic by focusing on five priority areas. They include: decreasing exposure and preventing new addiction, supporting the treatment of those with opioid use disorder, fostering the

development of novel pain treatment therapies, improving enforcement, and assessing risk-benefit.

FDA is committed to taking all of these steps transparently and in close cooperation with other Federal agencies and stakeholders. We have conducted significant outreach with stakeholders through the release of guidance documents, webinars, stakeholder listening sessions, docket requests for information, and seven public meetings and workshops in 2017. In addition, we actively participate in the groups coordinating those activities both within HHS and across all the relevant agencies of the U.S. government.

Combating Antibiotic Resistant Bacteria

Over the last few decades, antibacterial drug development has not kept pace with patient need. 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 in obtaining informed consent and completing trial enrollment procedures in a timely manner. In addition, many patients with serious infections have significant comorbidities that may render them less likely to be enrolled in a clinical trial.

Despite these considerable challenges in developing an antibacterial drug, there have been eight approvals of new antibacterial drugs over the past four years, all of which were qualified infectious disease products. The antibacterial product pipeline nevertheless remains very fragile. The regulatory science work described below is one of the many different components that is needed to facilitate development and informed use in this challenging area of drug development.

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 to collect data using electronic medical records from patients with blood infections to help 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 by CDER 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, which is essential to the development of new antibacterial drugs.

Guidances

Below are notable drug 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.[26]

Date	Docket #	Title	Description
Jan 2017	FDA-2014-D-1524	Repackaging of Certain Human Drug Products by Pharmacies and Outsourcing Facilities	Establishes FDA's policy regarding repackaging by State-licensed pharmacies, Federal facilities, and facilities that register with FDA as outsourcing facilities.
Jan 2017	FDA-2010-D-0026	Assessment of Abuse Potential of Drugs	Assists sponsors of investigational new drugs and applicants for approval of a new drug in evaluating whether their new drug product has abuse potential.
Aug 2017	FDA-2013-D-0744	Antibacterial Therapies for Patients with an Unmet Medical Need for the Treatment of Serious Bacterial Diseases	Assists sponsors in the development of new antibacterial drugs to treat serious bacterial diseases in patients with an unmet medical need.

[26] [1] For more information on guidances please visit http://www.fda.gov/RegulatoryInformation/Guidances/.

Date	Docket #	Title	Description
Sept 2017	FDA-2015-D-4644	Advancement of Emerging Technology Applications for Pharmaceutical Innovation and Modernization	Provides recommendations to pharmaceutical companies interested in participating in a program involving the submission of chemistry, manufacturing, and controls information containing emerging technology.
Nov 2017	FDA-2014-D-2300	Evaluating Drug Effects on the Ability to Operate a Motor Vehicle	Assists pharmaceutical sponsors in the evaluation of the effects of psychoactive drugs on the ability to operate a motor vehicle.
Nov 2017	FDA-2016-D-0785	General Principles for Evaluating the Abuse Deterrence of Generic Solid Oral Opioid Drug Products	Assists in the development and submission of an abbreviated new drug application (ANDA) that references an opioid drug product with abuse-deterrent properties described in its labeling.
Dec 2017	FDA-1999-D-4079	Product Name Placement, Size, and Prominence in Promotional Labeling and Advertisements	Clarifies the requirements for product name placement, size, prominence, and frequency in promotional labeling and advertisements for human prescription drugs.
Dec 2017	FDA-2017-D-6821	Systemic Antibacterial and Antifungal Drugs: Susceptibility Test Interpretive Criteria Labeling for NDAs and ANDAs	Provides recommendations on fulfilling the new labeling requirements for susceptibility test interpretive criteria for prescription systemic antibacterial and antifungal drugs as established by section 3044 of the 21st Century Cures Act.

Product Approvals

Below are some of CDER's recent generic product approvals. This list does not represent any degree of importance or priority ranking of products.[27]

Disease State	Approved	Generic Name	Reference Listed Drug	FDA-approved use on approval date
Heart Disease	Apr 2017	Ezetimibe and Simvastatin	Vytorin	To treat high cholesterol
	Jul 2017	Prasugrel Tablets	Effient	To reduce the risk of certain types of blood clots in patients with serious cardiovascular events requiring emergency treatment
	Aug 2017	Isoproterenol Hydrochloride Injection	Isuprel	To treat heart block and other serious cardiovascular events
	Oct 2017	Carvedilol Phosphate Extended-release Capsules	Coreg CR	To treat high blood pressure
Infectious Disease	Jun 2017	Emtricitabine and Tenofovir Disoproxil Fumarate Tablets	Truvada	To treat HIV and for pre-exposure prophylaxis (PrEP)
	Sep 2017	Caspofungin Acetate Injection	Cancidas	To treat fungal infections
	Nov 2017	Darunavir Ethanolate	Prezista	To treat HIV
	Nov 2017	Praziquantel Tablets	Biltricide	To treat parasitic worm infections
Other Diseases	May 2017	Atomoxetine Capsules	Strattera	To treat of Attention Deficit Hyperactivity Disorder (ADHD)
	Jul 2017	Mesalamine Delayed-release Tablets	Asacol HD and Lialda	To treat ulcerative colitis

[27] For more information on product approvals and designations visit http://www.fda.gov/NewsEvents/ProductsApprovals/

Disease State	Approved	Generic Name	Reference Listed Drug	FDA-approved use on approval date
	Jul 2017	Sevelamer Carbonate Tablets and Powder	Renvela	To control phosphorus levels in patients with chronic kidney disease on who are on dialysis
	Aug 2017	Docetaxel Injection	Taxotere	To treat cancer, including: breast cancer, non-small cell lung cancer, and squamous cell carcinoma of the head and neck

Rules

Below are rules recently published by CDER. Rules help address various issues. This list does not represent any degree of importance or priority ranking among the published rules.[28]

Date	Docket #	Purpose or Benefit
Aug 2015	FDA-2015-N-0648	Designation of Official Names and Proper Names for Certain Biological Products
Dec 2015	FDA-2015-N-1260	Fixed-Combination and Co-Packaged Drugs: Applications for Approval and Combinations of Active Ingredients Under Consideration for Inclusion in an Over-the-Counter Monograph; Proposed Rule
Mar 2016	FDA-2016-N-0001	Advisory Committee: Pharmaceutical Science and Clinical Pharmacology Advisory Committee
Apr 2016	FDA-2016-N-0543	Food and Drug Administration Review and Action on Over-the-Counter Time and Extent Applications; Proposed Rule
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

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

Date	Docket #	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-1999-N-0194	Additions and Modifications to the List of Drug Products That Have Been Withdrawn or Removed From the Market for Reasons of Safety or Effectiveness
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
Nov 2016	FDA-2016-N-0543	Food and Drug Administrative Review and Action on Over-the-Counter Time and Extent Applications

Enhance Oversight

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, packaged, tested, and stored. FDA also monitors the quality of finished drug products in distribution through sampling and analysis.

FDA's postmarket safety surveillance activities monitor the safety of drugs that are available to U.S. 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 these safety activities is to protect patients from adverse events or improper use of drug products that could result in potentially harmful effects.

Sentinel

The 2007 Food and Drug Administration Amendments Act (FDAAA) required FDA to establish an active 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. FDA officially integrated the Sentinel System into the Agency's routine safety

operations. All FDA Centers involved with medical products are now actively using the Sentinel System to monitor the safety of drugs and vaccines.

In FY 2017, the Sentinel System expanded surveillance to 223 million members, which is an increase of 30 million members from FY 2016. FDA held the Ninth Annual Sentinel Initiative Public Workshop in February 2017 to bring together stakeholder communities to discuss a variety of topics on active medical product surveillance and current and emerging Sentinel projects. Also in 2017, the FDA launched public access to the Sentinel System, enabling users such as members of the public, and representatives from industry and academia, to query this large database. The Innovation in Medical Evidence and Development Surveillance (IMEDS) program is a public-private partnership launched with the Reagan-Udall Foundation. It facilitates use of the Sentinel System as a national resource for generating broader public health and medical information based on real-world evidence. 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 responsibilities 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 July 1, 2017, 71 firms were 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 though 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.

Since enactment of the DQSA, and as of July 1, 2017, FDA has completed the following actions:

- Conducted 484 inspections of compounders (92 in fiscal year 2014, 116 in fiscal year 2015, 135 in fiscal year 2016, and 141 in fiscal year 2017), including over 100 inspections of compounders registered as outsourcing facilities. Approximately 30 percent of the 484 inspections of compounders since enactment of the DQSA have been for-cause, generally based on reports of serious adverse events or product quality issues such as drug contamination. FDA has issued a Form FDA 483, a list of inspectional observations identified by investigators, at the conclusion of almost all of its inspections.
- Issued over 180 warning letters to compounders, including one warning letter that addressed violations identified at four facilities.
- Issued over 70 letters to state agencies, referring findings from inspections of pharmacies in situations where FDA believes that any necessary follow-up can be overseen appropriately by the state.

Post-DQSA Actions					
	FY 2014	FY 2015	FY 2016	FY 2017	TOTAL
Inspections [29]	92	116	135	141	484
For-Cause Inspections [30]	37	35	47	25	144
Outsourcing Facility Inspections	28	31	26	39	124
Warning Letters	29	30	65	62	186
State Referral Letters	9	10	11	45	75
Recall Events	25	38	51	41	155

FDA has issued 21 draft and revised draft guidance documents regarding compounding and related activities, 10 of which have been finalized. FDA also issued four proposed rules, one of which has been finalized, and a draft memorandum of understanding. 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 patients' health from the risks associated with compounded drugs.

In addition, FDA re-established the Pharmacy Compounding Advisory Committee (PCAC), which provides advice on scientific, technical, and medical issues concerning drug compounding under sections 503A and 503B of the FD&C Act. FDA has held two meetings in FY 2015, three meetings in FY 2016, two meetings in FY 2017, and one meeting in FY 2018.

Further, the Agency uses funding to support stakeholder outreach and collaboration activities. FDA meets with stakeholder organizations including pharmacy, medical, hospital, insurer, and industry organizations, as well as consumer groups and outsourcing facilities, to hear their views on matters related to compounding. FDA has held five sets of listening sessions with more than 75 stakeholders. FDA also hosts intergovernmental working meetings with representatives of the state boards of pharmacy to increase and improve our collaborative efforts to oversee compounding facilities throughout the United States. FDA has held six such intergovernmental working meetings. In addition, FDA responds to numerous inquiries from stakeholders, including consumers, about compounding.

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. Therefore, FDA is continuing these efforts, which are critical to protect the public health.

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 human, finished, prescription drug products as they are distributed within the United States by 2023.

[29] Includes both for-cause and surveillance inspections of outsourcing facilities and other compounding facilities.

[30] Includes for-cause inspections of outsourcing facilities and other compounding facilities.

Since enactment of the DSCSA, FDA has issued seven draft guidance documents and four final guidances and held five public meetings as well as multiple stakeholder meetings. FDA is also working to develop regulations, standards, policy, and programs to implement the law[31].

Product Identification and Tracing: 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. In 2017, FDA held two public meetings on various strategies and issues related to the enhanced drug distribution security provisions of the DSCSA. FDA is holding a third public meeting on the topic in February 2018.

Licensing: FDA is actively working on regulations to implement the new licensing standards set forth in the DSCSA for wholesale drug distributors and third party logistics providers. FDA has also issued guidance specific to this issue and has received input from states, industry, and other stakeholders through stakeholder meetings, comments on guidance, questions to FDA staff, etc.

Promote Informed Decisions

FDA is responsible for protecting the public health by ensuring prescription drug information that healthcare professionals and consumers receive is truthful and not misleading, 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. In addition, CDER's Professional Affairs and Stakeholder Engagement (PASE) provides user-friendly information about the drug development and approval process. PASE also coordinates the Drug Trials Snapshots that inform consumers about who participated in clinical trials that supported FDA approval of new drugs. The information provided in these Snapshots also highlights whether there were any differences in the benefits and side effects among sex, race, and age groups.

Strengthen Organizational Excellence

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.

[31] [1] For more information on FDA's DSCSA-related activities, please visit https://www.fda.gov/Drugs/DrugSafety/DrugIntegrityandSupplyChainSecurity/DrugSupplyChainSecurityAct/default.htm.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2015 Actual	$1,369,889,000	$482,243,000	$887,646,000
FY 2016 Actual	$1,451,570,000	$487,299,000	$964,271,000
FY 2017 Actual	$1,549,170,000	$488,626,000	$1,060,544,000
FY 2018 Annualized CR	$1,611,475,000	$488,264,000	$1,123,211,000
FY 2019 President's Budget	$1,852,776,000	$686,364,000	$1,166,412,000

BUDGET REQUEST

The FY 2019 Budget Request is $1,852,776,000, of which $686,364,000 is budget authority and $1,166,412,000 is user fees. The budget authority is increased by $198,100,000 compared to the FY 2018 Annualized CR level and user fees increase by $43,201,000. The Center for Drug Evaluation and Research (CDER) amount in this request is $1,650,865,000. The Office of Regulatory Affairs amount is $201,911,000. The FY 2019 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 2019 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 2019 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 2019 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

FDA intends to focus its resources on promoting innovation and competition, and advancing the health and safety of American families. The targeted budget increases for FDA are intended to support these goals in a way that would also help American businesses capitalize on recent and emerging breakthroughs in technology and scientific knowledge. These breakthroughs include medical product innovation, improvements in manufacturing processes, and advances in scientific knowledge and data-gathering techniques.

The requested funding would enable FDA to implement regulatory improvements intended to advance these outcomes across a wide range of industries. FDA believes that these regulatory improvements would better enable industry to pursue innovation that will lead both to better health outcomes for American families and to U.S. economic development.

FDA proposes the following targeted budget requests for special initiatives, outside of-and in addition to-our core commitments and operating budget. These novel initiatives, that will require new investments, will advance the Agency's strategic priorities, and align with the Department's broader policy goals. In many cases, the improvements that would be made possible by a single request would help to advance multiple priorities simultaneously.

Medical Product Safety (+$198.1 million/ 46 FTE)

Foster Advancements in Manufacturing Innovation

Innovations in medical product manufacturing have the potential not only to improve the quality of the products being made-with direct benefits for the health of American families, but also to make the manufacturing process more efficient. Such improvements in efficiency can lead to lower costs for manufacturers which make it more attractive and feasible for manufacturers to locate their manufacturing and jobs in the U.S. and ultimately lower prices for consumers.

Promote Domestic Manufacturing: Advancing Modern Drug and Biological Product Manufacturing Technologies

CDER: +$35.0 million / 2 FTE

FDA recognizes that the U.S. pharmaceutical and biotechnology industries are moving toward advanced manufacturing technologies such as continuous manufacturing for both small-molecule drugs and biological products (e.g., monoclonal antibodies or vaccines) to improve the agility, flexibility, cost, and robustness of their manufacturing processes. This has great potential to enhance product quality, reduce product failures, avoid drug shortages, significantly reduce vulnerabilities in the U.S. drug supply, and enable rapid responses to domestic and global pandemic needs, thereby enhancing national security. Additional funding for this initiative will support advanced manufacturing technologies to also help accelerate product development and support new clinical development related to targeted therapies.

FDA promotes innovation in this area by evaluating innovative manufacturing technologies and creating a robust scientific base to define the impact of these new technologies on product quality, safety, and effectiveness. If FDA receives additional funding for this initiative, this improved analytical framework will allow FDA to develop clear scientific standards, guidance, and policy to support effective and efficient regulatory evaluation of advanced manufacturing technologies. Specifically, there are urgent needs to support advances in manufacturing science

and research from a regulatory perspective by providing better regulatory guidance and scientific frameworks in several key areas and funding is critical to make these advancements.

These areas include new processes for active pharmaceutical ingredients and final dosage forms that benefit from continuous manufacturing. For both small-molecule drugs and biological products, modular or plug-and-play type manufacturing equipment design with re-usable, flexible, or interchangeable parts will allow different types of continuous manufacturing process integration. Other processes may also include end-to-end continuous manufacturing from the raw material(s) to final product without isolated intermediates; enhanced in-line process analytical technologies to monitor critical quality attributes and provide feedback in real-time for rapid decision making regarding product quality; and advanced control systems and enhanced modeling for robust and efficient processes. FDA needs sufficient resources, including personnel who have the expertise and capacity to build a foundation for this initiative.

Based on the knowledge gained from research in novel manufacturing technologies, FDA is currently developing a guidance on continuous manufacturing for solid oral dosage forms to facilitate a broader implementation of these new manufacturing technologies in the pharmaceutical industry and simultaneously encouraging the industry to relocate drug manufacturing to the United States. Investments in FDA's work in this area will foster manufacturing innovations that will lead to lower drug prices, and improve the reliability and quality of the drug supply chain.

Advance a New Drug Industry: Establishing the Outsourcing Facility Sector as a Robust and Reliable Source of Compounded Products

CDER: +$22.3 million / 17 FTE

The Drug Quality and Security Act of 2013 created "outsourcing facilities" – a new sector of drug compounders held to higher production standards to protect patient health. Outsourcing facilities are intended to offer a more reliable supply of compounded drugs needed by hospitals, clinics, and other health care providers. It is particularly important that this sector be able to meet providers' needs for "office stock drugs" (compounded drug products that a provider holds in the office in anticipation of patients who will present with a medical need for a compounded drug), as it has the unique ability under the law to prepare such products. After three years, this domestic sector is still relatively small (approximately 70 entities), is experiencing growth challenges, and is not yet fulfilling its potential. Businesses have encountered market challenges and state regulatory complexities that limit entry and advancement, and FDA continues to find concerning quality and safety problems during inspections.

The FY 2019 budget request will allow the Human Drugs Program to establish a Center of Excellence on Compounding for Outsourcing Facilities, increase direct engagement with this sector to provide much-needed education and training, conduct research to help inform regulatory decision-making, and implement programs to harmonize and strengthen state oversight of compounding facilities.

The Center of Excellence on Compounding for Outsourcing Facilities created through a public-private partnership would provide training on current good manufacturing practice (CGMP) – the quality standard applicable to outsourcing facilities. The CGMP training would include in-depth, hands-on instruction and demonstrations offered in small settings to members of the sector with minimal cost to participants. The Center of Excellence would also conduct market research to

help inform regulatory decision-making by FDA and its external partners, including identification of key challenges and opportunities, as well as growth potential. FDA staff would work closely with a partner organization on engagement with outsourcing facilities, development of research initiatives and developing and executing CGMP training.

Increased direct FDA engagement is also essential. Outsourcing facilities consistently seek more in-depth information, prompt feedback, and timely inspections and site visits from the Agency. They frequently request FDA's views on, for example, facility design, production and testing methods, and new technologies. The requested resources will allow the Human Drugs Program to offer new programs for FDA review of method and process design and study protocols upon request, as well as conduct more meetings to provide prompt in-depth feedback. This approach has the potential to significantly reduce future compliance failures, thus improving confidence in the sector, and would also support technical advancements and encourage market entry and growth.

As part of our increased engagement initiative, FDA will also expand efforts to work with states to harmonize and streamline their approach to the outsourcing facility sector and improve the quality of compounded drugs. State quality requirements for compounding pharmacies not registered with FDA as outsourcing facilities also vary, as do the frequency and duration of inspections, often due to budgetary constraints. FDA often observes insanitary conditions at state-licensed compounding pharmacies. Additional funding will support training and outreach initiatives to strengthen state oversight of compounding facilities, as well as a pilot program of contracted state inspections. This pilot program would fund eligible states to conduct inspections under federal standards, to help ensure that compounding pharmacies not registered as outsourcing facilities provide solely patient-specific compounded drugs prepared under appropriate quality conditions (not insanitary) and outsourcing facilities become the sole source of compounded drugs for office stock prepared under CGMP.

Field: +$2.7 million / 10 FTE

The Office of Regulatory Affairs (ORA) is a critical partner in each of the activities described above. ORA will support the Center of Excellence on Compounding for Outsourcing Facilities and provide hands-on assistance to these facilities to improve compliance. ORA also will support training and outreach initiatives to strengthen state oversight of compounding, as well as a pilot program of contracted state inspections.

In addition, ORA will establish a specialized group of investigators who will spend a majority of their time on outsourcing facility inspectional activities. As discussed above, outsourcing facilities are in their early growth years and would benefit from more frequent FDA inspections and site visits, which outsourcing facilities in the past have requested. These visits would not only help the sector come into compliance, but also help address regulatory hurdles in states that refuse to license these facilities unless they receive annual inspections by FDA. Furthermore, outsourcing facilities are distinct from conventional manufacturers in numerous ways, and require specialized knowledge to inspect. A specially trained group of investigators who spend a majority of their time on outsourcing facility oversight will develop a highly sophisticated expertise; will become intimately familiar with the facilities, systems, and technologies that they routinely inspect; and will provide timely, consistent, substantive feedback when compliance issues are identified. This initiative will also help FDA meet annual inspection targets and conduct additional facility visits when requested by the outsourcing facility.

All of these ORA efforts will yield more substantive and efficient interactions with the outsourcing facilities, stimulating entry of new entities and expansion of existing outsourcing facilities.

Promote Innovation in Product Development and Scientific Knowledge

FDA is proposing measures to foster innovation and other scientific advancements in medical products for human and animal use. These advancements will help American families to lead healthier lives, including through medical breakthroughs leading to new treatments that were previously unavailable. Moreover, the more FDA can do to foster innovation, the more likely it will be that new technologies – and new jobs – will take hold in the U.S.

Create a New Medical Data Enterprise: Advance the Use of Real World Evidence to Improve Human and Animal Health

CDER: +$23.0 million / 2 FTE

Expanding FDA's capacity to utilize real world evidence to evaluate the safety and effectiveness of medical products would generate data that could be used to improve the efficiency of the regulatory process and reduce the burdens that drive up the time and cost required to bring innovative and life-saving products to the market. Leveraging real world evidence is also integral to advancing the public health where human and animal health challenges intersect, such as the public health threats posed by increasing antimicrobial resistance.

Within the Sentinel Initiative, FDA has built a cost-effective and scalable system, allowing FDA to answer numerous questions simultaneously and in a matter of weeks and months, rather than years. The per-study costs are a fraction of historical costs. FDA has completed 254 analyses using the Sentinel Common Data Model and reusable modular programs since the full activation of the Sentinel System in 2016, including 116 in 2016 and 138 in 2017. This result is many more than would have been possible without the improvements brought about by the Sentinel System. The creation of the Sentinel System and the companion Innovation in Medical Evidence and Development Surveillance (IMEDS) program, that provides access to the Sentinel infrastructure to stakeholders, has reduced the burden on pharmaceutical sponsors for conducting postmarketing studies.

Although large database systems, such as Sentinel, have been developed to help evaluate post-market safety, their utility for the evaluation of complex issues related to safety and their potential utility to evaluate effectiveness is less than optimal because to date Sentinel has relied primarily on claims data due to challenges with linking to more complete clinical data held in patients' medical records. Other systems, such as the National Evaluation System for health Technology (NEST), that rely primarily on registries, have been leveraged to evaluate safety and effectiveness, in some cases resulting in first in the world approvals, but also face challenges because they do not link to electronic health records.

Expanding on these successful distributed database models, the further development of a robust near-real-time, real-world evidence capability would serve to facilitate the development of drugs, biologics, and devices by allowing FDA and eventually sponsors to obtain critical information on aspects of the safety and effectiveness of marketed products.

Building on the accomplishments of the Sentinel System and NEST, the requested FY 2019 funding will be used to establish a new capability, including the development of data and

analytical tools, to conduct near-real-time evidence evaluation down to the level of individual electronic health records for at least ten million individuals in a broad range of healthcare settings in the United States for a broad range of medical products. The healthcare settings would be carefully selected to cover data gaps in the Sentinel and NEST systems for FDA-regulated products not currently easily assessed using existing systems. In addition to accessing more detailed clinical data, this effort would apply modern computational techniques, such as natural language processing and machine learning, to efficiently use these data elements for evaluating safety and effectiveness of marketed medical products. This would create a sustainable platform that could then be expanded through public-private partnerships.

This expanded real-world evidence capability will serve to facilitate the development of drugs, biologics, and devices by allowing FDA and eventually sponsors to obtain critical information on aspects of the safety and effectiveness of marketed products. Near-real-time access to data would result in the ability to shift more data collection into the postmarket setting to address residual uncertainties, to more rapidly identify and confirm relevant safety signals, and to facilitate product label expansion into new indications. Given the relatively large sample size, it would also allow FDA, potentially in collaboration with other federal partners, to rapidly evaluate emerging diseases potentially affecting the blood or tissue supplies.

A by-product of the development of a robust natural language processing and machine learning system also would be to significantly augment the efficiency of the existing manual review of passively reported adverse events by FDA staff. This investment will allow the optimization of human safety expert review while freeing resources to be redirected toward advancing product development, review, and approval. FY 2019 funding to support the activities above will enable FDA to address this critical initiative.

Applying Cutting Edge Science to Advance Drug Development and Review: Drug Innovation Platform

CDER: +$57.5 million / 5 FTE

Rapidly advancing science in drug development requires FDA to have up-to-date scientific standards and assessment tools, as well as evolving technologies, methods, and approaches. Without these tools, the Agency's ability to support innovation and review applications will lag behind the latest science and inhibit innovation. Currently, FDA has a number of drug development guidances where updates to assure new scientific information and new approaches to drug development are incorporated. In addition, guidances are needed in a number of disease areas where there is no existing guidance and therefore no articulated pathway to market for new treatments. FDA's decision-making rests on the regulatory and statutory framework, and on the scientific expertise of its staff, but would be supported and facilitated by a comprehensive knowledge management system that provides access to and analysis of prior regulatory decisions and previously submitted clinical trials information and other relevant datasets.

FDA requires a comprehensive knowledge management approach to its significant number of precedential decisions, and to the underlying data, including data from trials, data generated by FDA, and real-world data. Additional funding will support development of a knowledge management system that would provide rapid access to and in-depth analysis of the vast and diverse information submitted to FDA. Such a knowledge management system would advance

FDA's ability to rapidly develop scientific evidence as questions arise, including questions about drug safety or quality.

With this investment, FDA will build a knowledge management system and portal to previously submitted and ever-expanding information on drug development and regulatory precedents, advancing FDA's ability to provide consistent and fully-informed responses to regulatory questions. Such a knowledge management system may also help to enhance FDA's ability to rapidly respond to issues that arise, whether related to a regulatory decision or a safety signal, and support innovations in drug development by fully leveraging prior experience. This investment will also enable safety issues to be monitored along all phases of the drug lifecycle from animal studies to premarketing clinical trials to postmarket adverse events. FDA would also expand its capability to quickly evaluate new questions, using laboratory research or other appropriate methods.

Funding for this initiative would support a variety of components which includes building reliable, connected environments that allow reviewers/users to access data, tools, and knowledge. This includes templates, standardized data, tools and regulatory review knowledge and intelligence.

Additional FY 2019 funding will also support recruitment efforts of technical experts to help understand the requirements for scientific review and to develop the specifications for a future integrated platform for innovation that would also improve data sharing and allow testing of state-of-the-art tools and technologies. Such a platform would also support the enforcement of data standards and the acquisition of advanced analytical tools.

The FY 2019 funds requested will support refined oversight for investment and contract management functions to enable improved IT infrastructure to support regulatory review and knowledge management. In addition, FDA would have the capability to build IT environments that allow real-time testing of the latest tools and technologies, including data visualization and business intelligence tools.

With the advent of enforceable guidance, FDA must be prepared to accept and assess "data quality" and "data fitness" to fully utilize standardized data to support core analyses. This will entail increased infrastructure to support data management and data quality assessments as well as infrastructure to prepare data for standard analyses with core tools/technologies. In addition, with various data sources that can influence regulatory decision making, the Agency will need additional resources to have scientific computing environments enabled to support real time data analysis with state-of-the-art tools. FDA will also need considerable funding to develop and enhance regulatory intelligence systems to fully interface with the review work product to seamlessly capture metadata about the review.

Investments in this area would also facilitate training and understanding of advanced methodologies and emerging science to increase capacity to evaluate and propose innovative strategies for clinical outcome assessments and the endpoints derived from them. FDA will also have the additional capacity to develop advanced analytical methods/tools for the quantitative assessment of safety and increase training and exposure to quantitative assessment of complex innovative designs to increase capacity to evaluate, propose, and refine innovative strategies. Additional funding will support new and essential efforts to build a knowledge management framework that would enhance the overall drug development and review cycle within the Agency.

Overall, the development of this Drug Innovation Platform will make the review of drug applications and the management of postmarketing safety and efficacy supplements exponentially more efficient and effective, resulting in shorter review cycles and the ability to continuously evaluate and adopt innovative technologies and methodologies to support drug development and surveillance.

Stimulating Medical Product Development for Rare Diseases

CDER: +$20.0 million[32] / 5 FTE

A disease is considered rare if it has a prevalence of fewer than 200,000 affected individuals in the United States. There is great unmet need with nearly 7,000 diseases that lack treatment for an estimated 30 million Americans. Currently, there are large and growing gaps in the evidence available to help providers and patients make treatment decisions due to a lack of clinical data and understanding of how to develop the treatments in a given disease, often compounded by the small number of patients impacted by rare diseases.

FY 2019 funding will support FDA's commitment to advancing the evaluation and development of medical products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions. To foster innovation and medical product development for rare diseases, FDA will develop clinical trial networks to create an understanding of the natural history and clinical outcomes of rare diseases and leverage this framework when promising medical products have been identified on behalf of patients. FDA will stimulate medical product development for rare diseases by expanding and enhancing the understanding of rare diseases and related research and drug development processes.

FDA will also conduct assessments of current orphan drug incentives, including market exclusivity, to inform FDA's policy framework around primary and secondary drug indications. Included would be a better understanding of how FDA could best incentivize more drug development for ultra-rare diseases. The requested funding for this initiative will enable FDA to implement advances to support the public health mission of the Agency.

Modernizing Generic Drug Development and Review

CDER: +$37.6 million / 5 FTE

Timely development, review, and access to generic drugs are pivotal for enabling competition and providing affordable drugs for American patients. Currently, generic drug review is performed using text-based applications and assessments—in other words, 20th Century technology. An updated review platform will significantly modernize generic drug review and by improving clarity for generic sponsors and decreasing the rate of refusals-to-file, greatly increasing efficiency at FDA. This one-time platform investment will provide returns in the efficiency and effectiveness of the process for many years. As part of modernizing the regulatory processes for generic drugs, this investment will also support efforts to update generic drug labeling, with an initial focus on oncology products, as part of the FDA's efforts to ensure that patients and their providers have access to up-to-date information to inform clinical decisions.

The new Knowledge-aided Assessment & Structured Application (KASA) platform will support the capture and management of all the required information about a drug product, facilitate risk

[32] $10 million will support activities in CDER and $10 million will support policy related activities in FDA HQ.

identification, mitigation, and communication, and provide a structured template that will completely replace an unstructured text based narrative review. Instead of the current unstructured approach, information from the submission considered essential for the assessment would be structured and organized in tabular format. This investment will result in more consistent drug product evaluations and seamless knowledge management across generic and brand-name drugs that would enhance product surveillance based on quality risk. In addition, this new platform will enable the automation of elements of the application review that are currently performed manually, reducing overall application review cycle times.

The FY 2019 funding request for this new generic drug review platform will allow FDA to advance the quality assessment of sponsor-provided drug product applications and will lead to more predictability to the regulated industry, and thus facilitate generic entry. Additional funding will support resources and costs for IT investments as well as, structure for data management, contracts, and grants. Taken together, these programs will allow FDA to advance the quality assessment of sponsor-provided drug product applications and ultimately improve patient care and facilitate access to new and generic therapies.

USER FEES

Current Law User Fees: +$43.2 Million

Center: +$41.9 million / Field: +$1.3 million

The Human Drugs Program request includes an increase of $43,201,000 for user fees authorized under FDARA, which will allow FDA to fulfill its mission of promoting and protecting the public health by ensuring safety and efficacy of medical products and accelerating innovation in the industry.

PERFORMANCE

The Human Drugs Program's performance measures focus on premarket and postmarket 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 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
223210: Review and act on 90 percent of standard NME NDA and original BLA submissions within 10 months of the 60 day filing date. *(Output)*	FY 2016: 100% Target: 90% (Target Exceeded)	90%	90%	Maintain
223211: Review and act on 90 percent of priority NME NDA and original BLA submissions within 6 months of the 60 day filing date. (Output)	FY 2016: 100% Target: 90% (Target Exceeded)	90%	90%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
223212: Review and act on 90 percent of standard non-NME original NDA submissions within 10 months of receipt. *(Output)*	FY 2016: 96% Target: 90% (Target Exceeded)	90%	90%	Maintain
223213: Review and act on 90 percent of priority non-NME original NDA submissions within 6 months of receipt. *(Output)*	FY 2016: 92% Target: 90% (Target Exceeded)	90%	90%	Maintain
223215: Review and act on 90 percent of standard original Abbreviated New Drug Application (ANDA) submissions within 10 months of receipt. *(Output)*	FY 2016: 98% Target: 75% (Target Exceeded)	90%	90%	Maintain
223216: Review and act on 90 percent of priority original Abbreviated New Drug Application (ANDA) submissions within 8 months of receipt. *(Output)*	New Goal	90%	90%	Maintain
224211: Percentage of planned foreign and domestic high-risk human drug inspections. (Output)	FY 2017: 68% Target: 64% (Target Exceeded)	70%	70%	Maintain
292202: Number of people for whom FDA is able to evaluate product safety through Mini-Sentinel/Sentinel system. *(Outcome)*	FY 2017: 223 million Target: 198 million (Target Exceeded)	233 million	243 million	+10 million

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 goals of the PDUFA program are 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 goals of the GDUFA program are 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 2019 targets for the review goals align to the PDUFA VI and GDUFA II performance commitments.

Sentinel

The FDA's 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. Through the Sentinel System, the FDA is able to evaluate drug safety issues that may require regulatory action. In FY 2017, the Sentinel System expanded surveillance to 223 million members, which is an increase of 30 million members from FY 2016. FDA held the Ninth Annual Sentinel Initiative Public Workshop in February 2017 to bring together stakeholder communities to discuss a variety of topics on active medical product surveillance and emerging Sentinel projects. 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. The Sentinel System ensures FDA will continue to have the tools necessary to conduct active safety surveillance work.

New ORA Field Performance Measures

ORA has been working to improve the field performance measures to better aligned with ORA's Program Alignment initiative. In this submission, ORA has completed the process of adjusting the performance goals, so that the FY 2018 and FY 2019 targets now complete a certain percentage of the planned inspections in ORA's annual Workplan. The ORA Workplan is the necessary mechanism that takes into account all the complex variables (geography, commodity, risk, availability, efficiency, etc.) that allows ORA to plan which inspections to do. With these newly formulated performance goals, ORA is committing to complete a certain percentage of the initially planned inspections. This revision strengthens the importance of the Workplan, but allows the flexibility to respond dynamically to changing circumstances during the year, to better handle emerging risks and evolving public health priorities (i.e. the heavy hurricane damage this past year). This is a significant departure from the previous performance goals, so FY 2018 will be an important year in resetting the new baselines. Also, since the targets are now based on a planned number of inspections, it is possible to inspect more than what was planned and thus have an actual inspection rate over 100%.

PROGRAM ACTIVITY DATA

CDER Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
New Drug Review			
Workload – Submissions/Filings/Requests			
New Drug Applications/Biologic Licensing Applications (NDA/BLA)	154	154	154
Efficacy Supplements	231	231	231
Manufacturing Supplements	1,904	1,904	1,904
Commercial INDs (Drugs and Biologics) with Activity	7,047	7,047	7,047
Sponsor Requests: IND-Phase Formal Meetings	2,760	2,760	2,760
Sponsor Requests: Review of Special Study Protocols	160	160	160
Submissions of Promotional Materials	99,204	103,000	106,000
Outputs – Reviews/Approvals			
Reviews: Priority NDA/BLA	54	54	54
Reviews: Standard NDA/BLA	136	136	136
Approvals: Priority NDA/BLA	43	43	43
Approvals: Standard NDA/BLA	79	79	79
Mean time from Receipt to Approval: Priority NDA/BLAs (in months)	7.3	7.3	7.3
Mean time from Receipt to Approval: Standard NDA/BLAs (in months)	14.7	14.7	14.7
Median time from Receipt to Approval: Priority NDA/BLAs (in months)	7.6	7.6	7.6
Median Time from Receipt to Approval: Standard NDA/BLAs (in months)	10.1	10.1	10.1
Reviews: NDA Supplementals	3,186	3,186	3,186
Reviews: Clinical Pharmacology/ Bio-Pharmaceutic	4,868	5,111	5,366
Biologic Therapeutics Review			
Workload – Submissions/Filings/Requests			
Receipts: Commercial IND/IDE (Biologics Only)	143	143	143
Receipts: IND/IDE Amendments (Biologics Only)	26,050	26,050	26,050
Outputs – Reviews/Approvals			
Reviews: Total Original License Application (PLA/ELA/BLA)	18	18	18
Approvals: PLA/BLA	15	15	15
Reviews: License Supplement (PLA/ELA/BLA)	425	425	425
Generic Drug Review			
Workload – Submissions/Filings/Requests			
Receipts: Abbreviated New Drug Applications (ANDA)	1,306	1,000	1,000
Outputs – Reviews/Approvals			
Actions – ANDA	2,755	2,800	2,850
Approval Actions - ANDA (both Tentative and Full Approvals)	937	950	975
Median Review Time from ANDA Receipt to Approval (months)	37.26	37.00	36.75
Actions - ANDA Supplementals (Labeling and Manufacturing)	6,491	6,600	6,700
Over-the-Counter Drug Review			
OTC Monographs Under Development*	25	25	25
OTC Monographs Published*	1	5	5
*Category includes Proposed Rules, Final Rules, and Proposed and Final Orders under the Sunscreen Innovation Act			

CDER Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
Best Pharmaceuticals for Children Act			
Labels Approved with New Pediatric Information	17	13	13
New Written Requests Issued	22	19	20
Pediatric Exclusivity Determinations made	8	9	8
Post Exclusivity Safety Report	5	8	8
Patient Safety			
Workload – Submissions/Filings/Requests			
Submissions: Adverse Event Reports	1,769,061	1,830,922	1,894,946
Electronic Submissions: % of Total Adverse Drug Reaction Reports	100%	100%	100%
Electronic Submissions: % of Serious/Unexpected Adverse Drug Reaction Reports	100%	100%	100%
Submissions: Drug Quality Reports	14,372	15,000	16,000
Outputs – Reviews/Approvals			
Safety reviews completed by Office of Surveillance & Epidemiology	7,446	7,500	7,600
Number of drugs with Risk Communications	175	185	195
Administrative/Management Support			
Workload			
Number of Advisory Committee Meetings	27	32	32
Number of FOI Requests	3,364	3,300	3,300
Number of FOI Requests Processed	3,413	3,325	3,325
Number of Citizen Petitions Submitted (excluding suitability petitions and OTC monograph-related petitions)	129	109	109
Number of Citizen Petitions Pending on Last Day of Fiscal year (excluding suitability petitions and OTC monograph-related petitions)	178	171	171
Number of Citizen Petitions Completed [1] (excluding suitability petitions and OTC monograph-related petitions)	116	109	109

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

Field Human Drugs Program Activity (PAD)

Field Human Drugs Program Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS	***1,758***	***1,803***	***1,814***
Pre-Approval Inspections (NDA)	85	135	135
Pre-Approval Inspections (ANDA)	91	215	215
Bioresearch Monitoring Program Inspections	681	550	550
Drug Processing (GMP) Program Inspections	668	650	650
Compressed Medical Gas Manufacturers Inspections	63	50	50
Adverse Drug Events Project Inspections	83	88	88
OTC Monograph Project and Health Fraud Project Inspections	29	70	70
Compounding Inspections[1]	141	142	142
Domestic Laboratory Samples Analyzed	1,571	1,300	1,300
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS [2]	***1279***	***1360***	***1360***
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	87	98	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	165	190	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	307	255	255
Foreign Drug Processing (GMP) Program Inspections	799	900	900
Foreign Adverse Drug Events Project Inspections	8	10	10
TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS	***3,037***	***3,163***	***3,174***
IMPORTS			
Import Field Exams/Tests	14,300	10,000	10,000
Import Laboratory Samples Analyzed	741	620	620
Import Physical Exam Subtotal	**15,041**	**10,620**	**10,620**
Import Line Decisions	789,853	829,346	870,813
Percent of Import Lines Physically Examined	1.90%	1.28%	1.22%
GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS	***3,037***	***3,163***	***3,174***

[1] The number of compounding inspections includes inspections of compounders that are not registeredwith FDA as outsourcing facilities.

[2] The FY 2017 actual unique count of foreign inspections includes 105 OIP inspections (57 for China, 44 for India, & 4 for Latin America).

OFFICE OF ORPHAN PRODUCTS DEVELOPMENT

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actuals	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 President's Budget +/- FY 2018 CR
Office of Orphan Products Development (Budget Authority) 1,2,3.....	29,099,000	29,099,000	29,099,000	29,099,000	---
FTE.....	34	34	34	34	---

[1] FY 2017 includes $3 million added to PDC grant funds.
[2] FY 2017 amounts include $1.2 million of OOPD program funds to support Orphan Product Grants.
[3] Assumes approximately 50 percent of non-grant budget from user fees in 2017.

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 conditions. 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 for underserved populations. OOPD program activities directly support the Health and Human Services' strategic goal to advance scientific knowledge and innovation.[33]

Further, OOPD activities 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[34]

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

[33] http://www.hhs.gov/about/strategic-plan/strategic-goal-2/index.html

[34] FY 2017 includes $1.2 million of OOPD program funds to support Orphan Product Grants

promising new, drugs, biologics, devices, and medical foods through human clinical trials in very vulnerable populations often with life-threatening conditions.

Clinical Trial Grants Program

Over 600 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 2017, OOPD funded 15 new grant awards – out of 76 grant applications – and provided funding or continued support for approximately 70 other ongoing clinical study projects.

These grants are a modest investment to better ensure that product development occurs in a timely manner and helps reduce risk in the process for industry in these rare disease fields. 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 Grants Program

OOPD launched a new call for grant applications 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 funded six new research grants for natural history studies in rare diseases. Two of the six grants were able to be awarded through a partnership with the National Institutes of Health (NIH) National Center for Advancing Translational Sciences (NCATS). It is hopeful that these important studies will add valued data to help develop targeted therapies and lead to more efficient and better designed clinical trials.

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. Rare diseases and conditions are, in part, defined as one affecting fewer than 200,000 persons in the United States. OOPD evaluates requests from sponsors who are developing drugs to treat rare diseases to determine eligibility for orphan drug designation. Sponsors of designated orphan drugs 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 4,400 orphan drug designations OOPD issued since 1983 have resulted in over 650 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 2017, OOPD received a record 541 new applications for orphan drug designation. These included potential treatments for many kinds of rare cancers, sickle cell disease, and Ebola. OOPD designated 449 orphan drugs in FY 2017. FDA approved 63 orphan designated drugs for marketing in FY 2017.

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.

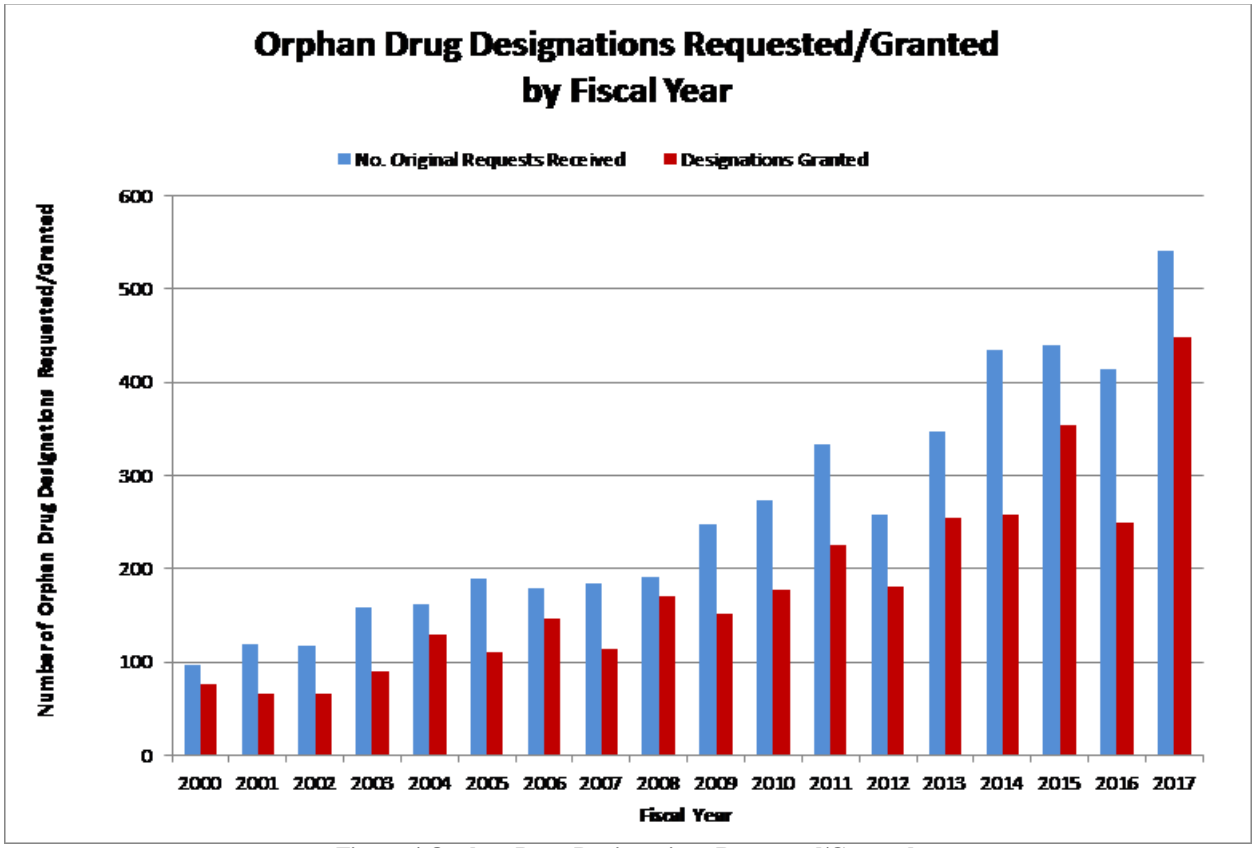

Figure 4 Orphan Drug Designations Requested/Granted

Product Designations

Below are examples of Orphan Product designations that occurred in 2017.[35]

Date	Product	Purpose or Benefit
May 2017	Larotrectinib	Treatment of solid tumors with NTRK-fusion proteins. This is the first orphan drug designation for a tissue agnostic cancer diagnosis, based on a molecular marker.
July 2017	Tocilizumab	Treatment of patients with severe or life-threatening cytokine release syndrome resulting from use of genetically modified T-cell therapies for treating cancer increasing the safety associated with the first gene therapy.

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

[35] For more information on designations and product approvals, visit http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm

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 a 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 2017, OOPD received 60 new rare pediatric disease designation requests plus one consult from submitted marketing applications needing rare pediatric disease determinations. Of these, OOPD determined that 39 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 FY 2017, 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 Designation Activity

The Humanitarian Use Device (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, 72 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 FY 2017, 15 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 2017, OOPD received 20 new HUD applications and designated 8 devices. Of the eight devices that were designated, four designations were based on HUD applications originally submitted in prior years. In FY 2017, two devices received an HDE approval from CDRH. Also, in FY 2017, one manufacturer who received HDE approval was authorized to market their device for profit.

Additionally, on December 13, 2016, Section 3052 of the 21st Century Cures Act (Pub. L. No. 114-255) changed the population estimate required to qualify for HUD designation from "fewer than 4,000" to "not more than 8,000." Accordingly, a HUD is now defined as a medical device

intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the United States per year. Since this change, seven devices have received HUD designation for population estimates between 4,000 and not more than 8,000.

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. On August 18, 2017, FDA Reauthorization Act of 2017 extended the program through September 30, 2022. FDA anticipates posting a new Request for Applications for PDC grants program in late 2017.

Most recently, the Consolidated Appropriations Act, 2017 increased funding for the program from $3 million to $6 million.

The FDA Pediatric Device Consortia Grant Program, administered in OOPD, supports nonprofit consortia that promote the development of pediatric medical devices. In FY 2017, the consortia funded in this program are based out of 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 $31.4 million has been awarded to the consortia. Collectively, the consortia have supported the development of more than 800 potential pediatric devices, many of which are in the early stages of development. Over 15 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 AnemoCheck, which is a point of care diagnostic for determining total hemoglobin and calculated hematocrit in whole blood; and PIVO device, which is a needle-free blood collection device that attaches to peripheral IV systems. The consortia collectively have also raised more than $135 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 2017, OOPD participated in 71 individual industry outreach meetings. In addition, OOPD received more than 70 invitations to speak and participate at orphan product stakeholder meetings and conferences to discuss different rare disease issues. OOPD made presentations and participated in 34 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 2017 include conducting training courses for researchers and reviewers, and presentations to national and international rare disease patient groups. In FY 2018 through FY 2020, OOPD will continue the mission critical 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 [3]	User Fees
FY 2015 Actual	$23,599,000	$23,599,000	$0
FY 2016 Actual	$29,099,000	$29,099,000	$0
FY 2017 Enacted	$29,099,000	$29,099,000	$0
FY 2018 Annualized CR	$29,099,000	$29,099,000	$0
FY 2019 President's Budget	$29,099,000	$29,099,000	$0

[3] Assumes approximately 50 percent of non-grant budget from user fees in 2017.

BUDGET REQUEST

The FY 2019 Budget Request is $29,099,000. 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 continue to fund six grants for natural history studies targeted on expediting the development of products for these rare conditions.

PROGRAM ACTIVITY DATA

Program Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
Grant Programs			
Total Orphan Product Grant (New and Continuations)	85	90	90
Total Pediatric Consortia Grants (New and Continuations)	7	7	7
Total Natural History Grants (New and Continuations)	6	7	7
Orphan Drug Designation Requests/Designations Granted/Orphan Drug Approvals			
New Orphan Drug Designation Requests	541	550	550
Drug Designations Granted	449	350	350
FDA Orphan Drug Marketing Approvals	63	60	60
HUD Requests and Designations			
New HUD Designation Requests	20	27	27
HUD Designations	8	14	14
Rare Pediatric Disease Priority Review Voucher Requests and Designations			
New RPD Requests	61	65	65
RPD Designations	39	45	45

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BIOLOGICS

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
Biologics	**339,492**	**340,016**	**358,025**	**403,268**	**45,243**
Budget Authority	***215,317***	***215,443***	***213,854***	***251,854***	***38,000***
User Fees	***124,175***	***124,573***	***144,171***	***151,414***	***7,243***
Center	296,066	296,923	315,328	360,492	45,164
Budget Authority	173,937	174,052	172,755	210,755	38,000
User Fees	122,129	122,871	142,573	149,737	7,164
Prescription Drug (PDUFA)	*109,704*	*111,173*	*127,961*	*134,872*	*6,911*
Medical Device (MDUFA)	*10,508*	*10,826*	*13,405*	*13,639*	*234*
Generic Drug (GDUFA)	*1,088*	*872*	*1,032*	*1,048*	*16*
Biosimilars (BsUFA)	*829*	---	*175*	*178*	*3*
Field	43,426	43,093	42,697	42,776	79
Budget Authority	41,380	41,391	41,099	41,099	---
User Fees	2,046	1,702	1,598	1,677	79
Prescription Drug (PDUFA)	*1,847*	*1,517*	*1,397*	*1,472*	*75*
Medical Device (MDUFA)	*199*	*185*	*201*	*205*	*4*
FTE	**1,414**	**1,414**	**1,375**	**1,383**	**8**

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); Food and Drug Administration Reauthorization Act of 2017 (FDARA) (P.L. 115-52).

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 its mission, CBER also seeks 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 of, 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 navigate the challenges and opportunities of 21st Century medicine successfully. 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 2017, the Biologics Program contributed to the improvement of public health with the following accomplishments, among others:

- Established the Regenerative Advanced Medicine Therapy (RMAT) designation to expedite the development of certain cell therapies, therapeutic tissue engineering products, human cell and tissue products, and certain combination products that meet the designation criteria.
- Issued landmark approvals of the first cell-based gene therapies available in the United States, Kymriah, a treatment utilizing a patient's own T-cells to combat the patient's cancer, and Luxturna a directly administered gene therapy that works by delivering a normal copy of the defective gene directly to retinal cells.
- Effected the seizure of one product, and issued five Warning Letters and one Untitled Letter to manufacturers of biological products due to deviations from the Federal Food, Drug, and Cosmetic Act, Public Health Service Act, and the applicable regulations in Title 21, Code of Federal Regulations (21 CFR).

The following selected accomplishments demonstrate the Biologics Program's delivery of its regulatory and public health responsibilities within the context of current priorities.[36]

Improve and Safeguard Access

FDA's Biologics Program is committed to helping to expedite the development and review 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

[36] Please visit http://www.fda.gov/ for additional program information and detailed news items

those representing ground breaking treatments, the exciting medical promise of precision medicine; and treatment options where very limited options exist. These products can include additional vaccines against pandemic influenza and other infectious diseases; cellular and gene therapies; or new technologies to enhance the safety and availability of blood and blood products.

Modernizing the Regulatory Process

Advances in science and technology show great promise for the development of safe and effective biological products and FDA is taking steps to foster innovation. 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.

FDA programs such as the RMAT Designation, Fast Track, Breakthrough Therapy Designation, Accelerated Approval, and Priority Review are used when appropriate to expedite the development and review of innovative biological products. Since the inception of the Breakthrough Therapy Designation process in July 2012, CBER has granted 35 Breakthrough Therapy designations, with 25 of the 35 products being for rare diseases (Orphan Product designation).[37] In FY 2017, FDA granted nine Breakthrough Therapy designations, seven of which were cell or gene therapy products.

The Biologics Program has utilized a variety of regulatory programs to help facilitate therapies for the treatment of cancer and other serious and life-threatening diseases coming to market. Notable examples are the approvals of three separate cell-based gene therapies available for the first time in the United States. Kymriah and Yescarta are both part of an innovative class of cell based gene therapies for cancer patients with few other options. Each dose is a customized treatment created using an individual patient's own T-cells, a type of white blood cell. The patient's T-cells are collected and sent to a manufacturing center where they are genetically modified to include a new gene that directs the T-cells to target and kill cancer cells. Once the cells are modified, they are infused back into the patient to kill the cancer cells. FDA granted both therapies Priority Review and Breakthrough Therapy designation. They were reviewed using a coordinated, cross-agency approach with the clinical review coordinated by the FDA's Oncology Center of Excellence, and CBER conducting all other aspects of the reviews and final product approvals.

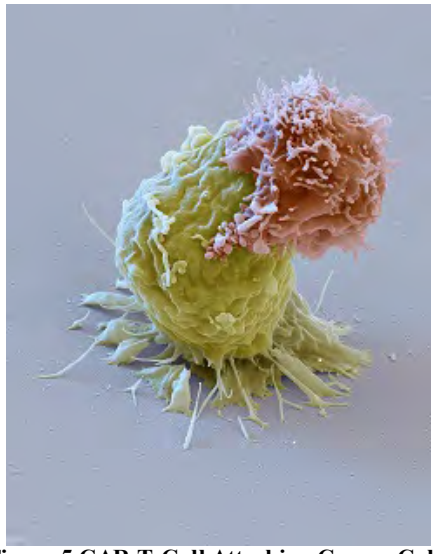

Figure 5 CAR-T Cell Attacking Cancer Cell

Luxturna is a directly administered gene therapy that works by delivering a normal copy of the defective gene directly to retinal cells. These retinal cells then produce the normal protein that converts light to electrical signal in the retina to restore patient's vision loss. FDA granted this therapy Priority Review and Breakthrough Therapy and Orphan drug designation. Luxturna is the first gene therapy in the U.S. that treats an inherited disease caused by mutations in a specific gene. This signals another development in the field of gene therapy and underscores the potential

[37] As of December 31, 2017

promise of the field of gene therapy for treating other serious and life-threatening diseases with no known cures.

In FY 2017, FDA established a new program to foster development and approval of regenerative medicine therapies: the RMAT Designation program. Upon receiving RMAT Designation, sponsors are eligible for increased and earlier interactions with FDA to help facilitate an efficient development program, including discussion of which approval pathways would be appropriate and advice on clinical trial design, including trial size and endpoints. The Agency has granted 13 RMAT Designations since program inception[38].

In November 2017, FDA announced its comprehensive policy framework for the development and oversight of regenerative medicine products, including novel cellular therapies. The framework, outlined in a suite of four guidance documents builds upon the FDA's existing risk-based regulatory approach and is intended to clarify what products are regulated as drugs, devices, and/or biological products. The suite of guidance documents also delivers on important provisions of the 21st Century Cures Act. This modern framework intends to balance the agency's commitment to safety with mechanisms to drive further advances in regenerative medicine so innovators can bring new, safe, and effective therapies to patients as efficiently as possible.

To improve efficiency in the review process, CBER expanded the capabilities of its Electronic Managed Review Process IT system to include electronic processing of efficacy supplements, uploading of approval letters and filing checklists, and expedited document sign-off. CBER also developed and implemented the Device Submissions Tracking System, to improve regulatory tracking of 510(k) device applications and expedite the medical device review process.

Facilitate Product Development Through Applied Research

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 and conduct research to address scientific gaps and provide effective regulatory responses to public health emergencies and new technologies. FDA leverages this considerable scientific expertise to develop new tools, models, and methods, often harnessing new technologies designed to expedite product development.

Pathogen Reduction Technologies for blood components, are a potential solution to transfusion-transmitted sepsis or viral infections, however, there are still technical challenges with implementing them to avoid compromising the quality of the blood component. FDA is evaluating new and better photosensitizers, and new proofs-of-concepts as potential alternatives to existing technologies. To support the agency's efforts to fight the Zika virus, FDA has also undertaken efforts to evaluate the impact of red blood cell storage on virus infection, develop rapid, sensitive methods to assess vaccine effectiveness in animal studies and clinical trials, and explore how long the Zika virus persists in body tissues.

FDA hosted the 20th US-Japan Cellular and Gene Therapy Conference, on March 9, 2017, in conjunction with Japan's Ministry of Education, Culture, Sports, Science, and Technology, under

[38] As of December 31, 2017

the US-Japan Cooperative Research Program. Ideas were exchanged on cutting edge and diverse areas of biomedical research, and enhanced opportunities for collaborations, focusing on CRISPR (Clustered Regularly Interspaced Short Palindromic Repeat) methods.

CBER developed two new influenza vaccine potency assays as alternatives to the traditional potency assay. Both assays were evaluated in a large international collaborative study to compare alternative influenza vaccine potency assays on blinded vaccine samples. The International Federation of Pharmaceutical Manufacturers & Associations sponsored the study and participants included vaccine manufacturers, regulatory agencies, and other public health agencies. Data collected in FY 2017 demonstrated that both alternative assays were able to quantify proteins indicative of specific influenza strains in the vaccines, suggesting their promise as alternatives to the traditional potency assay.

To enhance the efficiency and accuracy of using next generation sequencing to detect adventitious viruses in cell substrates, CBER developed a new reference virus database (RVDB). In FY 2017, version 10.2 of the database was completed and made publicly available in the high-performance integrated virtual environment at the George Washington University. The RVDB is expected to detect existing and novel viruses by including nucleotide sequences of all viral sequences, complete or partial genomes, including endogenous retroviruses and retrotransposons. Members of the Advanced Virus Detection Interest Group performed test analysis of the database, which reported overall satisfaction and improvement compared to other public databases.

In May 2017, CBER convened the Vaccines and Related Biological Products Advisory Committee (VRBPAC) to discuss considerations for clinical trial evaluation of vaccines candidates to protect against Respiratory Syncytial Virus (RSV) disease, which is a leading cause of hospitalizations and health care visits in children less than five years of age. Currently, there are no vaccines licensed for the prevention of RSV. VRBPAC discussed the preclinical data needed to support studies and the need for standardized assays, viruses, and animal models. FDA is conducting research aimed at developing new serological assays (tests) to evaluate protective antibody responses to RSV. This research will facilitate the design and evaluation of vaccines, and help to identify vaccine candidates with the greatest potential for preventing RSV disease. Figure 6 is a graphic illustrating reduction of disease in the 21st century compared to the 20th century with the widespread use of vaccines.

A graphic of the impact of vaccines in the 20th and 21st centuries[39] follows:

[39] Source: Adapted from the CDC Epidemiology and Prevention of Vaccine-Preventable Diseases, 13th Edition "Pink Book". Available at: https://www.cdc.gov/vaccines/pubs/pinkbook/index.html

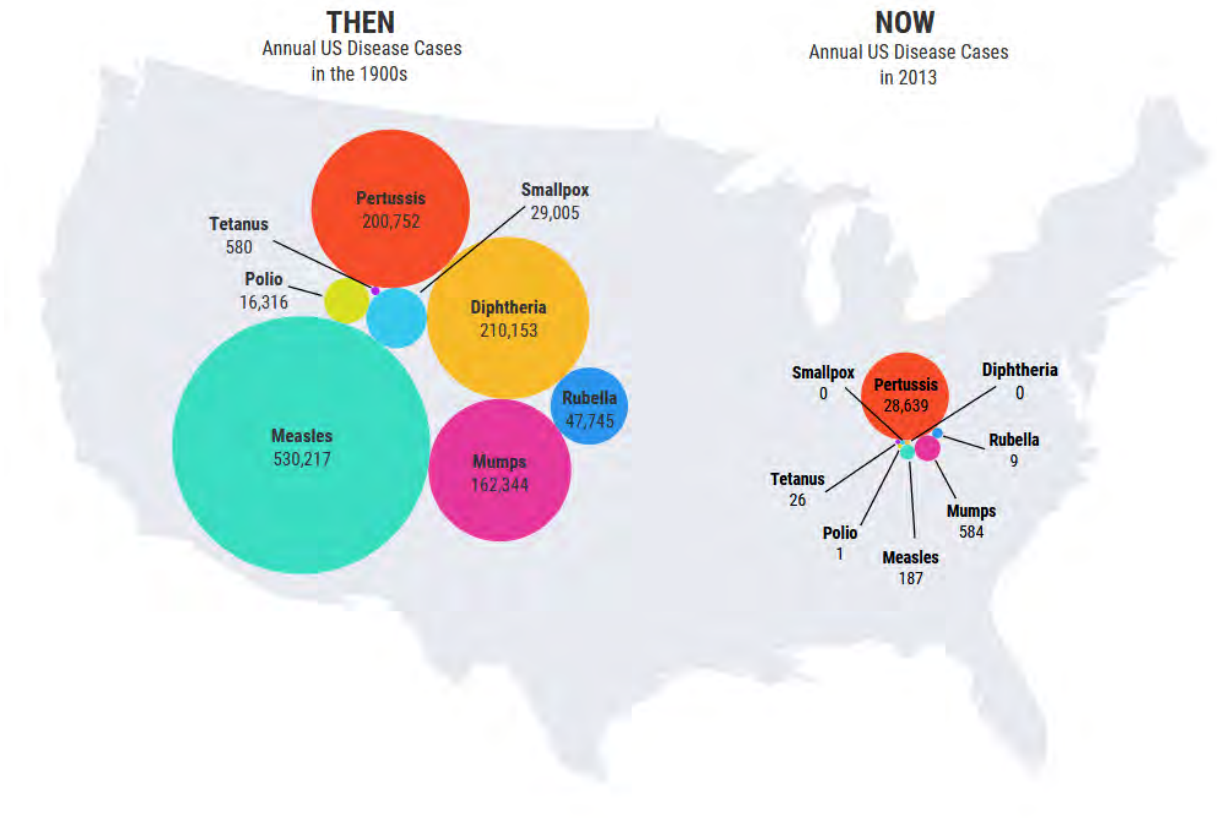

Figure 6 Impact of Vaccine in the 20th and 21st Centuries

Patient and Stakeholder Engagement to Bring Products to Market

To foster the development of innovative new therapies and address public health priorities, FDA engages a broad range of stakeholders. This includes fostering greater inclusion of patient engagement in the medical product development process, including regulatory decision-making for product review, post-market requirements, direct-to-consumer promotion, and risk communication.

FDA is working with the National Institute of Standards and Technology to coordinate and prioritize the development of standards and consensus definitions of terms for regenerative medicine advanced therapies. These standards and terms will help foster the development, evaluation, and review of regenerative medicine therapies, including with respect to the manufacturing processes and controls for such products.

In January 2017, FDA met with the Friedreich's Ataxia Research Alliance (FARA) to discuss potential gene therapies for Friedreich's Ataxia (FA), and to inform FARA and the research community of areas where more work may be needed to support development of gene therapies. In June 2017, an externally led Patient- Focused Drug Development Meeting gave patients with FA the opportunity to tell the FDA and drug developers about living with the disease.

In March 2017, in collaboration with NIH, CMS, and the Kidney Health Initiative FDA participated in, "Innovative Alternatives to Renal Replacement Therapy: Developing a Roadmap." This public workshop was held to discuss the scientific, technical, and regulatory

challenges needed to be addressed in a roadmap outlining steps towards bioartificial or bioengineered alternatives to dialysis. Topics included patient engagement, scientific challenges, and the path forward to address scientific barriers.

In June 2017, CBER participated in the Drug Information Association 2017 Annual Meeting held in Chicago, IL, chairing the forum entitled "Update from CBER: Advancing the Development of Complex Biologic Products." This meeting was held to foster the international exchange of actionable insights to improve health globally through the advancement of lifesaving medicines and technologies, enabling participants to build on their knowledge in the development of new therapies and accelerate efforts to enhance health and well-being.

In June, 2017 FDA with the University of California San Francisco-Stanford CERSI, and San Francisco State University Collaborative held a workshop with stakeholders to discuss whether Natural Language Processing can be applied to unstructured text in clinical notes. Potential uses could be used to identify indication or reason for medical product use, adverse outcomes or events associated with use of these products, and confounders or personal behaviors that may modify risks associated with use of these products. Protocol design, feasibility, recruitment efforts and execution of clinical trials was also discussed.

In July 2017, FDA and NIH/NIAID held a public workshop entitled ―Bacteriophage Therapy: Scientific and Regulatory Issues. The public workshop brought together government agencies, academia, industry, other stakeholders involved in research, development, and regulation of bacteriophages intended for therapeutic use in humans. The workshop stimulated discussion on this critical alternative to antibiotics in the treatment of infection and help facilitate development and rigorous clinical assessment of bacteriophage therapy products.

In September 2017, FDA held a public meeting on Patient-Focused Drug Development for Hereditary Angioedema (HAE), to obtain patient and caregiver perspectives on the impact of Hereditary Angioedema on daily life views on treatment options and participation in clinical trials.

FDA continues to provide scientific and regulatory advice to sponsors and stakeholders and to collaborate with other agencies and international regulatory authorities (WHO and EMEA) on the development and evaluation of vaccines for Zika virus. For example, FDA is actively engaged with NIH/NIAID and BARDA, and contributed to an HHS white paper outlining regulatory considerations for Zika vaccine licensure.

In October 2017, CBER representatives participated in the WHO Expert Committee on Biological Standardization meeting in Geneva Switzerland to establish WHO Biological Reference Preparations and written standards relevant to the manufacturing, licensing, and control of biological products. CBER representatives also serve as members of the WHO Blood Regulators Network, a forum for international blood regulatory authorities to share insights and address threats and opportunities to promote global blood product safety, efficacy, and availability, and attended the October 2017 meeting in Geneva.

Selected Product Approvals in 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
Biallelic RPE65 Mutation-Associated Retinal Dystrophy	Dec 2017	LUXTURNA	voretigene neparvovec-rzyl	First gene therapy in US that treats an inherited disease caused by mutations in specific gene (Priority Review, Breakthrough Therapy and Orphan drug)
Herpes Zoster (shingles)	Oct 2017	SHINGRIX	Zoster Vaccine Recombinant, Adjuvanted	For prevention of herpes zoster (shingles) in adults aged 50 years and older.
Large B-cell Lymphoma	Oct 2017	YESCARTA	Axicabtagene Ciloleucel	Second gene therapy available in the US for adults with large B-cell lymphoma.(Priority Review, Breakthrough Therapy Orphan drug)
Blood Screening	Oct 2017	cobas Zika	cobas Zika, Nucleic acid test for use on the cobas 6800/8800 systems	The first approval of a Zika virus detection test to screen donor samples for Zika virus RNA in plasma samples from individual human donors.
Acute Lymphoblastic Leukemia	Aug 2017	KYMRIAH	Tisagenlecleucel	First gene therapy available in the US for patients up to 25 years old with a form of acute lymphoblastic leukemia. (Priority Review, Breakthrough Therapy and Orphan drug)
Rabies Infection	Aug 2017	KEDRAB	Rabies Immune Globulin (Human)	For passive, transient post-exposure prophylaxis of rabies infection, given immediately after contact with a rabid animal and concurrently with full course of rabies vaccine.
Hereditary Angioedema	June 2017	HAEGARDA	C1 Esterase Inhibitor Subcutaneous (Human)	The first C1 Esterase Inhibitor for under the skin administration to prevent Hereditary Angioedema attacks in adolescent and adult patients.
Hemophilia B	May 2017	REBINYN	Coagulation Factor IX (Recombinant), GlycoPEGylated	Indicated for on-demand treatment and control of bleeding episodes, and for the perioperative management of bleeding in adults and children with hemophilia B.

Enhance Oversight

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.

Protect the Public Health from Infectious Disease

FDA collaborates with Department of Health and Human Services (DHHS) agencies, federal government partners, the WHO, National Regulatory Authorities, and stakeholders from the private and public sector to help ensure that blood, blood components, and HCT/Ps remain free of infectious agents and contaminants. This work helps decrease the spread of infectious disease, which may be spread through contact with infected individuals, travel to endemic areas, arthropod vectors, risk behaviors, and many other mechanisms.

Figure 7 is a graphic of Infectious Diseases and their Global Impact.[40]

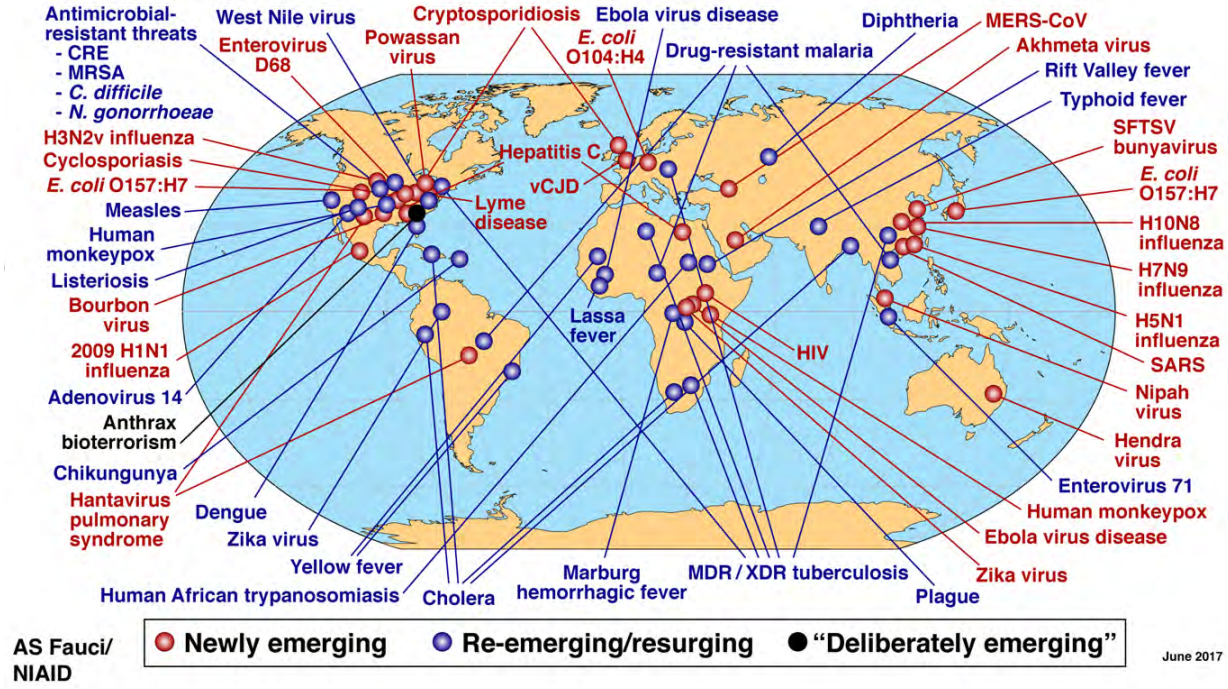

Figure 7 Infectious Diseases Globally

FDA has been working aggressively to combat the Zika virus outbreak. 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. FDA is continuing to monitor the evolving scientific and epidemiologic data on Zika virus and will

[40] "Global Examples of Emerging and Re-Emerging Infectious Diseases." Dr. Anthony S. Fauci, MD. National Institute of Allergy and Infectious Disease (NIAID)

update guidances as necessary to protect the safety of our nation's supply of blood and human cells, tissues, and cellular and tissue-based products.


Figure 8 Blood Donation

In October 2017, FDA approved the Roche Molecular Systems cobas Zika test, the first FDA-licensed donor screening test for Zika. The test is intended for use by blood collection establishments to detect Zika virus in blood donations, and for testing living organ donors, not for the individual diagnosis of Zika virus infection. Prior to this approval, several blood collection establishments used the cobas Zika test under IND to follow the recommendations in the FDA's 2016 guidance document. The approval is the result of a commitment by the manufacturer to work rapidly and collaboratively with the FDA and the blood collection industry to respond to a public health crisis and ensure the safety of blood in the U.S. and its territories.

In April 2017, FDA, in collaboration with the blood collection industry, the National Heart, Lung and Blood Institute, the Department of Defense and the Department of Health and Human Services, held a public workshop on emerging tick-borne diseases and blood safety. The workshop addressed tick-borne pathogens that continue to emerge as threats to blood safety, the effectiveness of current and potential mitigation strategies, and approaches to decision making on blood safety interventions.

Transfusion-transmitted babesiosis has emerged as a significant risk to the US blood supply. Human babesiosis is a disease transmitted primarily through tick vectors caused by Babesia microti, which is a rodent parasite. In response to this threat, FDA scientists developed a highly sensitive enzyme immunoassay test based on novel antigens for screening blood donors against Babesia microti, the causative agent of human babesiosis. B. microti is endemic prevalent in many parts of northeastern United States and is the most prevalent top ranking transfusion-transmissible infection for which no licensed donor screening test is available.

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 to gather scientific evidence on the feasibility of moving from the existing time-based deferrals related to risk behaviors as recommended in FDA's December 2015 guidance to alternative options, including the use of individual risk assessments. FDA presented a summary of responses submitted to the docket at its April 2016 Blood Products Advisory Committee meeting. FDA will assess the impact of current donor deferral recommendations and continue to gather the scientific evidence necessary for any future policy change.

Each year, FDA, WHO, CDC and other public health experts collaborate on the review of influenza disease surveillance and laboratory data collected from around the world to identify influenza strains that may cause the most illness in the upcoming season. Based on that information and the recommendations of FDA's Vaccines and Related Biological Products Advisory Committee (VRBPAC), which met on March 9, 2017, FDA selected the strains that should be included in the influenza virus vaccines for the 2017-2018 northern hemisphere influenza season. On October 4th, the VRBPAC met to select the strains to be included in an influenza virus vaccine for the 2018 southern hemisphere influenza season.

After the Ebola outbreak of 2014, it was recognized that the regulatory capacity and public health preparedness needed to be strengthened in African Countries. FDA worked with the WHO-coordinated committee African Vaccine Regulatory Forum to help revitalize the regional network to facilitate development and licensure of priority medical products in the region and increase capacity and preparedness to address future public health emergencies.

Selected Guidances in 2016 – 2017

Below are selected recent guidances issued by CBER, listed in date order. These guidances help address various issues.[41]

Date	#	Title	Description
Nov 2017	FDA-2017-D-6146-0001	Regulatory Considerations for Human Cell, Tissues, and Cellular and Tissue-Based Products: Minimal Manipulation and Homologous Use; Guidance for Industry and Food and Drug Administration Staff	Intended to improve stakeholders' understanding of the definitions of minimal manipulation and homologous use in FDA's regulations. Finalizes two draft guidances and certain material related to adipose tissue.
Nov 2017	FDA-2014-D-1584-0221	Same Surgical Procedure Exception under 21 CFR 1271.15(b): Questions and Answers Regarding the Scope of the Exception	Finalizes draft guidance dated October 2014, as well as, certain material related to adipose tissue that was included in the draft guidance from December 2014 (Adipose Draft Guidance).
Nov 2017	FDA-2017-D-6154-0001	Evaluation of Devices Used with Regenerative Medicine Advanced Therapies; Draft Guidance for Industry	When finalized, will provide information of Agency's current thinking of concepts related to evaluation of devices used in the recovery, isolation, and delivery of RMATs.
Nov 2017	FDA-2013-D-0575-0036	Expedited Programs for Regenerative Medicine Therapies for Serious Conditions; Draft Guidance for Industry	Provides information about expedited programs available for certain regenerative medicine therapies, including the Regenerative Medicine Advanced Therapy (RMAT) designation program established in the Cures Act.
Sep 2017	FDA-2015-D-4386-0011	Deviation Reporting for Human Cells, Tissues, and Cellular and Tissue-Based Products Regulated Solely Under Section 361 of the Public Health Service Act and 21 CFR Part 1271	Provides establishments manufacturing non-reproductive human cells, tissues, and cellular and tissue-based products (HCT/Ps) regulations and recommendations to comply with requirements to investigate and report HCT/P deviations.

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

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

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 Current Good Manufacturing Practices 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.

In August 2017, the U.S. Marshals Service seized five vials of Vaccinia Virus Vaccine (Live) – a vaccine that is reserved only for people at high risk for smallpox, such as some members of the military. The seizure came after FDA inspections at two stem cell clinics confirmed that the vaccine was used to create an unapproved stem cell product (a combination of excess amounts of vaccine and stromal vascular fraction – stem cells derived from body fat). The vaccine was then administered to cancer patients with potentially compromised immune systems and for those whom the vaccine posed a potential for harm, including myocarditis and pericarditis (inflammation and swelling of the heart and surrounding tissues). The unproven and potentially dangerous treatment was being injected intravenously and directly into patients' tumors.

In addition, Warning Letters were issued to two manufacturers of human cells, tissues, and cellular and tissue-based products (HCT/Ps) and one medical device manufacturer because their distributed products lacked appropriate FDA marketing authorization.

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 advance the use of real world experience, including large databases, from healthcare providers, insurers, and other partners to identify safety problems associated with biologic product use. In FY 2017 CBER launched a new pilot program, the Biologics Effectiveness and Safety system, as part of Sentinel to expand its use of electronic health record data in conducting post-market surveillance of biologic products in a more cost-effective and rapid manner. Using real world evidence may allow for a more comprehensive approach to product safety surveillance and help inform drug development and, as appropriate, regulatory decision making.

FDA, in collaboration with the National Heart Lung and Blood Institute and the DHSS Office of the Assistant Secretary launched the Transfusion Transmissible Infections Monitoring System (TTIMS) to help assure the continued safety of the US blood supply and monitor the effects of FDA's policy changes regarding donor deferral. TTIMS contractors are actively monitoring over 50 percent of the U.S. blood supply for HIV, hepatitis B virus and hepatitis C virus and conducting HIV recency testing.

Under FDASIA and the Drug Quality and Security Act, FDA gained additional authorities to enhance product safety through monitoring of drug shortages, including shortages of biologics products. For CY 2017, the Biologics Program has documented 4 new drug product shortages,

13 prevented shortages, 3 ongoing shortage, 50 notifications from 23 different manufacturers. CBER has used regulatory flexibility to prevent or mitigate 2 shortages, and expedited 16 reviews to prevent or mitigate a shortage.

As an active member of the AABB Interorganizational Task Force on Domestic Disasters and Acts of Terrorism, CBER worked proactively with the blood collection industry and device manufacturers to ensure the availability of blood and blood components in areas of the continental U.S., Puerto Rico, and the Virgin Islands impacted by the hurricanes in 2017.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2015 Actual	$326,290,000	$211,362,000	$114,928,000
FY 2016 Actual	$329,156,000	$215,308,000	$113,848,000
FY 2017 Actual	$340,016,000	$215,443,000	$124,573,000
FY 2018 Annualized CR	$358,025,000	$213,854,000	$144,171,000
FY 2019 President's Budget	$403,268,000	$251,854,000	$151,414,000

BUDGET REQUEST

The FY 2019 Budget Request for the Biologics Program is $403,268,000, of which $251,854,000 is budget authority and $151,414,000 is user fees. This level provides a net increase of $45,243,000. Budget authority increases by $38,000,000 compared to the FY 2018 Annualized CR level and user fees increase by $7,243,000. The Center for Biologics Evaluation and Research (CBER) amount in this request is $360,492,000. The Office of Regulatory Affairs amount is $42,776,000.

The FY 2019 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 expedite the use of advanced technologies and methods to facilitate product development, production, and regulatory decision-making, such as newly identified clinical biomarkers, innovative clinical trial designs, and continuous manufacturing methodology for a broad range of complex and life-threatening diseases.

FDA will work to reduce review times and regulatory burden by enhancing FDA-sponsor communications in its user fee programs and continuing to use FDA's expedited programs such as the RMAT Designation, Fast Track Designation, Breakthrough Therapy Designation, Accelerated Approval, and Priority Review. These programs help expedite the development and review of innovative biological products, many of which address unmet medical needs in patients with rare, serious, or life-threatening conditions without compromising FDA's high standards for demonstrating the safety, efficacy, and quality of new medicines.

FDA will continue to protect the public against the threats of emerging infectious diseases and bioterrorism, including facilitating the development of prophylactic and therapeutic biologics and vaccines. Infectious diseases are not only spreading faster; they appear to be emerging more quickly than ever before. Since the 1970s, over 40 infectious diseases have been discovered. 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 current and emerging public health needs and meet ever-changing scientific and technological advancements. This program has helped CBER keep pace with the tremendous scientific advancements being made in the field.

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. This collaboration helps facilitate global access to vaccines and biological products that address critical health needs, including promoting research and sharing information to address global diseases and emerging threats impacting human populations. FDA also strategizes to harmonize existing regulatory standards and works with international scientific efforts to establish and maintain reference materials and standards for biologics.

To foster manufacturing innovation, flexibility, and adaptation, FDA will work in collaboration with federal partners and with input from regulated industry to develop or modernize regulations and guidances. These regulations and guidances range from protecting the blood and tissue supplies in the face of emerging infectious diseases, to addressing recent statutory mandates, to expediting the use of advanced technologies. The Biologics Program will continue early engagement to identify and discuss scientific considerations and challenges to help inform the development of biological products.

FDA will advance the use of real-world experience including large databases from healthcare providers, insurers, and other partners, to identify safety problems associated with biologic product use in a cost-effective and rapid manner. Using real world evidence may allow for a more comprehensive approach to product safety surveillance, and help inform drug development and, as appropriate, regulatory decision-making. Working with others in FDA, CBER will also support the 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

Medical Product Safety (+38 million / 8 FTE)

Promote Domestic Manufacturing: Advancing Modern Drug and Biological Product Manufacturing Technologies, Through the Development of Efficient Regulatory Pathways Center: +$15 million / 4 FTE

The budget increase will allow FDA to support new efforts to foster more investment and innovation in the development and creation of more modern, domestically-based manufacturing to improve the agility, flexibility, cost, and reliability of manufacturing processes. This includes continuous manufacturing of biological products, including vaccines and cell and gene-based therapies. With continuous manufacturing platforms, vaccine supply can be more easily ramped up on short notice, and certain vaccines can be rapidly modified to address infectious diseases, such as the flu. The application of this kind of enabling technology to vaccine production has long been a strategic priority for the U.S. Equipped with a robust scientific understanding of the requirements and the impact of these advanced manufacturing technologies, FDA can help industry make investments in these new technologies and grow these opportunities.

By developing a science-based framework that provides clarity for how products developed in these systems will be evaluated, and by funding research, development and testing of the enabling technologies, the agency can help reduce the cost and uncertainty of adopting these new manufacturing platforms, essentially de-risking them for adoption by industry. FDA would lead stakeholders in the development of clear scientific standards, policy, and guidance to support the effective and efficient adoption of these new manufacturing platforms, including the new inspectional methods they will require.

Create a New Medical Data Enterprise: Advance the Use of Real-World Evidence to Improve Human and Animal Health and Support Pre-Market Evaluation and Post-Market Safety

Center: +$23 million / 4 FTE

FDA will advance the use of real-world experience to better inform patient care and provide more efficient, robust, and potentially lower-cost ways to develop clinical information that can inform product review and promote innovation. FDA will establish a new capability, including the development of data and analytical tools, to conduct near-real-time evidence evaluation down to the level of individual electronic health records in a broad range of U.S. healthcare settings. FDA will also further explore the use of natural language processing and artificial intelligence to rapidly process information such as adverse event reports, allowing signal detection. Expanding FDA's capacity to utilize real-world evidence to evaluate the pre- and post-market safety and effectiveness of medical products would generate processes that could improve the efficiency of the regulatory process, better inform patients and providers about pre-and post-market safety, reduce some of the burdens that drive up the time and cost required to bring beneficial innovations to the market and address barriers that can make certain important safety and effectiveness information around the real-world use of products hard to collect and evaluate.

USER FEES

Current Law User Fees: +$7.243 Million

Center: +$7.164 million / Field: +$0.079 million

The Biologics Program request includes an increase of $7,243,000 for user fees authorized under FDARA, which will allow FDA to fulfill its mission of promoting and protecting the public health by ensuring safety and efficacy of medical products and accelerating innovation in the industry.

PERFORMANCE

The Biologics Program's performance measures focus on biological product review, manufacturing diversity and capacity for influenza vaccine production, strengthening detection and surveillance of FDA-regulated products and postmarket inspections 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 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
233207: Review and act on standard New Molecular Entity (NME) New Drug Application (NDA) and original BLA submissions within 10 months of the 60 day filing date. *(Output)*	FY 2016: 100% Target 90% (Target Exceeded)	90%	90%	Maintain
233208: Review and act on priority NME NDA and original BLA submissions within 6 months of the 60 day filing date. *(Output)*	FY 2016:100% Target 90% (Target Exceeded)	90%	90%	Maintain
233205: Complete review and action on complete blood bank and source plasma BLA submissions within 12 months after submission date. *(Output)*	FY 2016: NA (No submissions received)	90%	90%	Maintain
233206: Complete review and action on complete blood bank and source plasma BLA supplements within 12 months after submission date. *(Output)*	FY 2016: 99% Target: 90% (Target Exceeded)	90%	90%	Maintain
233211: Review and act on new non-user fee, non-blood product applications within 12 months of receipt. *(Output)*	FY 2016: 67% Target: 60% (Target Exceeded)	60%	60%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
234101: Increase manufacturing diversity and capacity for influenza vaccine production. *(Output)*	FY 2017: 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
231301: Percentage of Lot Distribution Reports that were entered into the Regulatory Management System - Biologics License Applications (RMS-BLA) within 7 Days.	FY 2017: 99% Target 85% (Target Exceeded)	85%	85%	Maintain
234212: Percentage of planned registered domestic blood bank and biologics manufacturing inventory inspections. (Output)	FY 2017: 106% Target: 99% (Target Exceeded)	95%	95%	Maintain
234213: Percentage of planned human foreign and domestic tissue establishment inspections. (Output)	FY 2017: 100% Target: 82% (Target Exceeded)	85%	85%	Maintain

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 2017, 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. A second international collaborative study comparing several alternative methods and involving multiple manufacturers and regulatory agencies was completed in FY 2017. Methods developed at CBER, including antibody capture-ELISA and receptor-binding assays, were shown to be feasible for quantifying H3N2 and influenza B hemagglutinin (HA) in vaccines. Additional development work on these methods is planned for FY 2018 and future years.

FDA continued evaluation of methods to assess the relative yields of candidate vaccine viruses. FDA investigated several methods to increase the yields of candidate vaccines by targeted manipulation, both for potential pandemic influenza vaccine viruses, such as H7N9 vaccine reference virus and seasonal influenza vaccine candidates. In particular, H7N9 candidate vaccine viruses, and seasonal influenza B candidate vaccine viruses produce relatively low influenza HA yields compared to other high yield seasonal vaccine viruses. Additional development work for H7N9 and influenza B candidate vaccine viruses is planned for FY 2018 and future years.

New ORA Field Performance Measures

ORA has been working to improve the field performance measures to better aligned with ORA's Program Alignment initiative. In this submission, ORA has completed the process of adjusting the performance goals, so that the FY 2018 and FY 2019 targets now complete a certain percentage of the planned inspections in ORA's annual Workplan. The ORA Workplan is the necessary mechanism that takes into account all the complex variables (geography, commodity, risk, availability, efficiency, etc.) that allows ORA to plan which inspections to do. With these newly formulated performance goals, ORA is committing to complete a certain percentage of the initially planned inspections. This revision strengthens the importance of the Workplan, but allows the flexibility to respond dynamically to changing circumstances during the year, to better handle emerging risks and evolving public health priorities (i.e. the heavy hurricane damage this past year). This is a significant departure from the previous performance goals, so FY 2018 will be an important year in resetting the new baselines. Also, since the targets are now based on a planned number of inspections, it is possible to inspect more than what was planned and thus have an actual inspection rate over 100%.

PROGRAM ACTIVITY DATA

CBER Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
Original Biologics License Applications (BLA)			
Workload [1]	20	20	20
Total Decisions [2]	74	36	36
Approved	33	33	33
BLA Efficacy Supplements			
Workload [1]	17	17	17
Total Decisions [2]	46	46	46
Approved	37	37	37
BLA Manufacturing Supplements			
Workload [1]	1,322	1,322	1,322
Total Decisions [2]	1,441	1,441	1,441
Approved	1,239	1,239	1,239
BLA Labeling Supplements			
Workload [1]	142	142	142
Total Decisions [2]	113	113	113
Approved	105	105	105
Original New Drug Application (NDA)			
Workload [1]	0	1	1
Total Decisions [2]	1	1	1
Approved	1	1	1
NDA Efficacy Supplements			
Workload [1]	0	1	1
Total Decisions [2]	0	1	1
Approved	0	1	1
NDA Manufacturing Supplements			
Workload [1]	24	24	24
Total Decisions [2]	23	23	23
Approved	18	18	18
NDA Labeling Supplements			
Workload [1]	1	1	1
Total Decisions [2]	1	1	1
Approved	1	1	1
Original Abbreviated New Drug Application (ANDA)			
Workload [1]	0	1	1
Total Decisions [2]	1	1	1
Approved	0	1	1
ANDA Efficacy Supplements			
Workload [1]	0	0	0
Total Decisions [2]	0	0	0
Approved	0	0	0

CBER Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
ANDA Manufacturing Supplements			
Workload [1]	1	1	1
Total Decisions [2]	3	3	3
Approved	2	2	2
ANDA Labeling Supplements			
Workload [1]	0	1	1
Total Decisions [2]	0	1	1
Approved	0	1	1
Device 510Ks			
Workload [1]	53	53	53
Total Decisions [2]	57	57	57
Final Decision - SE	39	39	39
Device Premarket Applications (PMA)			
Workload [1]	4	4	4
Total Decisions [2]	5	5	5
Approved	2	2	2
Device Premarket Applications (PMA) Supplements			
Workload [1]	59	59	59
Total Decisions [2]	65	65	67
Approved	17	17	17
Investigational New Drugs (IND)			
Receipts: IND (new)	456	456	456
Receipts: IND Amendments	10,848	10,848	10,848
Total Active IND [3]	2,624	2,624	2,624
Investigational Device Exemptions (IDE)			
Receipts: IDE (new)	17	17	17
Receipts: IDE Amendments	384	384	384
Total Active IDE [3]	161	161	161
Patient Safety			
Adverse Event Reports Received [4]	65,000	65,000	65,000
Biological Deviation Reports Received	52,250	50,000	50,000
Sponsor Assistance Outreach			
Meetings	453	453	453
Final Guidance Documents [5]	30	30	30
Admin/Management Support			
Advisory Committee Meetings Held	8	13	13
FOI Requests Processed	265	320	320

[1] Workload includes applications received and filed.

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

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

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

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

Field Biologics Program Activity Data (PAD)

Field Biologics Program Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,835***	***1,892***	***1,892***
Bioresearch Monitoring Program Inspections	75	100	100
Blood Bank Inspections	872	900	900
Source Plasma Inspections	192	190	190
Pre-License, Pre-Market Inspections	77	55	55
GMP Inspections	33	28	28
GMP (Device) Inspections	2	7	7
Human Tissue Inspections	621	650	650
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS	***67***	***47***	***47***
Bioresearch Monitoring Program Inspections	22	11	11
Foreign Human Tissue Inspections	0	0	0
Blood Bank Inspections	7	7	7
Pre-License, Pre-market Inspections	5	7	7
GMP Inspections (Biologics & Device)	33	20	20
TOTAL UNIQUE COUNT OF FDA BIOLOGIC ESTABLISHMENT INSPECTIONS	***1,902***	***1,939***	***1,939***
IMPORTS			
Import Field Exams/Tests	197	45	45
Import Line Decisions	157,080	168,076	179,841
Percent of Import Lines Physically Examined	0.13%	0.03%	0.03%
GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,902***	***1,939***	***1,939***

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ANIMAL DRUGS AND FEEDS

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
Animal Drugs and Feeds	**195,042**	**190,879**	**187,348**	**225,065**	**37,717**
Budget Authority	***162,835***	***162,852***	***161,729***	***180,284***	***18,555***
User Fees	***32,207***	***28,027***	***25,619***	***44,781***	***19,162***
Center	128,876	126,217	121,808	158,894	37,086
Budget Authority	98,205	98,205	97,538	115,673	18,135
User Fees	30,671	28,012	24,270	43,221	18,951
Animal Drug (ADUFA)	*20,879*	*17,977*	*15,890*	*26,971*	*11,081*
Animal Generic Drug (AGDUFA).	*9,792*	*10,035*	*8,268*	*16,138*	*7,870*
Third Party Auditor Program	---	---	*112*	*112*	---
Field	66,166	64,662	65,540	66,171	631
Budget Authority	64,630	64,647	64,191	64,611	420
User Fees	1,536	15	1,349	1,560	211
Animal Drug (ADUFA)	*427*	*15*	*307*	*427*	*120*
Animal Generic Drug (AGDUFA).	*302*	---	*235*	*326*	*91*
Food Reinspection	*807*	---	*807*	*807*	---
FTE	**942**	**942**	**959**	**1,043**	**84**

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).

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

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

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 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 accomplishes its public health responsibilities by evaluating new animal drug applications for safety and effectiveness, monitoring animal drugs,

animal foods, and animal devices on the market, reviewing animal food additives for safety and utility, and conducting research. The 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.

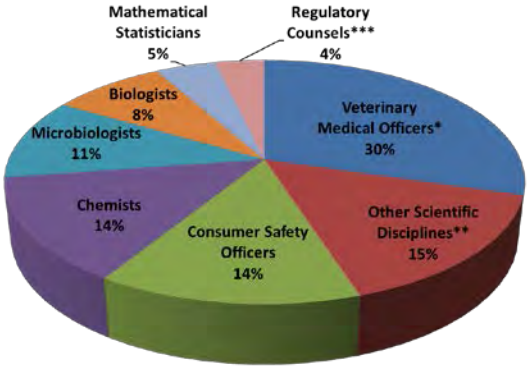

Figure 9 Scientific Disciplines at CVM

FDA's Animal Drugs and Feeds Program is administered by the Center for Veterinary Medicine (CVM) and is part of the Foods and Veterinary Medicine (FVM) Program. The FVM Program also includes the Foods Program, administered by the Center for Food Safety and Applied Nutrition (CFSAN), and a portion of the field activities performed by the Office of Regulatory Affairs (ORA). A combination of appropriations and user fee programs fund the regulatory process to ensure premarket drug safety and effectiveness and postmarket oversight of CVM regulated products.

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 new animal drug review processes to support the timeliness and efficiency of pioneer and generic new animal drug reviews. The Export Certificate program[42] helps promote the export of products marketed in the U.S. that are acceptable to the importing country.

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

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.

Animal Drug Review

The Animal Drugs and Feeds Program increases the availability and variety of safe and effective, quality manufactured and properly labeled animal drug products to support the health of food-producing, exotic, and pet (companion) animals, including minor species. The Program evaluates new animal drugs[43] to determine if they meet the safety and effectiveness standard necessary to obtain legal marketing status, including human food safety for food-producing animals, through a new animal drug approval, conditional approval, or index listing.

[42] For more information on the Export Certificate program, see: https://www.fda.gov/animalveterinary/newsevents/cvmupdates/ucm461415.htm

[43] For more information on new animal drug applications, see https://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/NewAnimalDrugApplications/default.htm

The animal drug and animal generic drug user fee acts require FDA to meet timeframes for review and action on 90 percent of new animal drug applications each fiscal year and FDA consistently exceeds these performance goals. In FY 2016, FDA completed review and action on 99.4 percent of pioneer drugs, or original New Animal Drug Applications (NADAs) and reactivations, and 98.1 percent of generic drugs, or original Abbreviated New Animal Drugs Applications (ANADAs) and reactivations.

In addition, the Animal Drugs and Feeds Program created a novel process, working with animal drug sponsors, for bringing innovative technologies and alternatives to antimicrobials to the marketplace. Over the last several years there has been an increase in the number of animal drug products brought forth by sponsors for review in the drug evaluation process. These new animal drug products come from both existing animal drug sponsors as well as sponsors new to the animal drug market. The increase in new animal drug products has contributed to an increase in the number of submitted applications for many novel drug classes and novel indications for both food-producing animals and companion animals.

FDA has been very active in the international arena working to enhance harmonization and collaboration with international organizations, other countries' regulatory agencies and regulated industry. For example, through the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) process, FDA has harmonized with over 55 guidelines describing regulatory requirements for the evaluation of new animal drug products with the European Union, Japan, Canada, Australia, New Zealand, South Africa, and the United States. This enables the animal drug industry to conduct studies that can be used for animal drug applications or registration in all member countries instead of having to conduct multiple studies to meet each country's regulatory requirements. This increases the availability of safe and effective animal drugs internationally and may lower the cost of drug development for drug sponsors.

FDA also partners with Health Canada through the U.S.-Canada Regulatory Cooperation Council (RCC), a council that works to minimize regulatory differences and duplicative procedures between the two countries, thereby providing more timely access to animal drug products on both sides of the border. FDA and Health Canada have simultaneously reviewed and approved 8 applications under the RCC program and the program continues to grow with 16 products currently under simultaneous review.

In June 2017, FDA launched the Phase 2 redesign of the *Animal Drugs @ FDA website*[44], continuing efforts to improve transparency and public access to information about approved new animal drugs. This redesign creates a one-stop-shop for veterinarians, pet owners, animal producers, and others to get information about approved animal drugs via a searchable database that includes Freedom of Information Summaries, Environmental Assessments, and Green Book Reports. The Green Book includes a list of all new animal drug product approvals and certain information regarding patents held for new animal drugs or their method of use.

Fostering Innovation in Animal Drugs

This is a period of exceptional innovation in American agriculture with the increasing development and use of innovative technologies. These innovations present the Animal Drugs

[44] For more information about the redesign of Animal Drugs @ FDA, go to: https://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm562359.htm

and Feeds Program with the challenge of assuring the public that human, animal, and environmental health are being safeguarded, while at the same time taking care that the regulatory process does not stifle the development of significant and beneficial technology. To address this challenge the Animal Drugs and Feeds Program has worked to define human and animal safety and effectiveness risks that must be addressed during the new animal drug development and application process.

FDA is currently considering public comments received on draft revised Guidance for Industry (GFI) #187, *Regulation of Intentionally Altered Genomic DNA in Animals*. GFI #187 outlines a risk based approach that animals with intentionally altered genomic DNA, including genetically engineered (GE) animals and animals developed using genome-editing technology, are regulated under FDA's new animal drug authorities. This is because the altered DNA is intended to affect the structure or function of the animal and, therefore, meets the definition of a drug. In October 2017, GFI #236, *Clarification of FDA and EPA Jurisdiction Over Mosquito-Related Products* was released. It clarifies which mosquito-related products are regulated by FDA and which are regulated by the Environmental Protection Agency (EPA) based on intended use associated with the product.

The Animal Drugs and Feeds Program has approved applications for recombinant DNA (rDNA) constructs in AquAdvantage Salmon, an Atlantic salmon that is genetically engineered to reach a growth marker important to the aquaculture industry faster than its non-GE counterparts, and domesticated goats that express in their mammary glands the human gene for antithrombin (which is intended for treatment in humans). The Animal Drugs and Feeds Program also approved an application for an rDNA construct in GE chickens that produce a recombinant form of human lysosomal acid lipase (LAL) protein in their egg whites, while the Human Drugs Program simultaneously approved Kanuma (sebelipase alfa), the human therapeutic biologic that is purified from those egg whites. Kanuma is the first treatment for humans with a rare disease known as LAL deficiency, which can lead to liver disease, cardiovascular disease, and other complications. The approval of Kanuma resulted from collaboration between FDA's Animal Drugs and Feeds Program and Human Drugs Program.

The Animal Drugs and Feeds Program is creating a more predictable and efficient pathway through the regulatory process to the marketplace for sponsors of intentionally genetically altered (IGA) animals. These more clearly defined processes help eliminate uncertainty for drug sponsors, and empower small and large businesses to venture into the development and marketing of IGAs. The Animal Drugs and Feeds Program anticipates a future with an increasing number of sponsors engaging in the development of IGAs, resulting in a growing number of safe, effective, and innovative IGA animals coming to market.

Another emerging technology is cell therapy, including stem cell therapy, for animals. The FDA published GFI #218 *Cell-Based Products for Animal Use*[45] to enable the stem cell industry to understand the varying levels of public health concern for different categories of therapies and the associated regulatory considerations. Publication of this guidance, as well as public outreach, has resulted in sponsors establishing investigational new animal drug files and working towards approval. FDA has worked on developing predictable, efficient pathways for these therapies. These efforts include developing guidance on donor eligibility and good manufacturing practices

[45] For more information on GFI #218, see: https://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM405679.pdf

specific to cell-based products. FDA anticipates interest in stem cell therapies will continue to grow with a similar increase in the number of sponsors and applications they submit to the Agency and is planning on this growth.

Animal Drug Inspections

FDA's Office of Regulatory Affairs (ORA) conducts preapproval inspections to support the review of applications for pioneer and generic new animal drugs. To help ensure the integrity of scientific testing and the reliability of clinical and non-clinical submission data, FDA also conducts bioresearch monitoring (BIMO) inspections of study facilities, clinical investigators, institutional review boards, and contract research organizations that submit data to FDA.

Post-approval, ORA conducts inspections of manufacturing establishments of marketed products to determine their ability to manufacture products to the specifications stated in their applications, and to ensure compliance with current good manufacturing practice requirements (CGMPs). FDA also inspects non-clinical laboratories that conduct testing to determine whether Good Laboratory Practices have been followed. Accurate test results are essential to the review and approval of new animal drugs, and helps to ensure that the rights and welfare of animals are protected.

Animal Food Safety

FDA reviews animal food additive petitions (FAP), generally recognized as safe (GRAS) notices, and animal food labels and labeling; monitors and establishes standards for feed contaminants; and directs the medicated animal feed and pet food programs to ensure the health and safety of livestock, poultry, fish, and other animals, including pets. Before marketing a new animal food additive or using an approved animal food additive in a new manner, a manufacturer or other sponsor must petition the FDA for its approval. Food additives used in animal foods are generally intended to supply nutrients, add aroma/flavor, aid stability or alter a food's characteristics. In FY 2017, FDA performed 99 animal FAP reviews and 80 reviews for investigational food additive files.

Substances that are GRAS for an intended use in food are not considered food additives. In FY 2017, FDA's GRAS final rule[46] went into effect, amending and clarifying the criteria used to determine if the use of a substance in food for humans or animals is not subject to the premarket approval requirements of the FD&C Act. The rule will help stakeholders to draw more informed conclusions about whether the intended conditions of use of a substance complies with the FD&C Act. While a voluntary program, manufacturers that submit animal food GRAS notices to FDA also benefit from clearer instructions on the GRAS notification process, which leads to more efficient reviews by FDA. FDA and the public benefit by having further information about the safety of the substances in the human and animal food supplies as more notices are filed with the Agency.

FDA evaluates safety information on new plant varieties (including genetically engineered plants) for food use submitted by developers of these technologies. In this process, a developer who intends to commercialize a bioengineered food may meet with the Agency to identify and discuss relevant safety, nutritional, or other regulatory issues regarding the bioengineered food in

[46] For more information on the GRAS final rule, see https://www.federalregister.gov/documents/2016/08/17/2016-19164/substances-generally-recognized-as-safe

an initial consultation. With or without an initial consultation, a developer may submit to FDA a summary of its scientific and regulatory assessment of the food. These submissions are designated biotechnology notification files. Many of these foods become a part of the animal food supply, and these evaluations assist the Agency in ensuring the safety of animal food.

Minor Use Minor Species

The Minor Use and Minor Species (MUMS) Animal Health Act, passed in 2004, helps FDA ensure that pharmaceuticals become available for animal species that are not major species (cattle, swine, chickens, turkeys, dogs, cats, horses). This law helps to increase the availability of drugs for minor species, including everything from farmed animals, like sheep and salmon, to zoo animals, like elephants. It also covers minor uses (rare diseases) in the major species, such as treating many types of cancer in dogs. Greater access to these "MUMS drugs" gives veterinarians more options for treating a wide range of unique species and uncommon conditions in major species.

One provision created a new pathway called "Conditional Approval" to incentivize bringing MUMS drugs to the marketplace. The conditional approval is valid for one year (and renewable for another four) and allows the drug company to legally sell the animal drug before proving it meets the "substantial evidence" standard of *effectiveness* for full approval. Drug *safety* must have been demonstrated to the full approval standard prior to marketing.

Another provision allows sponsors to apply for "Designation" status for MUMS drugs, which is a status similar to "orphan drug" status for human drugs. This gives sponsors eligibility to apply for grants to support their studies, and provides seven years of exclusive marketing rights following approval or conditional approval. To date, FDA has granted 139 MUMS drug designations.

In some cases, an animal drug needed for use in a species that is too rare or too varied to be the subject of the adequate and well controlled studies needed to support a drug approval can be legally marketed. In such cases, FDA may use an alternative process strictly limited to non-food minor species to add the drug to the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species (the Index). As of July 2017, FDA has a total of 13 animal drugs on the Index, and in September 2017, FDA published draft GFI #210, *The Index of Legally Marketed Unapproved New Animal Drugs for Minor Species*, describing this process in more detail.

Selected Product Approvals in 2017

Below are some of the most recent Animal Drugs and Feeds Program significant product approvals during calendar year 2017. 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 list does not represent any degree of importance or priority ranking.[47]

[47] For more information on product approvals and designations, visit http://www.fda.gov/NewsEvents/ProductsApprovals/

Date	Product Name	Purpose or Benefit
October 2017	Inteprity and Maxiban	For use in broiler chickens for the prevention of mortality caused by necrotic enteritis associated with *Clostridium perfringens* and for the prevention of coccidiosis caused by *Eimeria necatrix, E. tenella, E. acervulina, E. brunetti, E. mivati,* and *E. maxima.*
September 2017	Sentinel Spectrum	This supplement provides for the addition of the treatment and control of adult tapeworm *(Dipylidium caninum)* infections in dogs and puppies two pounds of body weight or greater and six weeks of age and older.
July 2017	Aivlosin	For use in swine for the addition of an indication for the control of Swine Respiratory Disorder (SRD).
July 2017	Banamine Transdermal	For use in certain calsses of cattle for the control of pyrexia associated with bovine respiratory disease and the control of pain associated with foot rot.
July 2017	Altren	For use in horses for the suppression of estrus in mares.

Selected Guidances Issued in 2017

Below are some GFIs issued by the Animal Drugs and Feeds Program in calendar year 2017.[48]

Date Issued	Docket #	Title	Description
October 2017	FDA-2016-D-44482	CVM GFI #236, *Clarification of FDA and EPA Jurisdiction Over Mosquito-Related Products"*	Provides information regarding regulatory oversight of mosquito related products, clarifying circumstances under which such products are regulated by the FDA as new animal drugs or by the EPA as pesticides.
September 2017	FDA-2017-D-2462	CVM Draft GFI #210, *"The Index of Legally Marketed Unapproved New Animal Drugs for Minor Species"*	Describes the process for adding a new animal drug to the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species (the Index). The Index is available for new animal drugs intended for use in minor species.

[48] For more information on FDA guidances, please visit http://www.fda.gov/RegulatoryInformation/Guidances

August 2017	FDA-2016-D-1248	CVM GFI #237, *"Oncology Drugs for Companion Animals"*	Makes recommendations to sponsors of investigational oncology drugs for use in companion animals (e.g., dogs, cats, and horses) on the target animal safety, effectiveness, and labeling technical sections of an NADA for oncology drugs administered as single agents.
August 2017	FDA-2015-D-1804	CVM GFI #232, *"Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: General Approach to Establish an Acute Reference Dose (VICH GL54)"*	Addresses the nature and types of data that can be useful in determining a toxicological acute reference dose (ARfD) for residues of veterinary drugs, the studies that may generate such data, and how the ARfD may be calculated based on these data.

Enhance Oversight

FDA's Animal Drugs and Feeds Program conducts surveillance of post-market product use to identify and rapidly respond to public health emergencies and product safety concerns. The surveillance activities provide oversight of production, manufacturing, and the global supply chain to ensure that consumers can have confidence in the products they buy.

Modernizing Food and Feed Safety

FDA faces unique challenges in the area of food and feed safety in the 21st Century, in part driven by globalization and the increasing complexity of international production and supply chains. Recognizing the urgent need to meet these challenges, in 2011 the Food Safety Modernization Act (FSMA) was signed into law. FSMA directs FDA to enhance current food and feed safety systems based on the public health principles of comprehensive prevention, risk-based resource allocation, and public-private partnerships with the goal to minimize food safety hazards. The FVM Program Strategic Plan[49] provides a framework for implementing FSMA and places a high priority on preventing foodborne illness of known and unknown origins.

The FSMA regulation, "Current Good Manufacturing Practice and Hazard Analysis and Risk-Based Preventive Controls for Food for Animals" (PCAF regulation) was published in September 2015. This regulation requires facilities that manufacture, process, pack, or hold animal food to adhere to current good manufacturing practices (CGMPs) and implement hazard analysis and risk-based preventive controls. Animal food includes pet food, animal feed, and the raw materials and ingredients. In July 2016, FDA finalized the final rule "Amendments to Registration of Food Facilities" to extend and clarify compliance dates for the PCAF regulation. In September 2017, the compliance date for large facilities was reached. FDA developed training courses for these regulations and is in the process of developing a training course for the regulation on hazard analysis and risk-based preventive controls for animal food.

[49] For more information on the FVM Strategic Plan, see: http://www.fda.gov/aboutfda/centersoffices/officeoffoods/ucm273269.htm.

While the PCAF regulation is the primary regulation impacting the animal food industry, there are three other FSMA regulations that apply to animal food: "Foreign Supplier Verification Programs for Importers of Food for Humans and Animals," "Sanitary Transportation of Human and Animal Food," and "Accreditation of Third-Party Certification Bodies to Conduct Food Safety Audits and Issue Certifications." FDA continues to develop relevant GFIs and resources to help the animal food industry comply with the new FSMA requirements, including publishing the following:

- in October 2017, GFI #235 Current Good Manufacturing Practice Requirements for Food for Animals to help facilities determine whether they need to comply with the CGMP Requirements for animal food;
- in August 2017, GFI Clarification on Food Establishment Waiver from Requirements of the Sanitary Transportation of Human and Animal Food Rule which provides clarification on the scope of the waiver for food establishments that provide food directly to consumers; and
- in May 2016, draft GFI Qualified Facility Attestation Using Form FDA 3942a (for Human Food) or Form FDA 3942b (for Animal Food) to allow qualified facilities, such as small businesses, to comply with a set of modified requirements for the FSMA PC rule.

In FY 2017 the Animal Drugs and Feeds Program continued to proactively engage with industry and regulatory partners on FSMA by conducting nearly 30 listening sessions, webinar, or meetings on FSMA related regulations and guidance documents in order to foster understanding and help educate stakeholders on how to comply. The Program also participates in the FSMA Technical Assistance Network (TAN)[50], a central source for information and questions related to FSMA rules, programs, and implementation strategies.

Preventing and Responding to Animal Food Emergencies

FDA evaluates industry compliance with safety standards throughout the production and handling stages of the global animal food supply chain using FDA and State regulatory partners. The Animal Drugs and Feeds Program provides funds to support Veterinary Laboratory Investigation and Response Network (Vet-LIRN) activities. This network of 40 state and university veterinary diagnostic laboratories assists with investigations into potential problems with animal feeds and drugs, as well as the development of new tests to detect feed contaminants and illegal drugs.

In FY 2017, Vet-LIRN network laboratories and FDA conducted dozens of investigations into consumer complaints of illness or death potentially due to animal food. One such complaint reported that five dogs in a single household had suffered acute neurological symptoms shortly after eating their pet food. Vet-LIRN initiated an investigation that found pentobarbital, a barbiturate that is used to euthanize animals, in the stomach contents of one of the dogs and in the leftover pet food. FDA inspected the firm and also confirmed pentobarbital in samples from unopened product. FDA advised pet owners not to feed their animals the adulterated pet food, and soon after, the companies voluntarily recalled the products.[51]

[50] For more information on the FSMA Technical Assistance Network (TAN), see: https://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm459719.htm

[51] For more information on the investigation related to pentobarbital, see: https://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm542265.htm

For the past 10 years, FDA has been closely monitoring complaints of illness related to the consumption of jerky pet treats. Due to significant Agency efforts, including import alerts, extensive product and patient testing, communications to stakeholders, and other FDA actions, concerns over jerky pet treats have been sharply reduced, declining more than 95 percent from hundreds per month to fewer than 15 between January and June 2017. Although a number of illegal drugs, including antibiotics and antivirals, have been identified and triggered product recalls and import alerts, a single agent that would explain all of the reported illnesses has not been found. FDA continues to monitor and follow-up as needed on consumer complaints.

FDA also participates in several programs to ensure preparedness for food emergencies. The Food Emergency and Response Network (FERN) and Vet-LIRN actively participate in activities coordinated by the Integrated Consortium of Laboratory Networks (ICLN). The ICLN was established, as required by FSMA, to provide a nation-wide, integrated system of laboratory networks to assist in responding to national events requiring an integrated laboratory response. FDA's and other Agencies' networks participation ensures timely, credible, and interpretable data is provided in support of effective surveillance, early detection, and response to large-scale contamination or disease incidents.

Antimicrobial Resistance

In order to address the challenge of antimicrobial resistance associated with foodborne pathogens, the Animal Drugs and Feeds Program is committed to supporting responsible antimicrobial stewardship and to addressing public health concerns associated with antimicrobial resistance and the use of antimicrobial drugs[52] in animals. Implementing stewardship principles in veterinary settings requires a collaborative effort that includes a broad interdisciplinary set of stakeholders, including veterinary pharmaceutical and feed manufacturers and distributors, veterinarians, animal producers, academic organizations, food safety advocacy groups, and a number of Federal, State, and local agencies.

FDA's judicious use strategy is intended to slow the rate of development of antimicrobial resistance associated with the use of antimicrobial drugs in veterinary settings through antimicrobial stewardship. The strategy has accomplished the following:

- established a framework in GFI #209 for ending production uses of medically important antimicrobials and bringing the remaining therapeutic uses of such drugs in food-producing animals under veterinary oversight
- provided detailed guidance to drug sponsors in GFI #213 for voluntarily removing production claims for medically important antimicrobials
- defined in the Veterinary Feed Directive (VFD) final rule the process for authorizing use of VFD drugs, which are animal drugs intended for use in or on animal feed that require the supervision of a licensed veterinarian
- provided veterinarians in all states with a framework for authorizing the use of medically important antimicrobials in feed when needed for specific animal health purposes in the VFD Final Rule
- in January 2017, FDA completed a three-year initiative that prohibits the use of antimicrobial drugs for production purposes (e.g., growth promotion), and requires

[52] The use of "antimicrobial drugs" refers to medically important antimicrobial drugs (i.e., those important for treating human disease).

veterinary oversight for the use of these drugs in the feed or drinking water of food-producing animals.

The implementation of this three-year initiative is a significant milestone in national efforts to address the use of medically important antimicrobials in food-producing animals. FDA is committed to ongoing collaboration with key stakeholders to support antimicrobial stewardship.

In September 2016, FDA announced its intent to focus for the first time on antimicrobial drugs used in animal feed or water that lack a defined duration of use, has reviewed public feedback on this effort and is developing a cross-functional working group to determine next steps. FDA also published a set of key initiatives it will focus on over the next five years. Moving forward, FDA intends to focus its efforts on such issues as (1) aligning antimicrobial drug products with the principles of antimicrobial stewardship in veterinary settings; (2) supporting efforts to foster stewardship of antimicrobials in veterinary settings; and (3) assessing the impact of strategies intended to slow the rate of development of antimicrobial resistance associated with the use of antimicrobial drugs in veterinary settings.

Antimicrobial Drug Sales and Use

Under Section 105 of the Animal Drug User Fee Amendments of 2008, Congress requires animal drug sponsors (i.e. drug manufacturers) to annually report to FDA the amount of antimicrobial active ingredient in the drug products they sell or distribute for use in food-producing animals. It also requires FDA to provide summaries of the sales and distribution information by antimicrobial class for classes with three or more distinct sponsors while protecting confidential business information.

FDA published 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). This new estimated species-specific data was submitted by sponsors in April 2017, along with other required sales and distribution data, and incorporated into an enhanced summary report on antimicrobials sold or distributed for use in food-producing animals that published in December 2017. The additional data will improve FDA's understanding about how antimicrobials are sold or distributed for use in major food-producing species and inform efforts to ensure judicious use of medically important antimicrobials.

In October 2017, FDA also published a paper proposing the use of a biomass denominator to adjust annual data on the amount of antimicrobials sold or distributed for use in food-producing animals in the United States. This adjusted estimate may provide insight into broad shifts in the amount of antimicrobials sold for use in food-producing animals and may give the agency a more nuanced view on sales increases or decreases over time in a manner that is specific to U.S. animal production. Such analysis could also support FDA's ongoing efforts to encourage the judicious use of antimicrobials in food-producing animals. FDA published the paper to engage stakeholders on the proposed biomass method, and to seek comment on the methodology and the utility of this type of data analysis.

In 2017, FDA funded for the second year the cooperative agreements originally awarded in September 2016. The two cooperative agreements were awarded for projects to characterize the use of animal drugs in food-producing animals: (1) Characteristics of Antimicrobial Use in Beef Feedlots and Dairies; and (2) Antimicrobial Use Data Collection in U.S. Poultry and Swine Production. Both projects have made significant progress in their first year and may be funded

for up to five years, if progress continues and funding is available. Once the data is collected, analyzed, and aggregated, FDA will have an opportunity to further refine platforms designed for long-term antimicrobial use data collection, benchmarking and analysis of trends in antimicrobial use over time.

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 mitigate the risk of antimicrobial resistance development.

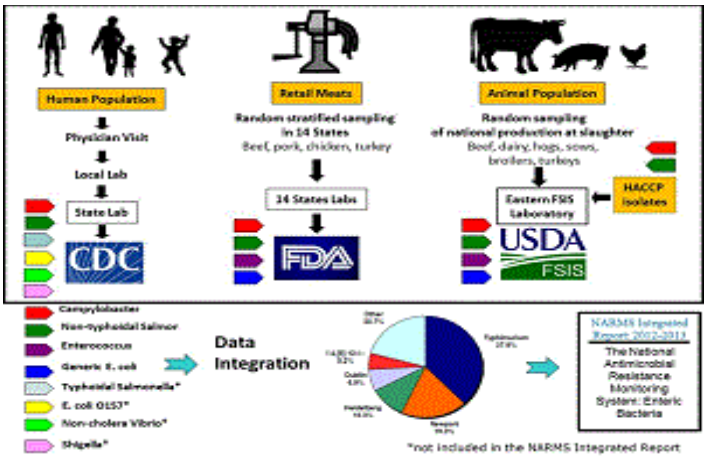

Figure 10 NARMS

In FY 2017, NARMS increased its surveillance and response capacity with the selection of five new collaborating laboratories, including universities for the first time. This expansion increases the geographic and population diversity of NARMS' surveillance, resulting in more representative data. NARMS also successfully implemented an enhanced reporting format in 2016 that leverages new data visualization software to make findings more accessible to a broad stakeholder base.

In October 2017, FDA published the 2015 NARMS Integrated Report[53], which includes seven new interactive online data displays, enabling more options for users to explore antimicrobial resistance trends according to their particular interests, and includes Whole Genome Sequencing (WGS) data. This WGS data provides definitive information on the genetic traits of bacteria, greatly strengthening FDA's ability to characterize the nature, origin and spread of resistant bacteria in foods. A new tool, Resistome Tracker, was developed by FDA and launched by NARMS in November 2017 to predict antibiotic resistance in all *Salmonella species data submitted* into its national database at National Institute of Health based on genomic DNA sequence alone. This tool will aid all countries in addressing antibiotic resistance in foodborne pathogens.

Innovative Microorganism Research

Whole genome sequencing (WGS) is a critical tool that helps FDA to provide scientific research solutions that ensure the safety of human and animal health. The high capacity and low costs of rapid DNA sequencing technology and advances in analytical software have made it possible to

[53] To review the NARMS 2015 Integrated Report, see: https://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/ucm059103.htm

routinely determine and interpret the complete DNA sequence obtained from microorganisms. During FY 2017, FDA sequenced 100 percent of its 4,859 historical Salmonella isolates. 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.

FDA is collaborating with scientists at the University of Georgia to develop a sequence-based serotyping tool. This will allow food safety scientists to switch from traditional, labor intensive, and expensive Salmonella serotyping to rapidly identifying the most commonly occurring 200 serotypes of Salmonella from the WGS data obtained from cultured bacteria. FDA sequenced *Salmonella* sp., *Campylobacter* sp. and *E. Coli* isolates recovered from retail meat are 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 publicly available via the NARMS interim report for Salmonella and NCBI.

FDA is collaborating with NCBI to build automatic analytical tools to predict antibiotic resistance based on WGS data alone. This work shows that WGS can predict resistance in over 95 percent of Salmonella isolates. Based on this work, the first phase of resistance gene analytics is now in place at NCBI and is providing resistance gene predictions for all deposited Salmonella genomes. FDA is involved in a related collaboration with Argonne National Laboratories to use WGS data to predict the concentration of drug (termed the MIC) needed to inhibit bacteria using machine learning tools. This has the potential to advance the use of WGS in both surveillance and clinical medicine.

In addition, the Veterinary Laboratory Investigation and Response Network (Vet-LIRN) continued 2017 implementation of a pilot project to monitor antimicrobial susceptibility and sequence selected veterinary pathogens. Veterinary diagnostic laboratories often have opportunities for early detection of emerging diseases, and are poised to play an increased role in biosurveillance for antibiotic-resistant bacteria that could affect humans. Twenty Vet-LIRN laboratories are gathering data on antibiotic susceptibility for *Salmonella* sp, *E. Coli* and *Staphylococcus pseudointermedius* and providing the isolates to four Vet-LIRN laboratories which have sequencing capabilities. The Vet-LIRN network provided equipment to multiple laboratories to increase the capacity for conducting state of the art susceptibility testing and genetic analysis. Integrated monitoring by these veterinary diagnostic laboratories could inform risk-based intervention strategies for FDA.

Adverse Event Program

The Animal Drugs and Feeds Program has the largest regulatory agency animal adverse event database in the world, containing real world safety and effectiveness data from nearly 700,000 adverse experience reports that involve more than 89,000,000 food animals and more than 700,000 companion animals. The Program continues to increase the functionality, utilization, and analysis of this pharmacovigilance database to improve 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, enabling approximately 99 percent of reports to be submitted electronically. Adverse event signal detection and management strategies are under development to assist with identification of potential safety and effectiveness issues and enable the program to monitor, detect and respond to products that could potentially put humans and animals at risk.

Unapproved and Compounded Animal Drug Products

The Animal Drugs and Feeds Program is concerned about unapproved animal drugs, because these drugs have not met the Agency's standards for safety and effectiveness and may not be properly manufactured or properly labeled. FDA conducts surveillance of firms selling illegal unapproved and compounded drugs and takes enforcement action when necessary to reduce the risk of harm to humans and animals from substandard or illegally marketed animal drugs. The Animal Drugs and Feeds Program 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.

Enforcement Strategies

The Animal Drugs and Feeds Program protects human and animal health by developing and implementing appropriate enforcement strategies 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 animal food establishments and products. When firms violate the FDA requirements of the FD&C Act, FDA takes appropriate 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 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.

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), 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.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2015 Actual	$175,024,000	$147,564,000	$27,460,000
FY 2016 Actual	$188,042,000	$158,629,000	$29,413,000
FY 2017 Actual	$190,879,000	$162,852,000	$28,027,000
FY 2018 Annualized CR	$187,348,000	$161,729,000	$25,619,000
FY 2019 President's Budget	$225,065,000	$180,284,000	$44,781,000

BUDGET REQUEST

The FY 2019 Budget Request for the Animal Drugs and Feeds Program is $225,065,000, of which $180,284,000 is budget authority and $44,781,000 is user fees. Budget authority increases

by $18,555,000 compared to the FY 2018 Annualized CR level and user fees increase by $19,162,000. The Center for Veterinary Medicine (CVM) amount in this request is $158,894,000. The Office of Regulatory Affairs amount is $66,171,000.

The Animal Drugs and Feeds Program is responsible for ensuring animal drugs and feed products are safe and effective, quality manufactured and properly labeled. This supports the health of food-producing and pet (companion) animals, including minor species, and enhances the availability and diversity of FDA approved products. CVM's responsibilities include all stages of the total product lifecycle such as ensuring safety and effectiveness of an animal drug before approval, conducting preapproval inspections, reviewing feed additives for safety and utility, and ensuring food for animals is safe, made under sanitary conditions, and properly labeled. The Animal Drugs and Feeds Program fosters a flexible, risk-based review framework for innovative technologies by engaging sponsors early in their drug development process.

In addition, as part of the product lifecycle, the Animal Drugs and Feeds Program bolsters critical post-market efforts by rapidly responding to product safety concerns as well as public health emergencies. The Program examines the safety and effectiveness of animal drugs on the market, including reviewing Adverse Drug Experience reports, monitoring the safety of animal devices, investigating livestock and pet illnesses, providing outreach and education, and conducting compliance and enforcement actions when appropriate. Ongoing risk-based efforts to reduce the distribution and use of unapproved animal drugs will continue. Efforts are ongoing to limit compounding to legitimate needs by veterinarians to treat animal disease where there are no alternatives and the compounded drug does not compete against approved products. Unapproved animal drugs, including compounded products, pose a public health risk because they have not been evaluated for safety and effectiveness and may not be properly manufactured or labeled.

The Animal Drugs and Feeds Program will continue prevention-focused efforts under the FDA Food Safety Modernization Act (FSMA) by working to build a modern, science- and risk-based animal food safety system through the establishment of and compliance with preventive control standards to protect human and animal health. The Program continues to develop guidance documents and conduct training, education, and outreach, in conjunction with our state regulatory and public health partners. CVM is working extensively with state partners to continue to build an integrated food safety system to support animal food standards, response efforts, and enhanced surveillance and communication systems.

The Animal Drugs and Feeds Program will continue surveillance efforts on antimicrobial resistance among enteric (intestinal) pathogenic bacteria via the National Antimicrobial Resistance Monitoring System (NARMS). Response efforts also will continue, such as using state and academia veterinary diagnostic laboratory capability and capacity via the Veterinary Laboratory Investigation and Response Network (Vet-LIRN) to assist FDA with responding to public health emergencies by investigating 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 to regulatory requirements that protect human and animal health. These activities in the FY 2019 Budget Request support mission critical activities, and Presidential, HHS, and FDA human and animal health priorities.

BUDGET AUTHORITY

Animal Drug Review (+$9.7 million / 32 FTE)

CVM: +$9.7 million / 32 FTE

This increase will enable the Animal Drugs and Feeds Program to review pioneer and generic new animal drugs within agreed-upon performance targets, meeting reduced timeframes, despite the continually increasing workload, and ensure the long-term stability of both programs moving forward. Additionally, with this funding increase, the Program will significantly mitigate the risk that FDA will not be able to meet the statutory conditions required by the FD&C Act to collect and spend user fees. User fees have been increasing on a yearly basis to cover their portion of additional workload, but FDA's direct budget authority has not correspondingly increased to sustain its proportional share of the cost burden while addressing the increased workload. These programs have had a significant impact on human and animal health, reducing review timeframes, and promoting the development of safe and effective drugs to reach the market sooner.

Medical Product Safety (+8.0 milliion / 4 FTE)

New Medical Data Enterprise

CVM: +$8.0 million / 4 FTE

With this funding increase, the Animal Drugs and Feeds Program will enhance its capacity to utilize real-world evidence from adverse experience reports to promptly detect, monitor, and learn from problems experienced with FDA-regulated animal health products. The data generated by this effort could be used to facilitate product expansion into new indications, to ensure that unsafe or ineffective products do not reach U.S. consumers, and to more rapidly identify and respond to public health threats. The Program will also support the judicious use of antimicrobial drugs in veterinary settings by enhancing collaboration with stakeholders and other Federal agencies to optimize the use of existing antimicrobial drugs and to foster innovation and the development of alternative animal health products. The Program will act on recommendations from the FDA's Science Board, including expanding the scope of the National Antimicrobial Resistance Monitoring System (NARMS) to test farm-raised seafood products at retail, test other pathogenic foodborne bacteria and enhance data collection capabilities to provide a framework for improvements that will strengthen the scientific basis for regulatory decision-making and public health interventions to address this important medical challenge.

Food Safety (+ $0.435 million)

CVM: +$0.435 million / 0 FTE

The FY 2019 funding level restores the Animal Drugs and Feeds Program food safety funding levels to maintain FY 2017 funded activities.

USER FEES

Current Law User Fees: +$19.2 Million

Center: +$18.951 million / Field: +$0.211 million

The Animal Drugs and Feeds Program request includes an increase of $19,162,000 for user fees proposed for reauthorization, which will allow FDA to fulfill its mission of promoting and protecting the public health by ensuring safety and efficacy of animal drug products.

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 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
243201: Complete review and action on original New Animal Drug Applications (NADAs) and reactivations of such applications received during the fiscal year. *(Output)*	FY 2016: 99.4% w/in 180 days Target: 90% w/in 180 days (Target Exceeded)	90% w/in 180 days	90% w/in 180 days	Maintain
243202: Complete review and action on Non-administrative original Abbreviated New Animal Drug Applications (ANADAs) and reactivations of such applications received during the fiscal year. *(Output)*	FY 2016: 98.1% w/in 270 day Target: 90% w/in 270 days (Target Exceeded)	90% w/in 270 days	90% w/in 270 days	Maintain
244212: Percentage of planned domestic and foreign high-risk animal drug and feed inspections. (Output)	FY 2017: 107% Target: 99% (Target Exceeded)	95%	95%	Maintain
244203: Percentage of planned targeted prohibited material BSE inspections. (Output)	FY 2017: 97% Target: 99% (Target Not Met)	95%	95%	Maintain
244204: 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. *(Output)*	FY 2017: 59% w/in 25 working days Target: 50% w/in 25 working days (Target Exceeded)	50% w/in 25 working days	50% w/in 25 working days	Maintain
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 2017: 40 Target: 36 (Target Exceeded)	40	40	Maintain

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

New Animal Drug Application Review

CVM exceeded all ADUFA performance goals for the last 13 years, except for two submissions, and all AGDUFA performance goals for the last eight years, except for one goal in one year where six of seven submissions were completed on time. In FY 2016, CVM completed review and action on 99.4 percent of original NADAs and other ADUFA sentinel submissions and completed review and action on 98.1 percent of original ANADAs and other AGDUFA sentinel submissions.

Vet-LIRN

Veterinary Laboratory Investigation and Response Network (Vet-LIRN) had 40 state and university veterinary diagnostic laboratories in FY 2017 that contributed to the initiation of 170 case investigations that provided pivotal data that resulted in either manufacturer recalls of contaminated products, or data that helped FDA avoid major expenses for regulatory actions because the investigation results demonstrated that certain products were unlikely to have caused the illnesses.

New ORA Field Performance Measures

ORA has been working to improve the field performance measures to better aligned with ORA's Program Alignment initiative. In this submission, ORA has completed the process of adjusting the performance goals, so that the FY 2018 and FY 2019 targets now complete a certain percentage of the planned inspections in ORA's annual Workplan. The ORA Workplan is the necessary mechanism that takes into account all the complex variables (geography, commodity, risk, availability, efficiency, etc.) that allows ORA to plan which inspections to do. With these newly formulated performance goals, ORA is committing to complete a certain percentage of the initially planned inspections. This revision strengthens the importance of the Workplan, but allows the flexibility to respond dynamically to changing circumstances during the year, to better handle emerging risks and evolving public health priorities (i.e. the heavy hurricane damage this past year). This is a significant departure from the previous performance goals, so FY 2018 will be an important year in resetting the new baselines. Also, since the targets are now based on a planned number of inspections, it is possible to inspect more than what was planned and thus have an actual inspection rate over 100%.

PROGRAM ACTIVITY DATA

Animal Drugs and Feeds Program Activity Data (PAD)

CVM Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
New Animal Drug Applications (NADAs) [1]			
Received	21	35	32
Completed	18	23	22
Approved	11	18	17
Pending [2]	16	28	38
New Animal Drug Application Supplements [1, 3]			
Received	521	625	600
Completed	636	500	480
Approved	517	380	390
Pending [2]	102	227	347
Abbreviated New Animal Drug Applications (ANADAs) [1]			
Received	21	65	60
Completed	19	58	55
Approved	8	60	56
Pending [2]	11	18	23
Abbreviated New Animal Drug Application Supplements [1, 3]			
Received	265	375	400
Completed	320	330	355
Approved	225	200	210
Pending [2]	134	179	224
Investigational New Animal Drug (INAD) Files [4]			
Received	3,428	3,550	3,600
Completed	3,452	3,400	3,450
Pending [2]	517	667	817
Generic Investigational New Animal Drug (JINAD) Files [4]			
Received	564	750	775
Completed	579	700	725
Pending [2]	359	409	459
Food (Animal) Additive Petitions Completed	99	100	100
Investigational Food Additive Petitions Completed	80	90	90
Adverse Drug Event (ADE) [5]			
ADE Reports Received	101,811	104,000	98,000
Post-Approval ADE Data Reviews	180	180	180

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

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

[3] A 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.

[4] An 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.

Field Animal Drugs and Feeds Program Activity Data (PAD)

Field Animal Drugs & Feeds Program Activity Data (PAD)									
Field Animal Drugs and Feeds Program Workload and Outputs	**FY 2017 Actual**			**FY 2018 Annualized CR**			**FY 2019 President's Budget**		
	Total	**Animal Drugs**	**Feeds**	**Total**	**Animal Drugs**	**Feeds**	**Total**	**Animal Drugs**	**Feeds**
FDA WORK									
DOMESTIC INSPECTIONS									
UNIQUE COUNT OF FDA DOMESTIC ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***1,710***	***206***	***1,517***	***1,664***	***298***	***1,398***	***1,664***	***298***	***1,398***
Pre-Approval /BIMO Inspections	28	28	0	79	79	0	79	79	0
Drug Process and New ADF Program Inspections	178	178	0	175	175	0	175	175	0
BSE Inspections	1,050	0	1,050	1,205	0	1,205	1,205	0	1,205
Feed Contaminant Inspections	26	0	26	25	0	25	25	0	25
Illegal Residue Program Inspections	312	0	312	450	0	450	450	0	450
Feed Manufacturing Program Inspections	242	0	242	200	0	200	200	0	200
Domestic Laboratory Samples Analyzed	1,599	22	1,577	1,560	20	1,540	1,560	20	1,540
FOREIGN INSPECTIONS									
UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS [1]	***95***	***89***	***6***	***74***	***69***	***5***	***74***	***69***	***5***
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	18	18	0	40	40	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	76	76	0	33	33	0	33	33	0
Foreign Feed Inspections	6	0	6	5	0	5	5	0	5
BSE Inspections	4	0	4	0	0	0	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***1,805***	***295***	***1,523***	***1,738***	***367***	***1,403***	***1,738***	***367***	***1,403***
IMPORTS									
Import Field Exams/Tests	3,847	614	3,233	3,795	495	3,300	3,795	495	3,300
Import Laboratory Samples Analyzed	704	3	701	867	2	865	867	2	865
Import Physical Exam Subtotal	**4,551**	**617**	**3,934**	**4,662**	**497**	**4,165**	**4,662**	**497**	**4,165**
Import Line Decisions	426,484	52,702	373,782	447,808			470,199		
Percent of Import Lines Physically Examined	1.07%	1.17%	1.05%	1.04%			0.99%		
STATE WORK									
UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS	***3,085***	***0***	***3,085***	***3,503***	***0***	***3,503***	***3,503***	***0***	***3,503***
State Contract Inspections: BSE	3,005	0	3,005	3,500	0	3,500	3,500	0	3,500
State Contract Inspections: Feed Manufacturers	614	0	614	620	0	620	620	0	620
State Contract Inspections: Illegal Tissue Residue	124	0	124	130	0	130	130	0	130
State Contract Animal Drugs/Feeds Funding	$3,389,745	0	$3,389,745	$3,491,437	0	$3,491,437	$3,596,180	0	$3,596,180
State Contract Tissue Residue Funding	$271,600	0	$271,600	$263,452	0	$263,452	$255,548	0	$255,548
Total State Funding	**$3,661,345**	**$0**	**$3,661,345**	**$3,754,889**	**$0**	**$3,754,889**	**$3,851,728**	**$0**	**$3,851,728**
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***4,893***	***295***	***4,611***	***5,241***	***367***	***4,906***	***5,241***	***367***	***4,906***

[1] The FY 2017 actual unique count of foreign inspections includes 11 OIP inspections (10 for China and 1 for India).

DEVICES AND RADIOLOGICAL HEALTH

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
Devices	**448,114**	**450,799**	**504,844**	**635,635**	**130,791**
Budget Authority	***329,681***	***329,764***	***327,442***	***455,442***	***128,000***
User Fees	***118,433***	***121,035***	***177,402***	***180,193***	***2,791***
Center	348,788	354,520	406,021	536,776	130,755
Budget Authority	246,261	246,319	244,588	372,588	128,000
User Fees	102,527	108,201	161,433	164,188	2,755
Prescription Drug (PDUFA)	---	---	*1,237*	*1,305*	*68*
Medical Device (MDUFA)	*96,150*	*102,451*	*153,819*	*156,506*	*2,687*
Mammography Quality Standards Act (MQSA)	*6,377*	*5,750*	*6,377*	*6,377*	---
Field	99,326	96,279	98,822	98,858	36
Budget Authority	83,420	83,445	82,853	82,853	---
User Fees	15,906	12,834	15,969	16,005	36
Medical Device (MDUFA)	*2,014*	*1,873*	*2,077*	*2,113*	*36*
Mammography Quality Standards Act (MQSA)	*13,892*	*10,961*	*13,892*	*13,892*	---
FTE	**2,215**	**2,215**	**2,394**	**2,416**	**22**

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 of 1997 (FDAMA); Medical Device User Fee and Modernization Act of 2002 (MDUFMA); Project Bioshield Act of 2004 (21 U.S.C. 360bbb-3); Medical Device User Fee Stabilization Act of 2005; Patient Protection and Affordable Care Act of 2010; FDA Amendments Act of 2007 (FDAAA); FDA Safety and Innovation Act of 2012 (FDASIA); FDA Reauthorization Act of 2017 (FDARA) (P.L. 115-52).

Allocation Methods: Direct Federal/Intramural

PROGRAM DESCRIPTION AND ACCOMPLISHMENTS

The modern Devices and Radiological Health Program (the Devices Program) began in 1976, when President Gerald Ford signed the Medical Device Amendments of 1976, which amended the Federal Food, Drug, and Cosmetic Act to outline a risk-based classification system for devices. The Devices Program operates with appropriations and user fees and is comprised of the Center for Devices and Radiological Health and the Office of Regulatory Affairs.

The Devices Program is responsible for the regulation and oversight of medical devices, from simple tongue depressors to complex programmable pacemakers with micro-chip technology and laser surgical devices. In addition, medical devices include in vitro diagnostic products, such as general purpose lab equipment, reagents, and test kits. To protect the public from unnecessary exposure to radiation, the Devices Program also regulates radiation-emitting electronic products that include microwave ovens, X-ray equipment, and medical ultrasound and MRI machines. The Devices Program also monitors mammography facilities to make sure the equipment is safe and properly operated.

Mission

The Devices Program assures that patients and providers have timely and continued access to safe, effective, and high-quality medical devices and safe radiation-emitting products. The Devices Program provides consumers, patients, their caregivers, and providers with understandable and accessible science-based information about the products it oversees. The Devices Program 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.

Vision

The vision of the Devices Program is that patients in the United States have access to high-quality, safe, and effective medical devices of public health importance first in the world. The United States 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 United States and remain safe, effective, and of high-quality.

The following strategic priorities describe important areas that the Devices Program has recently focused on to achieve this vision. The priorities are to:[54]

- Establish a National Evaluation System for Medical Devices
- Incorporate Patient Input into Decision Making
- Promote a Culture of Quality and Organizational Excellence.

By actively taking steps to realize these priorities, the Devices Program aims to help medical device developers choose the United States as the first country in which to make their innovative technologies available to patients.

Recent accomplishments of the Devices Program include the following:

- The number of early feasibility studies approved has more than doubled—from 26 in FY 2014 to 57 in FY 2017
- Approved 91 novel medical devices in 2016—the highest number since the advent of the medical device user fee program in 2003 This followed the second highest number from 2015 and continued a 7-year trend that has resulted in a marked increase in the annual number of novel device approvals since 2009.
- Approved the Micra Transcatheter Pacing System, which is the first pacemaker that does not require the use of wired leads to provide an electrical connection between the pulse-generating device and the heart
- During FY 2016, ORA conducted 2,499 domestic and 815 foreign inspections of medical device and radiological health facilities to help ensure the safety and effectiveness of products.

The following selected accomplishments demonstrate the Devices Program's delivery of its regulatory and public health responsibilities.

[54] For more information about our strategic priorities, please visit http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHVisionandMission/default.htm

Improve and Safeguard Access

The Devices Program focuses on flexible, smart regulation, and 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.

The Devices Program has evolved alongside changes in medical technology and the global marketplace. In addition, 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 being 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.

For example, since 2009, the number of innovative devices FDA has approved has almost quadrupled. In 2016, FDA approved 91 innovative devices—the highest of any year since the medical device user fee program began in 2003. These novel technologies, which help to improve the quality of life for patients—especially those that require day-to-day maintenance and ongoing attention—are reaching patients earlier, reducing suffering, and improving public health.

The Devices Program supports FDA's strategic priorities through efforts including the implementation of the 21st Century Cures Act, improvements to the Clinical Trial Enterprise, and qualification of Medical Device Development Tools.

Guidance Documents

Below are selected guidance documents recently issued by the Devices Program that support Improving and Safeguarding Access. This list does not represent any degree of importance or priority ranking among the published guidances.

Date	#	Title	Description
Nov 2017	FDA-2012-D-0384	Pediatric Information for X-ray Imaging Device Premarket Notifications	This guidance document recommends that manufacturers include dose reduction features in their equipment designs and pediatric resources when they develop and manufacture X-ray equipment.
Oct 2017	FDA-2015-D-5966	Breakthrough Devices Program - Draft Guidance for Industry and Food and Drug Administration Staff	This guidance document describes policies that FDA intends to use to implement a breakthrough devices program as required by section 515B of the Federal Food, Drug, and Cosmetic Act (FD&C Act).

Sep 2017	FDA-2015-D-4852	Design Considerations and Premarket Submission Recommendations for Interoperable Medical Devices	This guidance document highlights considerations that should be included in the development and design of interoperable medical devices and recommendations for the content of premarket submissions.
Jan 2017	FDA-2015-D-1777	Factors to Consider When Making Benefit-Risk Determinations for Medical Device Investigational Device Exemptions	This guidance document provides clarity to industry regarding the principal factors that FDA considers when assessing the benefits and risks of IDE applications for human clinical studies.
Dec 2016	FDA-2015-D-0025	Medical Device Accessories – Describing Accessories and Classification Pathway for New Accessory Types	The purpose of this guidance document is to provide the definition of a medical device accessory and includes recommendations for industry about the regulation of medical device accessories.

21st Century Cures

The 21st Century Cures Act (Cures Act), signed into law on December 13, 2016, is designed to help accelerate medical product development and bring new innovations and advances to patients more quickly and more efficiently. The law enables FDA to speed the development and review of novel medical products, such as through the expansion of FDA's Expedited Access Pathway (EAP) program into the Breakthrough Devices Program. The Breakthrough Devices Program allows for earlier and greater interaction with FDA during device development and review and will provide more timely patient access to devices intended to treat life-threatening or irreversibly debilitating diseases or conditions. By the 1-year anniversary of the Cures Act, FDA had designated 49 technologies as breakthrough and approved the first breakthrough PMA.

The Cures Act also includes authorities to help streamline and improve FDA's review and oversight of devices. As required by the Cures Act, FDA exempted many Class I and Class II device types from the requirement to submit a 510(k) prior to marketing because premarket notification to FDA for those device types was not value-added. FDA exempted more than 70 Class I device types and more than 1,000 Class II device types, which allows us to focus our oversight on higher risk products with greater impacts to public health.

FDA also provided training about the least burdensome concept to all Devices Program staff—not just those involved in the premarket review of device submissions (as required by the Cures Act)—because the least burdensome concept is integral to how we conduct business. Further, we revised our guidance on when a 510(k) is needed for a change to an existing device to clarify the least burdensome approach for FDA review of changes to a device while improving consistency based on feedback from FDA staff and the device industry about how the guidance was being interpreted.

Lastly, the Cures Act provided FDA an important authority to require instructions for use and validation data regarding cleaning, disinfection, and sterilization for certain reusable devices,

such as duodenoscopes. As required by the Cures Act, FDA published a list of reusable devices for which the requirement applies, and we believe this will ensure that the premarket requirements for these device types are clear and predictable, facilitating more efficient review of these devices and safer products for patients.

Clinical Trial Enterprise

The Devices Program is committed to improving U.S. patient access to new devices by strengthening and streamlining the clinical trial enterprise so that medical device clinical trials are conducted in the U.S. while maintaining appropriate human subject and patient protections. By reducing the time of every regulatory stage of the total product life cycle (including the review of medical device submissions) while still assuring robust but appropriate and least burdensome evidence generation and high-quality decision making, the Devices Program helps patients get access to safe and effective medical technologies while fostering innovation.

Manufacturers submit Investigational Device Exemptions (IDEs) for certain devices they want to study in human subjects. The Devices Program reviews an IDE submission before a manufacturer can begin to collect clinical data that may be used to support marketing a device. Through improvements to the device clinical trials program, the Devices Program slashed the median time to approve an IDE study by more than 1 year, from 442 days in FY 2011 to 30 days in FY 2017. Furthermore, based on the FY 2017 metrics, 56% of IDEs are fully approved in the first round, and 78% of IDEs are fully approved within two rounds.

In addition, in FY 2017, FDA and NIH announced the availability of a final template for investigators to use when developing clinical trial protocols, which are roadmaps for conducting a clinical trial. Clinical trial protocols are critical components of any medical product development program because they describe the objectives, design, methodology, statistical considerations, and organization of the trial. A standard format will help facilitate the review of clinical trial protocols by FDA and others (e.g., institutional review boards). FDA's goals for the template are that it will:

- Help investigators prepare protocols that are consistent and well organized;
- Contain the necessary information for the clinical trial to be properly reviewed; and
- Follow the International Conference on Harmonisation (ICH) E6 Good Clinical Practice guidelines.

By clarifying expectations, the template will enable time-saving and money-saving efficiencies.

Early Feasibility Studies

In addition to dramatically improved performance in reviewing IDEs, the Devices Program has encouraged the use of innovative methodologies and study designs in clinical trials. Innovators tend to market their technologies sooner in countries where they conducted early clinical studies. We recognize that manufacturers need the Devices Program's input early and often so that review of a device submission can proceed quickly and smoothly.

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. These studies allow for early clinical evaluation of devices to provide proof of principle and initial clinical safety data, and may be appropriate early in device development when clinical

experience is necessary because nonclinical testing methods are unavailable or inadequate to provide the information needed to advance the development process.

The number of early feasibility studies approved recently has more than doubled – from 26 in FY 2014 to 57 in FY 2017 – providing evidence that the EFS Program remains robust and permits efficient clinical trial progression in the U.S. while providing appropriate human subject protections.[55]

Medical Device Development Tools

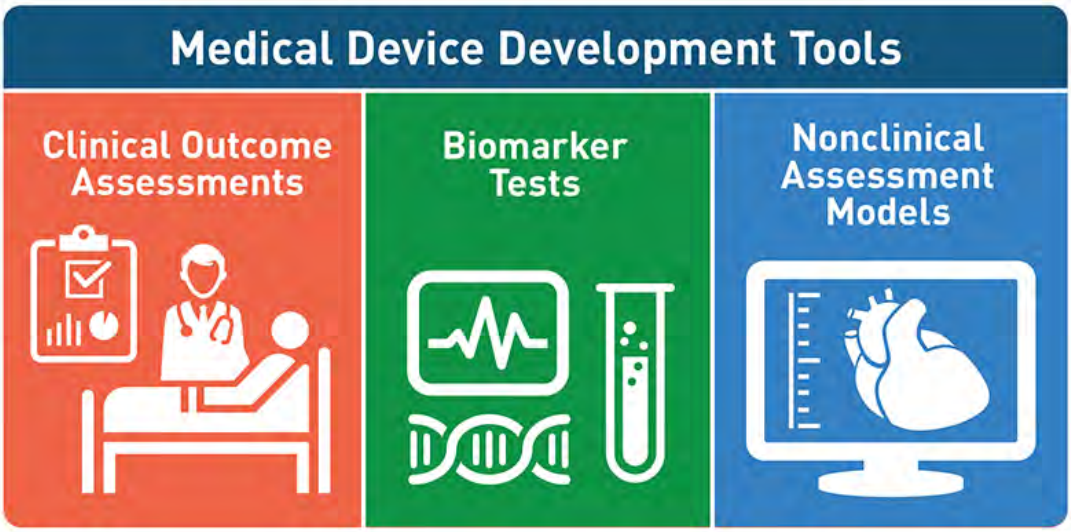

Figure 11 Medical Device Development Tools

The Devices Program relies on tools to efficiently and accurately measure a product's performance at all stages of its lifecycle. The Medical Device Development Tools (MDDT) program can help address questions about data validity and reduce the time and other resources needed for new product development while maintaining patient safety. The voluntary MDDT program is intended to reduce regulatory burden for tool developers and FDA reviewers by qualifying tools that can aid in the development and evaluation of medical devices. Tools provide a more efficient and predictable means for collecting information necessary to support regulatory submissions. MDDT is an exciting way that FDA is promoting innovation, supporting the manufacturer of high-quality products, and speeding the rate at which safe and effective medical technologies are made accessible to patients. Qualified tools should help lead to more efficient and robust medical device development, for example, by minimizing the use of animals, reducing testing duration or sample sizes, or by optimizing patient selection for a device clinical study.

MDDTs qualified by FDA can be used in clinical trials by the medical device industry to support both device submissions and post-approval studies. The MDDT program also offers developers increased opportunities to discuss early concepts of tool development, foster collaboration, and increase the potential that tools will be used and adopted. October 24, 2017, the Devices Program qualified the first MDDT tool, the Kansas City Cardiomyopathy Questionnaire (KCCQ)

[55] For more information visit https://blogs.fda.gov/fdavoice/index.php/tag/early-feasibility-studies-efs/

Patient Reported Outcome (PRO), which can be used to quantify the experiences of patients who have experienced heart failure.

Patient Preference Initiative

Since the Patient Preference Initiative was introduced into the Devices Program's regulatory decision-making process, we have seen increasing evidence of the benefits of soliciting patient feedback—most recently, in giving kidney patients more therapy options and enhancing the safe use of a glucose monitor by pediatric patients with Type 1 diabetes.

For example, in August 2017, for the first time, FDA cleared an expanded indication for a home hemodialysis machine so it can be used without a care partner being present. The clearance decision was based in part on asking kidney patients about their tolerance for risk. Home dialysis may improve a patient's quality of life, allowing them to undergo lengthy dialysis treatments in the comfort of their home rather than traveling several times each week to a dialysis center. However, due to a risk of rare but serious events associated with performing hemodialysis alone in the home, FDA had previously required the presence of a care partner during the treatment.

Collecting qualitative feedback from patients is another important technique and proved helpful in enhancing the safety of the Dexcom G5 Continuous Glucose Monitoring (CGM) System and Animas Vibe System, a continuous glucose monitor with an insulin pump, for children. FDA discussed with patients, care partners, and patient groups their concerns about the safety of using an insulin pump in pediatric populations. These conversations included how the device would be used once approved by FDA for pediatric populations and what kind of safety considerations might be relevant. Patient preference information led to a safer device on the market, and parents can now have greater confidence with managing their child's diabetes.

These are examples of how medical device companies are leveraging different types of patient preference information to support device submissions, information which is likely to vary depending on the device, the disease, the level of risk, and its regulatory purpose. Patient preference is an evolving area of regulatory science, supported in part by the nonprofit Medical Device Innovation Consortium (MDIC) FDA encourages further research in this field.

Patient Engagement Advisory Committee (PEAC)

The Devices Program believes that to successfully achieve our mission and vision in the service of patients, we must interact with patients as partners and work together to advance the development and evaluation of innovative devices and monitor the performance of marketed devices. That is why the Devices Program convened the Patient Engagement Advisory Committee (PEAC), which discusses topics regarding patient input throughout the total product lifecycle of a device. For the first time, an FDA advisory committee will focus specifically on patient-related issues. While patient representatives currently participate in many FDA advisory committee meetings, we have never had a committee wholly focused on patient-related issues.

In October 2017, the Devices Program held the inaugural meeting of the Patient Engagement Advisory Committee (PEAC). The topics covered included the challenges of clinical trial design, conduct, and reporting identified by patients. The Devices Program chose this subject because patients often have concerns about participating in clinical trials or drop out after enrolling in a trial. Inconsistent or minimal participation in clinical trials can make it difficult to reach reliable conclusions or to determine the level of benefit for patients. The nine core voting members of the

patient advisory committee, including the chair and the consumer representative, all have direct experience as a patient or as a care partner for a patient.

Digital Health

The widespread adoption and use of digital health technologies is creating new and innovative ways to improve health and health care delivery. In one of the biggest de-regulatory actions for the Devices Program in decades and to foster greater innovation in the digital health space while promoting public health, we have exercised enforcement discretion to stop subjecting certain lower-risk medical devices (such as apps for patient care management and medication reminders) to medical device requirements. Other recent efforts related to creating an oversight paradigm tailored to digital health products include:

- The "Software Precertification (PreCert) Pilot Program" that will enable us to develop a tailored approach toward regulating software by evaluating the software developer and/or digital health technology developer, rather than focusing on the product
- Examining whether and how, under current authorities, we can create a certification program under which lower risk digital health products could be marketed without FDA premarket review and higher risk products could be marketed with a streamlined FDA premarket review
- Providing guidance to clarify the regulatory status of products that contain multiple software functions for which some functions fall outside the scope of FDA regulation but others do not.

For digital health technologies to reach their fullest potential, it is critical that FDA be forward-leaning in making sure that we have implemented the right policies and regulatory tools and communicated them clearly to encourage safe and effective innovation. Greater certainty regarding what types of digital health technology is subject to regulation and regarding FDA's compliance policies will help foster innovation and will help the Devices Program devote more resources to higher risk priorities.

Product Approvals

Below are examples of selected Devices Program product approvals during calendar years 2016 and 2017. This list does not represent any degree of importance or priority ranking of products.[56]

[56] For a complete list of product approvals, clearances, and designations, visit http://www.fda.gov/NewsEvents/ProductsApprovals/.

Date	Product Name	Description
Nov 2017	Foundation Medicine's FoundationOne CDx	An in vitro diagnostic test that uses next-generation sequencing (NGS) to detect certain abnormalities in 324 genes and genomic signatures. This is the first approval of a device that went through the Breakthrough Devices Program.
Nov 2017	Memorial Sloan Kettering Cancer Center's (MSK) IMPACT	An in vitro diagnostic test that uses next-generation sequencing (NGS) to rapidly identify the presence of mutations in 468 unique genes, as well as other molecular changes in the genomic makeup of a person's tumor.
Nov 2017	RxSight Inc. Light Adjustable Lens and Light Delivery Device	The first medical device system that can make small adjustments to the artificial lens' power after cataract surgery so that the patient will have better vision when not using glasses.
Jul 2017	Embrace Neonatal MRI System	The first magnetic resonance imaging (MRI) device specifically for neonatal brain and head imaging in neonatal intensive care units.
Jun 2017	Sapien 3 Transcatheter Heart Valve (Expanded Indication)	A transcatheter heart valve as a valve-in-valve treatment offers U.S. patients with failing surgical bioprosthetic aortic or mitral valves a less-invasive treatment option.

Enhance Oversight

The Devices Program oversees approximately 175,000 medical devices on the U.S. market, more than 18,000 medical device manufacturers, and more than 25,000 medical device facilities worldwide. Each year, the Devices Program receives more than 1.4 million reports on medical device adverse events and malfunctions.

Ensuring that manufacturers comply 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. In addition, the Devices Program also 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.

Guidance Documents

Below are other selected guidance documents recently issued by the Devices Program that support enhancing oversight. These guidance documents help address various issues. This list does not represent any degree of importance or priority ranking among the published guidances.[57]

[57] For more information on guidance please visit http://www.fda.gov/RegulatoryInformation/Guidances/.

Date	#	Title	Description
Dec 2016	FDA-2015-D-5105	Postmarket Management of Cybersecurity in Medical Devices	This guidance clarifies FDA's postmarket recommendations and emphasizes that manufacturers should address cybersecurity vulnerabilities and exploits as part of their postmarket management of medical devices.
July 2016	FDA-2016-17750	Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices	Draft guidance to clarify how to evaluate real-world data to determine whether it may be sufficiently relevant and reliable to generate the types of real-world evidence that can be used in FDA regulatory decision-making for medical devices.
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 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 (NEST)

The National Evaluation System for health Technology (NEST) is a multi-stakeholder collaboration intended to drive down time and cost and increase the value and use of real-world evidence to support the needs of the medical device ecosystem by applying market-based principles. NEST is not a government-owned or government-operated system; it is operated by medical device ecosystem stakeholders who comprise a governing committee directing NEST activities. The Devices Program is leading the establishment of NEST to enable more timely identification and resolution of safety concerns, better characterization of real-world performance of medical devices, and facilitation of premarket clearance or approval of new devices and new uses of currently marketed devices.

The Devices Program intends for NEST to increase the quality and use of real-world data (RWD) collected as part of routine clinical care, which would also help to reduce the time and cost of evidence generation. Ongoing implementation of the Unique Device Identification (UDI) system also will enable NEST to perform enhanced analyses of devices on the market, providing a clear and standard way to identify devices in electronic medical records.

The Devices Program is already relying on RWE to approve new devices, expand the indications for marketed devices, and reduce the time and cost for device makers to meet their postmarket study requirements. In 2017, the Devices Program documented access to more than 100 million electronic patient records (from national and international clinical registries, claims data, and electronic health records) that included device identification. The Devices Program spearheaded the work of 12 National Coordinated Registry Networks and 4 international Registry Consortia through grants to the Medical Device Epidemiology Network (MDEpiNet), creating infrastructure for device evaluation including minimum core data sets, harmonized definitions, basic governance, and informatics and methodological alignment.

The Devices Program also awarded $3 million to the Medical Device Innovation Consortium (MDIC) to establish the NEST Coordinating Center. The MDIC—a 501(c)(3) public-private partnership—is an organization that fosters collaboration between patient organizations, nonprofit organizations, industry, and other federal agencies to find solutions for common medical device challenges. MDIC is focused 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.

Although FDA does not own or operate NEST, the Devices Program has been establishing strategic alliances among data sources to accelerate NEST's launch with the initial version of a fully operational system anticipated by the end of 2019.[58]

Unique Device Identification (UDI)

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 as a standard in electronic health records (EHRs), clinical information systems, billing systems, and registries will enable the National Evaluation System for health Technology (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).

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. To fully realize the value of UDI, FDA will need to increase

[58] Available at http://mdic.org/

engagement with demonstration projects and early UDI adopters, other government agencies, and with global regulatory agencies who are developing their own UDI systems.

It is expected that the next five years will be crucial for transitioning from development to use and sustainability of the UDI system to demonstrate improvements to safety, patient outcomes and economic returns to supply chain, clinical systems and outcomes research. As of October 31, 2017, more than 4,600 labelers have submitted more than 1.5 million device identification records in the GUDID.

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 are interconnected, we must take steps to secure them from hackers and cyberattacks. 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.

FDA partnered 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. The partnership will help to proactively address cybersecurity threats and vulnerabilities that may impact patient safety.

It is the goal of the Devices Program to encourage a coordinated approach of vigilance, responsiveness, resilience, and recovery that fits our culture of continuous quality improvement. This means taking a total product lifecycle approach, starting at the product design phase when we build in security to help foil potential risks, followed by having a plan in place for managing any risks that might emerge, and planning for how to reduce the likelihood of future risks. The Devices Program encourages medical device manufacturers to proactively update and patch devices in a safe and timely manner. The concept of updates and patches, while not new to traditional information technologies, is complex when it comes to critical safety systems and requires a collaborative approach to finding solutions.

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.

Medical Device Single Audit Program (MDSAP)

The Medical Device Single Audit Program (MDSAP) is an international coalition of trusted regulatory authorities working together to eliminate the need for multiple medical device manufacturer audits and inspections. The Medical Device Single Audit Program allows an MDSAP-recognized Auditing Organization to conduct a single regulatory audit of a medical device manufacturer that satisfies the relevant requirements of the regulatory authorities participating in the program. Single and shared audits help lower costs to industry and taxpayers by eliminating duplicate audits and inspections of medical device manufacturing facilities.

From 2014 to 2016, FDA, alongside its international partners, participated in a Medical Device Single Audit Program Pilot. In June 2017, a report was generated summarizing the outcomes of prospective "proof-of-concept" criteria established to confirm the viability of the Medical Device Single Audit Program. The outcomes documented in the Final MDSAP Pilot Report are based on data generated during the 3-year pilot. Based on its evaluation of the MDSAP Final Pilot Report, the MDSAP Regulatory Authority Council (the international MDSAP governing body) determined that the MDSAP Pilot had satisfactorily demonstrated the viability of the Medical Device Single Audit Program.

FDA is accepting MDSAP audit reports as a substitute for routine Agency inspections. FDA aims to have increased information with which to perform its risk-based work planning, allow for greater efficiency in FDA's use of resources, and provide broader understanding of regulated industry. This program will lead to greater regulatory and consumer confidence in the medical device supply chain and allow for safe and effective medical device products for the U.S. market.

Promoting a Culture of Quality and Organizational Excellence

Our focus on promoting a culture of quality and organizational excellence recognizes manufacturers that promote practices and behaviors that result in higher quality outcomes for patients. The Devices Program is working with stakeholders to identify and promote quality and patient-centric practices during device design and production. These practices range from design improvements to controlling production errors and increasing the speed of detecting quality issues.

The Devices Program worked collaboratively with the Medical Device Innovation Consortium (MDIC) and industry partners to develop a quality-maturity appraisal method, which will be conducted by third-parties. The appraisal moves away from assessing compliance with the quality system regulation alone toward assessing an organization's ability to drive continuous improvement and deliver quality products to its customers. The Devices Program intends to launch a voluntary pilot that leverages that maturity appraisal method to collect objective performance metrics from participating firms. FDA developed modified review and submission processes for certain regulatory programs that facilitate rapid improvement of manufacturing processes and promotion of device quality.

Additionally, through this activity, the Devices Program has learned that there is a significant lack of investment in technologies to improve data analytics and manufacturing practices in the medical device industry. As part of our efforts to promote a culture of quality and organizational excellence, the Devices Program is working to simplify and reduce regulatory burdens associated with implementing these technologies. In the next few years, these combined efforts will change how the Devices Program evaluates product and manufacturing quality and enable us to incentivize industry competition on a quality basis.

The Devices Program is also promoting a culture of quality and organizational excellence within the Center for Devices and Radiological Health. This framework embraces the core values and concepts of both ISO 9001 (a set of international standards for management and verification of good quality management practices) and Baldrige Criteria for Performance Excellence. The Quality Management framework includes the following components:

- Infrastructure, including Policy & Process Alignment and Policy & Process Improvement
- Leadership

- Support & Operations (Resource and Life Cycle Management)
- Performance Evaluations & Improvements (QM Evaluation System)

Quality Practices across the Devices Program include document control system development, quality training and education, leadership engagement in quality, quality improvement initiatives, and building a quality community of practice.

Mammography Quality Standards Act Program

Figure 12 Nurse Assisting Patient Undergoing Mammogram

FDA's mammography program—authorized by the Mammography Quality Standards Act (MQSA)—helps to ensure all women in the United States have access to quality mammography for the detection of breast cancer in its earliest, most treatable stages. The program also ensures that patients receive their mammogram results within 30 days (sooner if there are problems) and in plain language they can understand.

As part of the mammography program, FDA and its state 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 2017, 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.

The Devices Program recently enhanced the inspection process by creating our Enhancing Quality Using the Inspection Program (EQUIP) initiative, which adds inspection questions related to existing regulations about image quality. In this way, we can ensure that facilities have processes in place to help them maintain image quality and detect issues early so that they can be rapidly corrected, benefiting both patients and facilities.

Over the last 25 years, breast imaging technology has moved from screen film technology to full field digital mammography (first cleared by FDA for marketing in 2000) to digital breast tomosynthesis (a new technology that takes x-ray "slices" to improve visualization of breast tissue). The advances in mammography technology, combined with FDA's scientific expertise and regulatory authority in this area, have served the public well.

Thanks in large part to early detection of the disease through quality mammography under the MQSA, as well as improved therapies, the five-year survival rate for all women diagnosed with breast cancer in the United States between has improved by over 15 percent since 1977, from 74.8 percent to 90.8 percent, the Centers for Disease Control and Prevention reported earlier this year. Moreover, today's mammograms require very small doses of radiation, far less than was required decades ago.[59]

Radiological Health Program

The Radiological Health Program protects public safety by monitoring industry's compliance with regulatory performance standards to reduce the incidence and severity of radiation injury. The program reviews initial and periodic reports as well as inspects establishments that manufacture radiation emitting electronic products to determine compliance with the law. The program also prioritizes product types for sampling and testing at FDA's Winchester Engineering and Analytical Center, as well as engages with regulatory scientists to identify high-priority projects develop new and revised methods to evaluate evolving technologies.

The Radiological Health Program has initiated multiple efforts to improve the efficiency and effectiveness of the program with a focus on high-risk products. Initiatives include manufacturer engagement, reliance on international standards, public safety notices, and proposals to reduce or eliminate unnecessary reporting. Recent successes include engaging with Customs and Border Protection and major online distributors to identify and prevent sale of non-compliant products as well as preparing outreach material to proactively engage industry and new manufacturers with information on basic safety requirements.

FDA supports and collaborates with state agencies on projects to understand current levels of radiation exposure. The Nationwide Evaluation of X-ray Trends (NEXT) is completing a survey on patient exposures during dental radiography. Information from the report will be published to help industry and practitioners to optimize their systems to improve patient safety.

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.

[59] Available at: http://www.fda.gov/Radiation-EmittingProducts/MammographyQualityStandardsActandProgram/Regulations/ucm489348.htm

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2015 Actual	$442,689,000	$320,793,000	$121,896,000
FY 2016 Actual	$447,605,000	$323,157,000	$124,448,000
FY 2017 Actual	$450,799,000	$329,764,000	$121,035,000
FY 2018 Annualized CR	$504,844,000	$327,442,000	$177,402,000
FY 2019 President's Budget	$635,635,000	$455,442,000	$180,193,000

BUDGET REQUEST

The FY 2019 Budget Request for the Devices Program is $635,635,000 of which $455,442,000 is budget authority and $180,193,000 is user fees. Budget authority increases by $128,000,000 compared to the FY 2018 Annualized CR level and user fees increase by $2,791,000.

The FY 2019 Budget allows the Devices Program to continue to assure the quality, 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 2019 Budget also enables the Devices Program to make historic leaps in new, least burdensome regulatory approaches to support rapid innovation cycles that will reduce the time and cost of market entry for new products while assuring appropriate patient safeguards, and create jobs by driving manufacturing back to the United States. By fully and consistently implementing its priorities, along with continuing efforts to transform review and oversight, the Devices Program can realize its vision of U.S. patients having access to high-quality, safe, and effective medical devices of public health importance first in the world.

BUDGET AUTHORITY

Medical Product Safety (+$128 million / 22 FTE)

Bring MedTech Manufacturing Home

Center: +$12.0 million / 4 FTE

Advances in medical device manufacturing provide the potential to not only improve patient safety, but also encourage medical device manufacturers to innovate production methods and shift more of their production to the United States. However, manufacturing innovation has stagnated in recent years as manufacturers have focused on meeting the basic requirements to ensure compliance with FDA regulations. To overcome this challenge, FDA will establish a more modern and nimble framework that will make it more efficient for device developers to implement smart manufacturing solutions and innovate manufacturing processes in ways that can allow devices to better meet the needs of patients and providers.

The new framework will include a voluntary program for device manufacturers to receive certification for meeting objective manufacturing and product quality criteria. This voluntary program will encourage device manufacturers to make investments to retool their development and manufacturing processes in ways that can facilitate manufacturing innovation; encourage

investment in new production methods, technologies, and materials; create more jobs in the United States; and lead to higher quality medical products and better patient outcomes. Manufacturing innovations include adopting intelligent, automated processes that monitor and record manufacturing quality metrics that manufacturers can leverage to incorporate new features to improve manufacturing capabilities more efficiently and predictably.

FDA's investment in this area will enable further collaboration with industry, patients, providers, and payers through the Medical Device Innovation Consortium (MDIC) to develop the parameters of the program and enable adoption of innovative manufacturing practices. FDA will recognize third-party certifiers and offer regulatory incentives for manufacturers who demonstrate capability and transparency around their manufacturing and product performance.

These actions will increase manufacturing innovation, accelerate availability of high-quality devices to patients, and foster a competitive marketplace around device quality similar to other industries, such as automotive, consumer electronics, and aerospace. In turn, these improvements will advance device innovations, reduce manufacturing costs, and improve the quality and safety of medical devices. As medical devices become more complex and given the frequent modifications made to devices, spurring advanced manufacturing, and creating a competitive marketplace for device quality is critical for both driving technological innovations and assuring patient safety.

Facilitate Growth and Spur Transformation of the Digital Health Technology Industry

Center: +$70.0 million / 13 FTE

Digital health technologies offer the opportunity to improve patient care, empower consumers, and reduce health care costs. However, investment in the U.S. digital health technology industry has lagged due to market uncertainty over both the high cost of regulatory burdens and the uncertainty of adequate patient safeguards. To help this industry grow and reach its full potential, FDA will create a Center of Excellence on Digital Health, whose responsibilities will include establishing a regulatory paradigm for these products, building new capacity to evaluate and recognize third party certifiers, and create a cybersecurity unit to complement the advances in software-based devices as well as to aid in review of cybersecurity advances affecting the more traditional, hardware and software-based medical devices.

A Center for Excellence on Digital Health will address current concerns by establishing a new review and oversight paradigm for digital health technologies based on risk. Under this paradigm, a company could market lower-risk products without FDA premarket review. Higher-risk products could be marketed following a streamlined FDA premarket review if the company is certified by a third party as one that engages in high-quality software design and testing (validation) and ongoing maintenance.

FDA's forward-leaning stance in medical device cybersecurity also seeks to address an unmet gap in the healthcare and public health sector related to currently marketed medical devices. At present, a multi-disciplinary, device-focused team does not exist that brings together a broad range of requisite expertise (including hardware, software, networking, biomedical engineering, and clinical expertise) to fully assess and validate high-risk/high-impact vulnerabilities and incidents, including the potential patient safety implications of such vulnerabilities and incidents.

FDA will establish a public-private entity, comprised of subject matter experts from multiple disciplines across the government, academia, and private industry, to integrate the critical patient

safety and clinical environment dimensions into the assessment and validation of high-risk/high-impact vulnerabilities and incidents. This public-private entity will complement existing coordination and response mechanisms across the federal government without being duplicative.

In addition, to modernize its oversight of medical devices—such as those that are a part of the FY 2019 budget request—and to reduce inefficiencies and help industry bring innovative digital health and other technologies to market, FDA will implement the modern, agile information technology systems with cloud-based data storage necessary to support this new regulatory paradigm. These systems will foster the review of breakthrough device innovations, prevent and address cybersecurity vulnerabilities and incidents, facilitate the use of advanced manufacturing processing, and leverage real-world evidence. As part of this transformation, FDA will establish a knowledge management platform with customer friendly interfaces with industry, patients, and providers that will foster greater and more transparent interactions between FDA and its customers, including providing industry with the ability to track their premarket submissions. FDA will achieve time and cost savings to industry by integrating, redesigning, and streamlining at least 80 percent of its core business processes.

Implementing these regulatory innovations and information technology improvements are essential for advancing software-based and other technologies to improve the health and quality of life of patients while assuring critical safeguards, as the current regulatory framework is not well-suited for driving the development of safer, more effective software-based devices, including the use of machine learning and artificial intelligence.

Create a New Medical Data Enterprise

Center: +$46.0 million / 5 FTE

FDA will advance the use of real-world evidence to better inform patient care and provide more efficient, robust, and potentially lower-cost ways to develop clinical evidence that can inform medical device review and promote innovation. The Medical Device Data Enterprise, consisting of existing and emerging electronic health care data sources such as electronic health records (EHRs) and registries, will be expanded through ongoing development of data infrastructure and analytical tools to conduct near-real-time evidence evaluation down to the level of individual EHRs for at least ten million individuals in a broad range of health care settings in the United States. FDA, in collaboration with the National Evaluation System for health Technology (NEST) Coordinating Center, a public-private partnership under the Medical Device Innovation Consortium, will identify and work to address gaps in enterprise data infrastructure and analytic capabilities in a variety of health care settings. Filling these gaps will greatly enhance FDA's and the public's capacity to utilize real-world evidence to evaluate the pre- and postmarket safety and effectiveness of medical products, thereby reducing the time and cost of innovative device development and evaluation while providing greater patient safeguards at a lower cost. This approach will help drive the development of safer, more effective devices and more timely patient access to those devices. Key components related to the use of real-world evidence include the following investments.

<u>Active Surveillance</u>

Data infrastructure and methods/analytics development are key to active surveillance efforts. FDA will enable linkages across a variety of complementary data sources—including EHRs—to capitalize on the opportunity to evaluate broader sets of endpoints that are not easily captured

today. FDA will leverage established and evolving Coordinated Registry Networks (CRNs) that link claims, EHRs, and national and international device registries to transform the U.S. device surveillance infrastructure from passive to active. Active surveillance will improve access and analysis of data to ensure timely responses to public health threats.

Methods and Consensus Development

FDA will lead development and validation of standardized data extraction and analysis tools and active surveillance methods, such as learning effect algorithms and the use of natural language processing, based on stakeholder consensus recommendations, to efficiently monitor real-world data sources. In addition, FDA will help establish an open-source software repository consisting of Data Analytics Commons (DAC) to build national capabilities among a variety of stakeholders. A clinical evidence learning community will foster further capabilities, such as use of natural language processing, through establishment of a Learning Hub.

Enhancing UDI Quality

FDA will invest in research and analytics to further develop Unique Device Identifier (UDI) quality to link data and evaluate long-term patient outcomes after device use. UDI information, when part of real-world data such as EHRs, claims data, and registry data, will feed into NEST and promote accurate device identification and data aggregation, facilitating better analysis of information and improved regulatory decision-making. Support of data quality efforts is critical to ensure UDI adoption. The limited incorporation of UDI into electronic health information sources has limited the ability of industry and others to leverage real-world evidence to drive and reduce the time and cost of device innovation and timely patient access to safe and effective technologies.

Patient Engagement

Patient engagement is another key component related to the development of real-world evidence to evaluate medical devices, and mobile apps—often referred to as mHealth—play a key role. FDA will establish a Learning mHealth Research Community to advance the development and use of patient mHealth technologies in evidence generation and help mHealth companies save development time and increase marketability with a research design that returns insights to patients to encourage long-term use. FDA will also support the use of mHealth technologies to communicate with study participants to provide meaningful and understandable feedback of study progress and research results as well as promote easier participation in research through the awareness and adoption of standardized approaches for informed consent and patient privacy.

These investments will allow FDA to further leverage the use of real-world data to reduce the time and cost of clinical evidence development. Previous efforts have resulted in more efficient and informative postmarket data collection and more timely and lower cost approvals of new devices and expanded indications of already marketed devices, including for drug-eluting stents, pacing leads, companion diagnostics, spinal cord stimulators, and pediatric ventricular assist devices. In the case of transcatheter heart valves, leveraging real-world evidence has already resulted in a return on investment of more than 400 percent for industry, improved postmarket surveillance, and moved the United States from 42nd to, by some measures, first in the world in approvals for life-saving technologies.

Expanding the industry’s and FDA's capacity to utilize real-world evidence to evaluate the premarket and postmarket safety and effectiveness of medical products will improve the

efficiency of the regulatory process and reduce the time and cost required to bring beneficial innovations to the market, drive more timely patient access to safer, more effective technologies, and create more jobs in the United States.

USER FEES

Current Law User Fees: +$2.791 Million

Center: +$2.755 million / Field: +$0.036 million

The Devices Program request includes an increase of $2.8 million for user fees authorized under FDARA, which will allow FDA to fulfill its mission of promoting and protecting the public health by ensuring safety and efficacy of medical products and accelerating innovation in the industry.

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 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
253203: Percentage of received Original Premarket Approval (PMA), Panel-track PMA Supplement, and Premarket Report Submissions reviewed and decided upon. (Outcome)	FY 2015: 97% in 180 days Target: 90% in 180 days(Target Exceeded)	90% in 180 days	90% in 180 days	Maintain
253204: Percentage of 180 day PMA supplements reviewed and decided upon within 180 days. (Outcome)	FY 2015: 100% in 180 days Target: 90% in 180 days(Target Exceeded)	95% in 180 days	95% in 180 days	Maintain
253205: Percentage of 510(k)s (Premarket Notifications) reviewed and decided upon within 90 days. (Outcome)	FY 2015: 96% in 90 days Target: 95% in 90 days(Target Exceeded)	95% in 90 days	95% in 90 days	Maintain

253208: Percentage of De Novo requests (petitions to classify novel devices of low to moderate risk) reviewed and classified within 150 days. (Output)	FY 2016: 56% in 150 days Target: 50% in 150 Days (Target Exceeded)	50% in 150 days	55% in 150 days	+5%
253211: Percentage of planned Medical Device Bioresearch Monitoring (BIMO) inspections. (Output)	FY 2017: 91% Target: 91% (Target Met)	91%	91%	Maintain
252203: Percent of total received Code Blue MDRs reviewed within 72 hours during the year. (Output)	FY 2017: 95% Target: 90% (Target Exceeded)	90%	90%	Maintain
254202: Percentage of time CDRH meets the targeted deadline of 60 working days to review GMP information and issue Device Warning Letters. (Output)	FY 2017: 50% Target: 50% (Target Met)	50%	50%	Maintain
254203: Percentage of time CDRH meets the targeted deadlines for on-time recall classification (Output)	FY 2017: 83% Target: 85% (Target Not Met)	85%	85%	Maintain
254211: Percentage of planned domestic and foreign device inspections. (Output)	FY 2017: 91% Target: 57% (Target Exceeded)	80%	80%	Maintain
252101: Number of technical analyses of postmarket device problems and performance. (Output)	FY 2017: 52 Target: 50 (Target Exceeded)	50	50	Maintain
253207: Number of technical reviews of new applications and data supporting requests for premarket approvals. (Output)	FY 2017: 2,637 Target: 2,000 (Target Exceeded)	2,000	2,000	Maintain
254101: Percentage of an estimated 8,700 domestic mammography facilities that meet inspection standards, with less than 3% with Level I (serious) problems. (Outcome)	FY 2017: 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 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. In MDUFA IV (FY 2018 – FY 2022), De Novos are subject to performance goals for the first time. Performance goals are based on a percentage of the total number of De Novo requests for which a final decision (grant or decline) is rendered within 150 FDA days.

Recall Classifications

When the FDA learns of a company's correction or removal action, we review the strategy the company proposes to address the problem, determine if the problem violates applicable law, assign the recall a classification (I, II, or III) to indicate the relative degree of risk and post the information for the public. In FY 2017, FDA classified 83% (886 of 1069 recalls) of recalls within the targeted timeframe. In 2017, FDA recognized the need to train additional staff to perform recall classifications and subsequently trained 17 additional staff members to classify recalls. In September 2017, as new staff began classifying recalls, there was a temporary decrease in timeliness. In October and November 2017, timeliness improved to exceed performance targets (Oct 85% and Nov 87%).

Warning Letters

New ORA Field Performance Measures

ORA has been working to improve the field performance measures to better aligned with ORA's Program Alignment initiative. In this submission, ORA has completed the process of adjusting the performance goals, so that the FY 2018 and FY 2019 targets now complete a certain percentage of the planned inspections in ORA's annual Workplan. The ORA Workplan is the necessary mechanism that takes into account all the complex variables (geography, commodity, risk, availability, efficiency, etc.) that allows ORA to plan which inspections to do. With these newly formulated performance goals, ORA is committing to complete a certain percentage of the initially planned inspections. This revision strengthens the importance of the Workplan, but allows the flexibility to respond dynamically to changing circumstances during the year, to better handle emerging risks and evolving public health priorities (i.e. the heavy hurricane damage this past year). This is a significant departure from the previous performance goals, so FY 2018 will be an important year in resetting the new baselines. Also, since the targets are now based on a planned number of inspections, it is possible to inspect more than what was planned and thus have an actual inspection rate over 100%.

PROGRAM ACTIVITY DATA TABLES

Devices and Radiological Health Program Activity Data (PAD)

Devices and Radiological Health Program Activity Data (PAD)			
CDRH Workload and Outputs	**FY 2017 Actual**	**FY 2018 Annualized CR**	**FY 2019 President's Budget**
Original PMAs and Panel-Track Supplements (without Advisory Committee input)			
Workload [1]	57	64	64
Total Decisions [2]	67	65	65
Approved [3]	63	62	62
Original PMAs and Panel-Track Supplements (with Advisory Committee input)			
Workload	2	1	1
Total Decisions [2]	4	4	4
Approved	3	3	3
Modular PMAs			
Workload	91	92	92
Actions [4]	86	109	99
180-day PMA Supplements			
Workload	282	246	246
Total Decisions [5]	272	244	244
Approved	267	234	234
Real Time PMA Supplements			
Workload	337	333	333
Total Decisions [6]	327	335	335
Approved	312	320	320
510(k) Premarket Notifications			
Workload	4,100	3,944	3,944
Total Decisions [7] (SE & NSE)	3,253	3,285	3,285
Cleared [9] (SE)	3,117	3,131	3,131
Humanitarian Device Exemptions (HDE)			
Workload	5	4	4
Total Decisions [2]	3	4	4
Approved	3	3	3
Investigational Device Exemptions (IDE)			
Workload	311	290	290
Total Decisions [8]	324	309	309
Approved	195	188	188

Devices and Radiological Health Program Activity Data (PAD)			
Investigational Device Exemption Supplements			
Workload	1,624	1,640	1,640
Closures [10]	1,595	1,633	1,633
Pre-Submissions			
Workload	2,517	2,495	2,495
Closures [11]	2,479	2,475	2,475
De Novo			
Workload	101	60	60
Total Decisions [14]	58	66	51
Granted	29	33	25
Standards			
Total Standards Recognized for Application Review	1,261	1,250	1,270
Medical Device Reports (MDRs) [12]			
Reports Received	1,438,043	1,509,945	1,509,945
Analysis Consults [13]	633	655	655

[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.

[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 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC DEVICES ESTABLISHMENT INSPECTIONS	***2,648***	***2,498***	***2,498***
Bioresearch Monitoring Program Inspections	279	300	300
Pre-Market Inspections	61	60	60
Post-Market Audit Inspections	53	60	60
GMP Inspections	1,477	1,400	1,400
Inspections (MQSA) FDA Domestic (non-VHA)	787	700	700
Inspections (MQSA) FDA Domestic (VHA)	59	50	50
Domestic Radiological Health Inspections	61	50	50
Domestic Field Exams/Tests	5	100	100
Domestic Laboratory Samples Analyzed	191	170	170
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN DEVICES ESTABLISHMENT INSPECTIONS [1]	***782***	***613***	***613***
Foreign Bioresearch Monitoring Inspections	22	14	14
Foreign Pre-Market Inspections	24	30	30
Foreign Post-Market Audit Inspections	24	20	20
Foreign GMP Inspections	712	550	550
Foreign MQSA Inspections	12	14	14
Foreign Radiological Health Inspections	71	50	50
TOTAL UNIQUE COUNT OF FDA DEVICE ESTABLISHMENT INSPECTIONS	***3,430***	***3,111***	***3,111***
IMPORTS			
Import Field Exams/Tests	23,335	19,800	19,800
Import Laboratory Samples Analyzed	636	670	670
Import Physical Exam Subtotal	**23,971**	**20,470**	**20,470**
Import Line Decisions	20,584,138	22,025,028	23,346,529
Percent of Import Lines Physically Examined	0.12%	0.09%	0.09%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT DEVICES ESTABLISHMENT INSPECTIONS	***7,505***	***7,880***	***7,880***
Inspections (MQSA) by State Contract	1,060	6,800	6,800
Inspections (MQSA) by State non-Contract	6,398	1,060	1,060
GMP Inspections by State Contract	47	20	20
State Contract Devices Funding	$5,524	$5,690	$5,860
State Contract Mammography Funding	$10,383,992	$10,695,512	$10,909,422
Total State Funding	**$10,389,516**	**$10,701,202**	**$10,915,283**
GRAND TOTAL DEVICES ESTABLISHMENT INSPECTIONS	***10,935***	***10,991***	***10,991***

[1] The FY 2017 actual unique count of foreign inspections includes 12 OIP inspections (11 for China and 1 for India).

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NATIONAL CENTER FOR TOXICOLOGICAL RESEARCH

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
National Center for Toxicological Research (BA only).....	63,331	63,331	62,901	65,200	2,299
FTE.....	314	314	314	314	---

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, 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
- understand the risks and benefits of nanoscale materials used in FDA-regulated products
- 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 accomplishments demonstrate NCTR's delivery of its regulatory and public-health responsibilities within the context of current priorities.

Enhance Oversight

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 this area, NCTR conducts research in pediatric medicine, detection of bacterial and microbial contamination, cancer-drug toxicity, antimicrobial resistance, and the human microbiome.

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 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 on children.

Maternal and perinatal (developmental stage before and after birth) research has been a cornerstone of NCTR regulatory science research for more than 30 years. Throughout the years, this work has been conducted collaboratively with the FDA Product Centers such as the Center for Drug Evaluation and Research (CDER), external partners such as the Mayo Clinic, and academic institutions such as the University of Arkansas for Medical Science. NCTR research on pediatric anesthetics has led to several recent FDA Drug Safety Communications. Specifically in FY 2017, the FDA approved label changes[60] for the use of general anesthetics and sedation drugs in young children. The changes to the labeling includes a warning about cummulative exposures for long periods of time (several surgeries), as well as one-time exposures of more than three hours that may affect the developing brain.

Also in collaboration with CDER, NCTR scientists conducted exposure assessments in early FY 2017 on pediatric exposure to the gaseous anesthetic, desflurane. An abstract for the study can be found in the March issue of *The Toxicologist*[61] created for the 2017 Society of Toxicology Annual Meeting and ToxExpo™ In general, these data provide the scientific framework critical to updating the best practices for minimally-invasive pediatric anesthetic-assessment methods. A related study that continues into FY 2018, is evaluating the utility of neural stem-cell models in predicting the effects of the pediatric anesthetics sevoflurane and isoflurane in combination with nitrous oxide.

The effects of pediatric anesthesia are also being studied in collaboration with colleagues at the Mayo Clinic in Rochester, Minnesota using an NCTR-developed method for assessing brain function in children. This method has been used extensively in nonhuman primate studies conducted at NCTR. This collaborative study has completed the participant enrollment phase and has entered the data analysis and interpretation phase. 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. A manuscript summarizing progress of this study has been submitted for publication.

The FDA Opioid Action Plan[62] provides comprehensive guidance for reestablishing safe-use standards for these products. NCTR scientists supported opioid research in FY 2017 by completing a methods-development protocol which enabled FDA to gain hands-on-experience in neural stem-cell growth and differentiation. Based on the success of and insight gained from this initial experiment and in relation to perinatal-related FDA Drug Safety Communications[63], NCTR recently initiated a larger study to assess perinatal opioid exposure. NCTR will report preliminary findings regarding opioid exposure to brain cells during perinatal development in FY 2018 and finalize data on its potential neurotoxicity in FY 2019.

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,

[60] For more information on label changes visit: https://www.fda.gov/Drugs/DrugSafety/ucm554634.htm

[61] For more information visit: http://www.toxicology.org/pubs/docs/Tox/2017Tox.pdf

[62] For more information visit: http://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm484714.htm

[63] For more information visit: https://www.fda.gov/Drugs/DrugSafety/ucm429117.htm

also called biomarkers, of liver injury. A manuscript, published in FY 2017 verifies hemeoxygenase 1 (HMOX1) as a biomarker of APAP liver injury in blood plasma and can be found in *Proteomics Clinical Application*.

Rapid Detection of Bacterial and Microbial Contamination

Figure 13 NCTR scientist conducting bacterial detection analysis.

In FY 2017, NCTR scientists significantly improved and published a method for rapidly detecting low levels of harmful bacteria such as *E-coli* O157:H7 in foods. This method measures single bacterial cells without requiring a time-consuming period of growth on a Petri dish and is proven to be superior to the current FDA regulatory method. Information about this research may be found in *Frontiers in Microbiology*[64].

NCTR scientists also finalized a study in FY 2017 focused on the emerging public-health concern of genetic diversity in *shiga*-toxin producing *Escherichia coli* (STEC). The bacteria in the study were gathered from humans, cattle, and some food samples. NCTR 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. A manuscript describing this study can be found in *International Journal of Food Microbiology*[65].

Ongoing collaborative research efforts by NCTR and CFSAN scientists include looking for ways to rapidly detect:

- *Listeria monocytogenes* faster using genetic tags
- lower numbers of the Listeria cells in foods, such as cantaloupe, avocado, or carrots
- large numbers of samples as to the likelihood that they came from a particular source
- microbial contaminants—including mycobacteria—in tattoo inks.

The goals of an NCTR collaborative research study with CFSAN that began in late FY 2017 are to 1) survey tattoo inks previously used in NCTR toxicology tests for microbial contamination and 2) develop a reliable method for the rapid detection and evaluation of pathogenic mycobacteria, including *Mycobacterium chelonae*, in tattoo inks. This study continues in FY 2018. The results of this study will:

[64] For more information about rapid pathogen detection: Frontiers in Microbiology: http://journal.frontiersin.org/article/10.3389/fmicb.2017.01493/abstract

[65] For more information about STEC research: International Journal of Food Microbiology: http://www.sciencedirect.com/science/article/pii/S0168160515300970

- ensure the test and control groups are not affected by microbial contamination of tattoo inks used in animal studies, which may alter the research outcome and interpretation
- increase understanding of tattoo-related infectious diseases and their impact on public health
- provide FDA and the public with data and methods for determining the safety of tattoo inks from a microbiological-risk perspective.

Cancer-Drug Toxicity

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.

A continuing study in FY 2018 with 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 differentially expressed in heart mitochondria (a major target of DOX) before and after the occurrence of drug-induced cardiac injury. The study seeks to understand the molecular basis for different susceptibility to DOX toxicity between males and females. Researchers also found that pre-treatment of mice with a high dose of the heart-protecting drug, dexrazoxane, significantly reduced the severity of DOX-mediated gene expression changes and completely eliminated evidence of cardiac pathology. The most recent information about the study is available in *Toxicology and Applied Pharmacology*[66].

A new study aimed at testing cardiotoxicity of various drugs including those used in chemotherapy began in FY 2017. The goal of this preliminary study is to develop a mouse model of DOX-induced delayed cardiotoxicity in mice that will facilitate identification of early biomarkers for predicting risk of delayed cardiotoxicity. The mouse model will be designed to mimic the delayed cardiotoxicity observed in human cancer survivors. This study is targeted for completion in FY 2018 and may give rise to a larger study using the same model of cardiotoxicity.

Another drug, cyclophosphamide, is used to treat cancers and autoimmune diseases. It is used to quickly control the disease. Because of its toxicity, it is replaced as soon as possible by less toxic drugs. Regular and frequent laboratory evaluations are required to monitor kidney function, avoid drug-induced bladder complications and screen for bone marrow toxicity. A study involving the cognitive effects of both cyclophosphamide and doxorubicin is ongoing at NCTR. This study analyzes the neurobehavioral effects of single and combined treatment with these chemotherapy drugs using an animal model similar to a breast-cancer patient. This study is in collaboration with CDER and the University of Arkansas for Medical Sciences. A publication describing this research has been accepted and will be published in FY 2018.

Antimicrobial Resistance (AMR) and the Human Microbiome

The 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

[66] For more information on the study of dexrazone: http://www.sciencedirect.com/science/article/pii/S0041008X16300266

spread of drug resistance in bacterial pathogens that compromise our ability to treat foodborne illnesses. These projects support FDA's regulatory needs related to the pool of AMR genes and bacterial pathogens in feed, foods, clinical and environmental samples; and the potential effects of transmission of resistant bacteria on human health.

NCTR scientists, in collaboration with CVM, 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 AMR and enhanced disease-causing ability. Results showed that when certain *Salmonella* strains were exposed to different concentrations of specific antibiotics, there was an increase in the rate of resistance transfer by plasmids. A manuscript published in early FY 2018 regarding this research can be found in *BMC Genomics* NCTR and CVM continue their efforts in this vastly understudied area of research — comparing the impact of antimicrobial exposure on the spread of plasmids that can transfer AMR and the potential for increased pathogenicity to a cell. This study continues in FY 2018 and a manuscript describing this research can be found at *Genome Announcements*[67].

Microorganisms associated with the human gut are known collectively as the "human microbiome" or "microbiota" and play an important role in health and disease. The use of veterinary antimicrobial agents in food-producing animals may result in continual exposure of humans to low levels of antimicrobial residues in food as part of their daily diet. There is concern that antimicrobial agents at residue-level concentrations could potentially disrupt the microbial colonization that serves as a protective barrier in the gastrointestinal tract — important in combating certain diseases. These issues as well as other drug, bacterial, and food interactions associated with the human microbiome are becoming an increasingly more important research area for FDA.

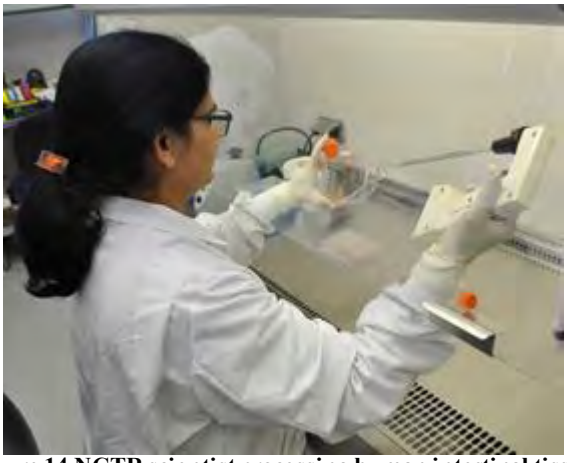

Figure 14 NCTR scientist processing human intestinal tissue to study its absorbency.

Pathogenic bacteria constitute a significant public-health problem worldwide. These microbes cause illnesses ranging from mild diarrhea to severe symptoms, and — in some instances — death. The prevalence of these pathogenic bacteria as a means of contamination during food harvesting and processing should be monitored more rapidly and precisely than is currently available. An ongoing project at NCTR aims to develop and assess a simple, sensitive, cost-effective, and rapid approach for the identification of potential bacteria contaminants in foods, feed, clinical samples, and other FDA-regulated products. This research, that continues in FY 2018, involves collecting and analyzing large sets of Next Generation Sequencing (NGS) data on different strains of *Salmonella enterica*. The goal of this study is to detect genetic clues from the NGS data that will help FDA monitor and detect the presence of *Salmonella enterica* in foods.

[67] For more information in Genome Announcements: http://genomea.asm.org/content/4/5/e01122-16.abstract

Improve and Safeguard Access

NCTR conducts research to evaluate FDA-regulated products in a more predictable, consistent, and efficient way and is often sought as a collaborator and advisor due to its exemplary reputation in the research community. Within this area, NCTR conducts research in precision medicine and genetic prediction, nanotechnology, bioinformatics and text mining, and bio-Imaging, and participates in the Global Summit on Regulatory Science and bioinformatics collaborations.

Precision Medicine and Genetic Prediction

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.

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.

Figure 15 NCTR scientist looks at cells through microscope.

In FY 2017, scientists at NCTR used thioacetamide (TAA), a well-known hepatotoxicant which could be a liver carcinogen in humans, to discover microRNA biomarkers of liver toxicity. After administering the chemical to rats, scientists used next generation sequencing to discover early and sensitive microRNA biomarkers for liver injury and tumor progression. These biomarkers could improve cancer diagnosis, prognosis, and management. A paper summarizing the findings of this study can be found in *Scientific Reports*[68]. This research continues in FY 2018.

Other NCTR research efforts to discover microRNA biomarkers of liver injury are using easily obtainable body fluids, such as blood and urine. Research analyzing blood and urine in adults who suffered acute liver failure was conducted in FY 2017. Most of the recent findings suggest that microRNAs in the urine may not only aid the diagnosis of acute liver failure, but may also have predictive value in determining patient survival. Also in FY 2017, NCTR researchers developed a method to detect biomarkers of liver disease, in this case extracellular

[68] To read about the TAA study in Scientific Reports: http://www.nature.com/articles/s41598-017-02798-7.pdf

vesicles (EVs), in blood and urine. EVs are small membrane-bound bodies that are highly involved in cellular communication. The results of this study were published in *Biomarkers of Liver Disease*[69]. Detecting these biomarkers is critical to improving the delivery of precision medicine by allowing for earlier and targeted treatment in patients.

Also supporting precision medicine, researchers at FDA's 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. This project was completed in FY 2017.

A study specifically tailored to precision-medicine solutions for FDA was started in late FY 2017. The study is entitled "Sequencing Quality Control Phase 2 (SEQC2): A Consortium Effort to Assess Next-Generation Sequencing (NGS) for Enhanced Regulatory Science Research and Precision Medicine". Most FDA Centers have encountered NGS data in regulatory science research and/or regulatory applications. This effort seeks to facilitate development of the quality metrics and standard analysis protocols for NGS and other similar technologies. Thus, the outcome from SEQC2 has the potential to significantly impact multiple FDA projects and practices and prepare FDA for the effective use and review of NGS data.

Nanotechnology

The NCTR/ORA Nanotechnology Core Facility (NanoCore) supports collaborative research efforts within FDA, and between FDA and other government agencies and universities. This work provides information on issues related to the safety of nanotechnology-based materials that may be used in FDA-regulated products.

The NanoCore conducts regulatory science research to better understand the effects of nanomaterials on human health. For example, working with CDER and CVM, the NanoCore is studying how nanomaterials travel through the blood and distribute in different parts of the body. Additionally, NCTR scientists are conducting research to better understand the effects, if any, that nanomaterials have on the human microbiome and immune system.

In collaboration with FDA's Office of Women's Health, NanoCore is also evaluating the potential migration and corresponding toxicity to the vaginal tissue of silver nanoparticles when used in feminine-hygiene products. Such investigations generate critical scientific data and information that helps FDA to ensure the safety of FDA-regulated products containing nanomaterials, and to develop any necessary and relevant guidance for industry.

Bioinformatics and Text Mining

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

[69] To read about EV research in Biomarkers of Liver Disease: https://link.springer.com/referenceworkentry/10.1007/978-94-007-7742-2_38-1

technologies required to improve product development, safety assessments, and risk analysis. Below are examples of NCTR's bioinformatics program.

Publicly Available Dataset/Database Name	Description
DILIrank	Dataset listing 1,036 FDA-approved drugs ranked by potential to cause drug-induced liver injury (DILI); the largest publicly available annotated DILI dataset. The drugs in the dataset were defined and verified as shown below: • 192 "Most-DILI" concern • 278 "Less-DILI" concern • 312 "No-DILI" concern • 254 "Ambiguous-DILI" concern *Drug Discovery* [70]Today
Endocrine Disruptor Knowledge Base (EDKB)[71]	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.
Estrogenic Activity Database (EADB)[72]	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.
FDALabel Database — Drug Labelings[73]	Hundreds of new or updated drug and biological products labeling documents with information about product indications, target populations, and adverse drug reactions are added weekly. NCTR created and maintains two production versions of FDALabel that make previously unavailable information easy to access — one version for the research community at large and a second version for FDA staff who review labeling for the safety and effectiveness of drugs. FDALabel — that allows customizable searches of over 95,000 labeling documents — is regularly used by: • researchers for adverse drug-reaction studies • FDA medical officers for drug review • pharmaceutical companies for drug development and repositioning

[70] For more information about DILIRank visit: http://www.sciencedirect.com/science/article/pii/S1359644616300411

[71] For more information about EDKB visit: http://www.fda.gov/ScienceResearch/BioinformaticsTools/EndocrineDisruptorKnowledgebase/default.htm

[72] For more information about EADB visit: http://www.fda.gov/ScienceResearch/BioinformaticsTools/EstrogenicActivityDatabaseEADB/default.htm

[73] For more information about FDALabel visit: http://www.fda.gov/ScienceResearch/BioinformaticsTools/ucm289739.htm

	• physicians and consumers for drug-safety information. NCTR has produced training materials and conducted training sessions, and is working with CDER partners to refine usability for regulatory application.

Text-mining methods apply computation approaches to 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 identification of e-mail messages containing certain words. Text-mining allows scientists to organize and search large datasets, many of which already exist, and may lead to finding new or hidden information that benefits public health.

NCTR scientists, as requested by CDER reviewers, are applying text-mining techniques including pattern-matching and natural-language processing to extract information from FDA approval letters for New Drug Applications and Biologic License Applications. A relational database and web-based application have been developed to host the information for better query, view, and analysis. NCTR scientists are also using pattern-matching and natural-language processing to map free-text drug indications to standardized nomenclatures used in approval letters and other regulatory documents

A recently started bioinformatic study at NCTR, in collaboration with CDER, will develop a database for the study of cancer predisposition in rare diseases. The study will investigate whether the genetic mutations from both cancer and rare disease interact with the same functional protein domain and look for correlation among the data This project is currently ongoing at NCTR and the results should be finalized in FY 2018. The results of this study may lead to another larger-scale study on the same topic.

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. This 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 disease, dementia, and mild cognitive impairment. NCTR developed a method using MRI and image analysis of MRI files to screen brain samples for evidence of neuro-irregularities (presumed neurotoxicities). The data obtained from these studies are being readied to support the qualification of MRI signals as brain-toxicity biomarkers. Such signals will also be useful for locating affected brain tissue allowing for targeted brain-slice collection for assessment via traditional histopathological techniques. The method has been used to monitor the life cycle of neurotoxic lesions caused by a variety of neurotoxicants including hexachlorophene, a potent compound used to treat burns and to prevent *Staphylococcus aureus* infections in infants. Publications about this approach can be found in

Neurotoxicology (vol. 56)[74], *Neurotoxicology* (vol. 577)[75], *Regulatory Toxicology and Pharmacology*[76], and *Toxicological Sciences*[77].

In FY 2017, NCTR researchers validated a minimally invasive three-dimensional MRI technique to more accurately evaluate brain neurotoxicity. A set of MRI image-analysis software has been assembled and the experimental brain lesions created by six neurotoxicants have been analyzed. Eight more brain lesions caused by other known neurotoxicants are being processed. All microscopic slides of brain tissue taken from the areas of neurotoxicity identified using the MRI have been converted into digital images that will be used to produce digital maps of neurotoxic damage and will be compared to the obtained MRI data. This technique, once validated, will allow for the minimally invasive detection and location of brain lesions.

Also in FY 2017, NCTR, in collaboration with FDA Product Centers, performed research on the bioaccumulation of gadolinium in the brain. Gadolinium is an agent commonly used during MRI procedures. This research contributed to a FDA Drug Safety Communication on May 22nd, 2017[78] concerning gadolinium-based contrast agents (GBCAs) and their retention in the brain and will continue through FY 2018.

New and continuing imaging research at NCTR includes:

- studying the relationship of MRI findings with biological fluid biomarkers
- comparing MRI results to current assessment methods to assess MRI sensitivity and specificity.

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.

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[79]. Now in its eighth year, the Global Summit's goal is to engage the global community

[74] For more information visit Neurotoxicology (vol. 56): http://www.sciencedirect.com/science/article/pii/S0161813X16301516?via%3Dihub

[75] For more information visit Neurotoxicology (vol. 577): http://www.sciencedirect.com/science/article/pii/S0161813X16302212?via%3Dihub

[76] For more information visit Regulatory Toxicology and Pharmacology: http://www.sciencedirect.com/science/article/pii/S0273230014002153?via%3Dihub

[77] For more information visit Toxicological Sciences: https://academic.oup.com/toxsci/article-lookup/doi/10.1093/toxsci/kfv083

[78] For more information on GBCAs visit: https://www.fda.gov/Drugs/DrugSafety/ucm559007.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

[79] For more information visit: https://www.fda.gov/AboutFDA/CentersOffices/OC/OfficeofScientificandMedicalPrograms/NCTR/WhatWeDo/ucm289679.htm

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 2017 Global Summit on Regulatory Science was held September 18-20, 2017, in Brasilia, Brazil. The Summit hosted a record number of 170 registered attendees and presentations from scientists representing 10 different countries. The Summit reinforced the need for and initiation of scientific exchange and collaboration.

Bioinformatics Collaborations

NCTR and the Arkansas state university system held the third annual Arkansas Bioinformatics Consortium conference in April 2017 to leverage statewide bioinformatics capabilities. The conference — organized by NCTR, Arkansas Research Alliance, and the Arkansas Bioinformatics Consortium — focused on the "Microbiome and Biomedical Informatics."

NCTR scientists led two of the four workshops and two of the breakout sessions at this year's 14th Annual Mid-South Computational Biology and Bioinformatics Society (https://mcbios.org/MCBIOS[80]) Conference that was held March 23-25, 2017, in Little Rock, Arkansas. The theme of this year's conference was "Make Them Safer Make Them Better: Bioinformatics and the Development of Therapeuticals." There were approximately 200 conference participants with 68 poster presentations, 62 oral presentations, and a wide array of guest speakers.

Also in FY 2017 as a result of NCTR Science Advisory Board recommendations, NCTR initiated the creation of a new research branch within the Division of Bioinformatics and Biostatistics emphasizing the development of the R2R (review-to-research and return) program. This program strengthens the Division and increases NCTR's linkages with FDA Product centers.

NCTR scientists organized a drug-induced liver injury (DILI) workshop sponsored by the FDA Liver Toxicity Working Group. The workshop was held at NCTR in January 2017, with the theme "DILI: Cross-Talk Among Clinicians, Toxicologists, and Regulators." Eleven invited speakers presented their cutting-edge scientific research on DILI with 36+ scientists attending in person and ~200 FDA scientists participating remotely.

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.

[80] For more information about MCBIOS visit: https://mcbios.org/

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, and the graphene study continues into FY 2018.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2015 Actual	$63,312,000	$63,312,000	---
FY 2016 Actual	$63,329,000	$63,329,000	---
FY 2017 Actual	$63,331,000	$63,331,000	---
FY 2018 Annualized CR	$62,901,000	$62,901,000	---
FY 2019 President's Budget	$65,200,000	$65,200,000	---

BUDGET REQUEST

The FY 2019 Budget Request is $65,200,000, which is all Budget Authority. Budget Authority increases by $2,299,000 compared to the FY 2018 Annualized CR level. The FY 2019 Budget will allow NCTR to continue research to support emerging technologies and toxicology assessments required by FDA and increase the scope of NCTR's collaborative research. 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 FDA-regulated products
- integrate toxicology safety assessments maximizing existing and emerging technologies
- provide regulatory science capacity to evaluate FDA-regulated products in a more predictable, consistent, and efficient way
- provide valuable research data on FDA-regulated products using new technologies
- help FDA better understand and interpret diverse data submissions that are generated using new methodologies and techniques.

These research areas include, but are not limited to the advancement of bioinformatics technologies, precision medicine, biomarkers, bio-imaging, pediatric medicine, neurotoxicology, human microbiome, and nanotechnology. This research will be 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. Investments in these areas in recent years have enhanced the capabilities and expertise that allows FDA to capitalize on global scientific advancements and expand FDA's regulatory-science capacity and, ultimately, the American public. These funds will allow such efforts to continue and will give the programs and associated projects the opportunity to develop.

BUDGET AUTHORITY

Medical Product Safety (+$2.23M)

NCTR will be able to pursue the following activities to focus on supporting FDA's highest priorities for FY 2019:

- continue to provide the scientific-framework critical to updating the best practices for minimally-invasive pediatric anesthetic-assessment methods
- conduct research on the safety of, and precision medicine solutions for, chemotherapeutic drug regimens
- research the toxic potential of nanoparticles in feminine hygiene products and other FDA-regulated products.

Promote Domestic Manufacturing

As part of FDA's FY 2019 initiative to promote domestic manufacturing, FDA will help reduce the cost and uncertainty of adopting new manufacturing technologies by developing a science-based framework that includes the regulatory tools and guidance for how products will be evaluated, and by funding research, development and testing of these technologies. NCTR will:

- continue development of mathematical (pharmacokinetic and pharmacodynamic) and in silico (computer-based) models to be used as alternatives to animal studies
- generate data and increase collaboration focused on the developmental period briefly before and after the birth of a child, known as the perinatal period. The perinatal period, along with the lactation phase, represents a vastly understudied stage of development due to the lack of clinical trials.

Food Safety (+$0.069M)

NCTR will continue research related to antimicrobial resistance and the human microbiome.

PERFORMANCE

NCTR's performance measures focus on research to advance the safety of FDA-regulated products, to develop a strong FDA science base for emerging technologies, and to provide precision medicine solutions to protect and improve the health of the American public as represented by the following table.

Measure	Most Recent Result / Target for Recent Result	FY 2018 Target	FY 2019 Target
263103: Conduct translational and regulatory research to advance the safety of products that FDA regulates *(Output)*	FY 2017: Assembled a set of MRI image-analysis software which can produce digital maps of neurotoxic damage and can be used as an alternative to traditional, more invasive, methods (Target Met) FY 2017: A manuscript was published in *Toxicological Sciences* regarding the neurological effects of commonly used chemotherapy drugs doxorubicin and cyclophosphamide (Target Met)	Report preliminary data concerning opioid exposure during prenatal development on neural precursor cells Provide data regarding the development and evaluation of predictive models that can improve the assessment of drug-induced liver injury (DILI) risk during the Investigative New Drug (IND) phase	In collaboration with CDER, finalize data on the bioaccumulation of gadolinium, a heavy metal commonly used as a contrast agent during Magnetic Resonance Imaging (MRI) procedures Finalize data on the potential neurotoxic effects of opioids during prenatal development

Measure	Most Recent Result / Target for Recent Result	FY 2018 Target	FY 2019 Target
263201: Develop science base for supporting FDA regulatory review of new and emerging technologies *(Output)*	FY 2017: Finalized data gathered concerning the toxicity of graphene nanomaterials (Target Met) FY 2017: Identified and validated predictive biomarkers that can indicate the immune system has been harmed by exposure to nanomaterials (Target Met)	Conduct analysis and risk assessment of drug-nanocrystals on the human gastrointestinal tract Develop a more rapid and sensitive *in vitro* (non-animal) assay for the identification of cancerous substances as an alternative to the much longer classical animal bioassay	Finalize research regarding the toxic potential of silver nanoparticles in feminine hygiene products utilizing 3D mucosal models
262401: Develop biomarkers to assist in characterizing an individual's genetic profile in order to minimize adverse events and maximize therapeutic care (Output)	FY 2017: The metabolism of several drugs that were predicted to have differential toxicity effects in males and females was examined in both male and female animal models (Target Met)	Complete a study that will promote women's health by facilitating the development of personalized approaches to treat breast cancer Identify new clinical biomarkers that predict chemotherapy-induced cardiotoxicity prior to the occurrence of overt cardiac-tissue damage	Identify and validate potential early biomarkers for prostate disease using an animal model and human prostate cells Identify human cancer mutations that can be used as biomarkers to potentially speed the development of effective personalized cancer treatments

Measure	Most Recent Result / Target for Recent Result	FY 2018 Target	FY 2019 Target
264101: Develop risk assessment methods and build biological dose-response models in support of food protection *(Output)*	FY 2017: Developed a simple, sensitive, cost-effective, and rapid approach for the identification and characterization of potential bacteria contaminants in foods, feed, clinical samples, and other FDA-regulated products (Target Met)	Provide data on how exposure of the human gastrointestinal tract to low concentrations of antimicrobial veterinary drug residues in food will affect human intestinal microbiome	Explore and provide results of research on how fecal microbial transplant is an effective treatment for bacterial infections such as *Clostridium difficile*
263104: Use new omics technologies to develop approaches that assess risk and assure the safety of products that FDA regulates *(Output)*	FY 2017: A panel of biomarkers for kidney cancer were discovered. A publication can be found at *Scientific Reports* (Target Met)	Using a multi-omics approach, identify an antimicrobial resistance marker of *Staphylococcus aureus* associated with antimicrobial-coated medical devices commonly used in a hospital setting	Discover and validate early biomarkers of cardiotoxicity associated with an effective chemotherapy drug utilizing a variety of methods including whole RNA genome sequencing

Measure	Most Recent Result / Target for Recent Result	FY 2018 Target	FY 2019 Target
263102: Develop computer-based models and infrastructure to predict the health risk of biologically active products *(Output)*	FY 2017: Developed and refined FDALabel, a bioinformatic tool, with new functionalities based on feedback from FDA reviewers and scientists (Target Met)	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 mandatorily and voluntarily by patients, health care professionals, and manufacturers to support post-market drug safety surveillance	Facilitate the development of the quality metrics and standard analysis protocols for Next Generation Sequencing (NGS) and other similar technologies Develop novel *in silico* (computer-based) methods as alternatives to animal models

Advance the Safety of FDA-Regulated Products

NCTR research is vital to ensure the safety and effectiveness of the products that the FDA regulates. Two specific examples include research regarding opioids and gadolinium – a heavy metal commonly used as a contrast agent during MRI procedures. The FDA Opioid Action Plan provides comprehensive guidance for reestablishing safe-use standards for these products. In support of this effort, NCTR will report their preliminary findings regarding opioid exposure to brain cells during prenatal development in FY 2018 and finalize data on the potential neurotoxicity in FY 2019. Also in FY 2019, NCTR scientists will continue to advance the safety of FDA-regulated products by providing data on the bioaccumulation of gadolinium in the brain.

Develop Science Base for New and Emerging Technologies

The understanding of nanomaterials and their potential toxicity is of great importance to FDA. In FY 2018, NCTR scientists will conduct an analysis and risk-assessment of drug-nanocrystals on the human gastrointestinal tract. Nanocrystals increase a drug's ability to dissolve, which potentially increases the drug's effectiveness. However, if a drug does not easily dissolve, it may be not only ineffective, but the drug may also accumulate in the gastrointestinal tract causing unknown health consequences. Nanomaterial research will continue in FY 2019, as NCTR scientists conduct research regarding the toxic potential of silver nanoparticles in feminine hygiene products utilizing 3D mucosal models. In FY 2019, NCTR will also continue development of *in silico* (computer-based) methods as alternatives to animal models.

Precision Medicine

NCTR continues to support FDA in its pursuit for precision medicine solutions through cutting-edge research that uses an individual's or demographic groups' genetic information to tailor treatment regimens for safety and effectiveness. Among the products that NCTR investigates are post-market chemotherapy drugs and new alternative drugs and methods available to cancer patients. Specifically, in FY 2018, NCTR will conduct a study that will promote women's health by facilitating the development of personalized approaches to treat breast cancer.

In FY 2019, a projected entitled "Sequencing Quality Control Phase 2 (SEQC2): A Consortium Effort to Assess Next-Generation Sequencing (NGS) for Enhanced Regulatory Science Research and Precision Medicine" will be conducted. Most FDA Centers have encountered NGS data in regulatory science research and/or regulatory applications. This effort seeks to facilitate development of the quality metrics and standard analysis protocols for NGS and other similar technologies. Thus, the outcome from SEQC2 has the potential to significantly impact multiple FDA projects and practices and prepare FDA for the effective use and review of NGS data.

PROGRAM ACTIVITY DATA

Program Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
Research Outputs			
Research Publications	155	170	165
Research Presentations	148	135	145
Patents (Industry)	5	5	5
Leveraged Research			
Federal Agencies (Interagency Agreements)	3	3	3
Nongovernmental Organizations	19	19	18
Active Research Projects	158	155	159

OFFICE OF REGULATORY AFFAIRS - FIELD ACTIVITIES

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
Office of Regulatory Affairs	**1,154,001**	**1,108,570**	**1,139,274**	**1,148,674**	**9,400**
Budget Authority	***1,039,968***	***1,040,199***	***1,032,904***	***1,040,908***	***8,004***
User Fees	***114,033***	***68,371***	***106,370***	***107,766***	***1,396***
Prescription Drug (PDUFA)	*12,725*	*10,110*	*9,435*	*9,944*	*509*
Medical Device (MDUFA)	*2,213*	*2,058*	*2,278*	*2,318*	*40*
Generic Drug (GDUFA)	*55,973*	*33,185*	*53,104*	*53,943*	*839*
Biosimilars (BsUFA)	*1,416*	*213*	*1,120*	*1,140*	*20*
Animal Drug (ADUFA)	*427*	*15*	*307*	*427*	*120*
Animal Generic Drug (AGDUFA)	*302*	*---*	*235*	*326*	*91*
Tobacco Control Act	*14,900*	*11,435*	*14,799*	*14,550*	*-249*
Mammography Quality Standards Act (MQSA)	*13,892*	*10,961*	*13,892*	*13,892*	*---*
Food And Feed Recall	*1,000*	*---*	*1,000*	*1,000*	*---*
Food Reinspection	*5,382*	*---*	*5,382*	*5,382*	*---*
Voluntary Qualified Importer Program	*4,320*	*---*	*4,320*	*4,320*	*---*
Third Party Auditor Program	*1,141*	*---*	*144*	*144*	*---*
Outsourcing Facility	*342*	*394*	*354*	*380*	*26*
FTE	**5,001**	**5,001**	**5,080**	**5,097**	**17**

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); Drug Quality and Security Act of 2013; Food and Drug Administration Reauthorization Act of 2017 (FDARA) (P.L. 115-52).

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. As FDA's lead office for all agency field activities, ORA inspects regulated products and manufacturers, conducts sample analyses of regulated products, and reviews imported products offered for entry into the United States. These activities help protect consumers and enhance public health by maximizing compliance of FDA-regulated products and minimizing risk associated with those products, including 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 and two co-located medical product labs and one tobacco lab that conduct applied research and perform highly specialized analyses of domestic and imported products. ORA develops and maintains information technology systems used across the FDA necessary to support mission critical activities such as information sharing and risk based decision making. 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.

Program Alignment (PA)

In May 2017, as part of a broader agency initiative called Program Alignment, ORA implemented a program-based management structure that aligns staff by FDA-regulated product. This organizational approach replaces a management structure based on geographic regions. Specializing by FDA-regulated product type more closely mirrors the organizational model of FDA's centers and the industries we regulate. This will enhance the effectiveness of our communications, our processes, and our ability to keep pace with scientific innovation and protect public health.

Adapting to an Evolving Domestic and International Supply Chain

The supply of FDA-regulated products continues to grow in complexity, both domestically and globally. In response, ORA continues to build partnerships with Federal, State, and local agencies across the United States to strengthen public health safety. ORA increased the size of its foreign food cadre, conducting more than 1,500 foreign food inspections in FY 2017, which was an

increase from inspection under 1,300 in FY 2016. Through improvements to technology systems, FDA continues to increase transparency and access to importers and other government agencies, helping to improve the efficiency of import entry reviews.

Foreign Supplier Verification Program (FSVP)

FDA continues to work on implementing the Foreign Supplier Verification Program (FSVP). FSVP requires importers to conduct risk-based foreign supplier verification activities to verify that imported food is not adulterated and that it was produced in compliance with FDA's preventive controls requirements and produce safety standards, where applicable. ORA has implemented an internal training program and trained a cross section of investigators, supervisors, and compliance staff within FDA to enable the ongoing inspections under this program. The cross-section of staff that have been trained thus far ensure the agency has adequate staff throughout the life cycle of an FSVP inspection from initiation of the inspection, to managerial review of the inspection findings, compliance review and final classification of the inspection findings.

Enhance Oversight

Risk-Related Preventive Focus

Working with the FDA Centers, ORA uses a risk-based approach to target firms to inspect, enabling ORA to focus its on-site inspections on the highest risk facilities and industries both domestically and abroad. In addition, ORA actively advocates for enhanced partnerships with federal and state, local, tribal, and territorial (SLTT) public health regulatory partners. FDA provides support and funding to SLTT food safety partners to build an Integrated Food Safety System (IFSS) which helps enhance FDA's own coverage of the domestic inventory and better protect the American food supply. 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.

FDA has also begun the process of rethinking how the agency deploys sampling resources. Over the years sampling approaches have evolved 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 vision for the sampling process that is not just traditional surveillance and compliance based, but also serves as a mechanism to actively identify risks and when possible to identify areas where preventive controls should be put into place to better protect public health. As FDA increases its understanding of the sources of contamination in high risk commodities and practices, it can more effectively allocate resources to address public health risks through compliance sampling, targeted sampling or other risk mitigation strategies.

The Center for Food Safety & Nutrition (CFSAN) and ORA have developed the future state of sampling whereby various information sources, including those from our regulatory partners and external stakeholders can be used in shaping our sampling assignments. So, if a state or industry has done research on a certain product, ORA can leverage and use that research in our decision making on assignments.

The Center for Drug Evaluation and Research (CDER) and ORA have entered an unprecedented concept of operations (ConOps) agreement to integrate facility evaluations and inspections for human drugs. The agreement, Integration of FDA Facility Evaluation and Inspection Program for

Human Drugs: A Concept of Operations, outlines the responsibilities and the workflow for Pre-Approval, Post-Approval, Surveillance, and For-Cause Inspections at domestic and international facilities. ConOps will enable CDER and ORA to more effectively manage the growing complexity of the pharmaceutical landscape and to meet new challenges.

CDER and ORA are also working together to develop a new, more efficient inspection and reporting paradigm to better assess and record the state of quality in manufacturing facilities. This project, known as the New Inspection Protocol Project (NIPP), utilizes standardized electronic inspection protocols and templated and semi-automated inspection reports. Feedback from ORA and CDER stakeholders led to major improvements in the protocols. The new inspection protocol aims to enhance consistent and comprehensive coverage of critical areas, including targeting the highest risk products and processes.

IFSS and Program Standardization

FDA prioritizes its inspectional efforts in coverage of the highest risk products, facilities, and global marketplace. Therefore, to meet the responsibilities specified by FSMA, FDA has made significant investments in the development of IFSS. In support of IFSS and protection of the nation's food supply, FDA relies on the strength and capability of federal and SLTT 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. FDA currently has contracts with 48 regulatory agencies in 43 States and Puerto Rico for food safety inspections, with 34 regulatory agencies for animal food safety inspections, and with 7 regulatory agencies for egg safety inspections.

To ensure uniformity in the regulation and approach taken by our partners, FDA works collaboratively with SLTTs and numerous regulatory and public health associations to develop guidance, rules, and standards that provide a framework to the regulation of these partners. FDA also 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
- provide a collaborative vision and approach for a sustainable uniform electronic data exchange with IFSS partners.

FDA has worked collaboratively with its SLTT regulatory partners to develop three sets of national regulatory program standards: Manufactured Food Regulatory Program Standards (MFRPS), Animal Feed Regulatory Program Standards (AFRPS), and Voluntary National Retail Food Regulatory Program Standards (VNRFRPS). These standards establish a uniform foundation for the design and management of SLTT programs that have the responsibility for regulating human and animal food. One of the key principles of FSMA is the ability to rely on partner agencies to meet the inspection mandate set forth in FSMA. National standards increase consistency and uniformity among partner agencies, thus increasing the quality and overall confidence in the work conducted by these agencies and providing a solid platform for federal and state agencies to use each other's findings for effective, timely, and efficient actions to

protect public health. Standards also advance a nationally integrated approach to food safety and public health by promoting capacity building, accountability, cost efficiency, transparency, and exchange of best practices. Currently, there are 812 SLTT jurisdictions enrolled in VNRFRPS and FDA has granted 40 MFRPS awards and 22 AFRPS awards to SLTT regulatory agencies.

FDA has enhanced produce safety through advancing and implementing the Produce Safety Rule by awarding cooperative agreements to 43 states to enhance their capacity, coordination, and training efforts. Establishing these cooperative agreements helps leverage federal resources to provide the states the funding that they need to establish or expand their produce safety programs and ultimately make the food safety system work more integrated. FDA is also working with states and stakeholders to develop training to implement the Produce Safety Rule to draft the inspectional model for farms inspections. FDA is committed to working with state partners to develop educational materials, on-farm readiness reviews and on-farm educational visits. In FY2017 ORA continued to perform food and feed assessments of the states participating in the program, verifying the progress being made by our state regulatory counterparts.

FDA is also working with stakeholder groups for consideration of egg standards. In FY 2017, 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 their own state egg safety laws and regulations in comparison to the current federal egg safety laws and regulations; to develop and implement an agreement and protocol for sharing egg regulatory inspections and information between states and the FDA; and to identify gaps and areas of improvement between federal and state egg programs. By the end of this project, grantees are expected to work together in providing recommendations for national egg safety regulatory program standards for that states to may adopt.

In the coming years, multiple projects will be initiated by ORA to support a system for produce safety farm inventory and inspections, preventive controls inspections, state conducted sprout safety inspections, capabilities to support exchange of sample collection information, and continual improvement of data and document sharing with regulatory partners.

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 SLTT, federal, and global regulatory partners.

ORA is also 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. 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.

Under the Partnership of Produce Safety (PSP), our regulatory partners in Mexico are incorporating a system for risk reduction for produce and FDA continues to work with the government of Mexico to enhance produce safety controls on both sides of the border. FDA has also worked with our regulatory partners in Mexico on several produce related outbreaks that have been traced to that country. For example, experts from FDA and the Center for Disease Control and Prevention travelled to Mexico and worked with our regulatory partners in Mexico to trace outbreaks and enter farms within the State of Puebla to investigate. This collaboration has resulted in an import alert and has reduced the number of outbreaks related to cyclospora in cilantro.

ORA is actively engaged in CFSAN's efforts to expand the Agency's international arrangements under the Systems Recognition program. Systems recognition involves reviewing a foreign country's domestic food safety regulatory system to determine if it has a food safety system that provides a similar system of food safety protection to that provided by the FDA. This approach allows FDA to focus import screening efforts on areas of higher risk. To date, FDA has entered a System Recognition arrangements with New Zealand, Australia and Canada and is exploring additional opportunities including actively working with the European Union. 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).

Mitigating Significant Increases in Import Entry

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.

Import Operations

Program Area	2012	2013	2014	2015	2016	2016 Percent Growth*	2016 Percent of Total Lines	Estimate 2017	Estimate 2018	Estimate 2019
Foods	10,805,094	11,502,065	12,180,223	13,080,429	13,952,537	5%	37.70%	14,650,164	15,382,672	16,151,806
Cosmetics	2,349,615	2,433,747	2,596,057	2,930,682	2,939,034	4%	7.94%	3,056,595	3,178,859	3,306,014
Human Drugs	592,591	590,079	641,908	688,208	739,309	4%	2.00%	768,881	799,637	831,622
Animal Drugs & Feeds	331,505	368,447	391,388	416,860	434,384	5%	1.17%	456,103	478,908	502,854
Biologics	65,469	74,402	82,710	150,673	151,911	14%	0.41%	173,179	197,424	225,063
Medical Devices & Rad Health	13,651,985	14,320,961	16,668,422	17,252,283	18,757,725	6%	50.69%	19,883,189	21,076,180	22,340,751
Tobacco Products	17,757	19,316	20,161	16,680	32,972	8%	0.09%	35,610	38,459	41,535
Total	27,814,016	29,309,017	32,580,869	34,535,815	37,007,872	5%	100.00%	39,023,721	41,152,138	43,209,745

ORA works with the U.S. Customs and Border Protection (CBP) through several partnerships and Memoranda of Understanding to improve and streamline the import process to expedite the release of compliant products. FDA is one of 12 Partner Government Agencies present at CBP's Commercial Targeting and Analysis Center (CTAC). CTAC is designed to promote interagency collaboration to collectively target against high-risk shipments and increase compliance with Federal standards and regulations allowing the U.S. Government to more cohesively serve the U.S. public.

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. FDA continues to participate as an active member of Pharmaceutical Inspection Cooperation Scheme (PIC/S), the multinational organization that now contains 49 participating authorities representing the pharmaceutical inspectorate. The mission of PIC/S is to lead the international development, implementation, and maintenance of harmonized Good Manufacturing Practices (GMP) standards and quality systems of inspectorates in the field of medicinal products. For the first time since joining PICS in January 2011, the FDA is now a member of the Executive Board. This honor was earned by US being voted as Chair of the Sub-Committee on Strategic Development.

On November 27, 2013, the Drug Supply Chain Security Act (DSCSA) (Title II of Public Law 113-54) was signed into law. DSCSA outlines requirements to develop and enhance drug supply chain security by 2023 and includes product tracing requirements for manufacturers, repackagers, wholesale distributors and dispensers. The DSCSA directs FDA to establish national standards for licensing WDDs and 3PLs to improve drug supply chain security. The DSCSA also created a new licensing scheme for WDDs and 3PLs, whereby, if a state does not have a licensing program for wholesale distributors and 3PLs that is in accordance with the federal standards, FDA will license WDDs and 3PLs in that state. FDA continues to develop and will implement the licensure program, whose components can be categorized into three primary areas: accreditation, licensing, and inspection. These three areas must include, among other things, accepting and reviewing applications, developing a program for accrediting third parties to conduct inspections, developing an inspection program, and accepting user fees.

FDA and CBP continue to work together to assess recommendations from Commercial Operations Advisory Committee (COAC) for possible implementation. COAC is a 20-member council that meets quarterly and advises government agencies on the commercial operations of CBP and related functions, taking into consideration issues such as global supply chain security and trade facilitation, CBP modernization and automation, air cargo security, customs broker regulations, trade enforcement, U.S. government approach to trade and safety of imports, agriculture inspection, and protection of intellectual property rights.

FDA has worked with CBP and 46 partner government agencies to modernize the electronic entry process through the implementation of the Automated Commercial Environment/International Trade Data System (ACE/ITDS). ACE/ITDS is the single access point whereby industry can electronically submit all data required by various partner government agencies involved in international trade. This single window for trade unifies border coordination, fosters government and industry collaboration, and yields prosperous and secure trade worldwide. As of July 2016, all electronic data and messages associated with FDA regulated import commodities were and continue to be transmitted through the ACE portal, including final dispositions of goods presented for import. The implementation of ACE has led to improved system performance and improvements in the timeliness of providing feedback to trade on admissibility decisions associated with entry dispositions.

Over the past several years, FDA has worked with our internal stakeholders and partner government agencies such as CBP and the United States Postal Service (USPS) in the International Mail Facilities (IMFs) to develop and implement the necessary guidance and instructions to utilize new authority provided under section 708 of FDASIA. The authority under

the Food and Drug Administration Safety and Innovation Act (FDASIA) 708 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. In May 2017, FDA implemented the FDASIA 708 administrative destruction process across all nine IMFs. FDA is phasing in implementation of this rule, applying our destruction authority to the most egregious examples of impermissible drug products and will expand use as we assess the success of our activities and review any lessons learned.

ORA continues to work to implement the Voluntary Qualified Importer Program (VQIP). VQIP is a fee-based program that provides 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; controls supporting a high level of confidence in the safety and security of the food they import. Expedited entry incentivizes importers to adopt a robust system of supply chain management and further benefits public health by allowing FDA to focus its resources on food entries that pose a higher risk to public health. FDA's policy regarding participation in the program by importers of food for humans or animals is outlined in a Guidance for Industry document published November 2016. FDA anticipates that the agency will begin to accept applications from importers who wish to participate in VQIP in 2018.

FDA has developed and implemented an account management functionality to allow for bilateral communications with importers and other industry stakeholders. This system the Industry Trade Auxiliary System (ITACS) allows for additional information to be requested by FDA on entries and submitted from trade. Additionally, and perhaps just as importantly it allows for the electronic notification of trade of FDA actions rather than requiring the information to be sent out through traditional mail. The system which went live in September of 2017 is voluntary but has received accolades from industry and already saved the FDA approximately $10,000 by implementing an electronic notification process. This cost savings is expected to increase over time.

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 these 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 take part in developing assignments.

ORA funds and manages the Food Emergency Response Network (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 (CAP) laboratories 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 provides International Organization for Standardization (ISO)/International Electrotechnical Commission (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.

Figure 16 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 formed two groups at Pacific Regional Lab Southwest and New York Regional Labs that specialize in pharmaceutical testing research programs. 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 August 2017, FDA has approved five biosimilar drugs to be used in the United States.

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.

Surveillance of FDA-Regulated Products

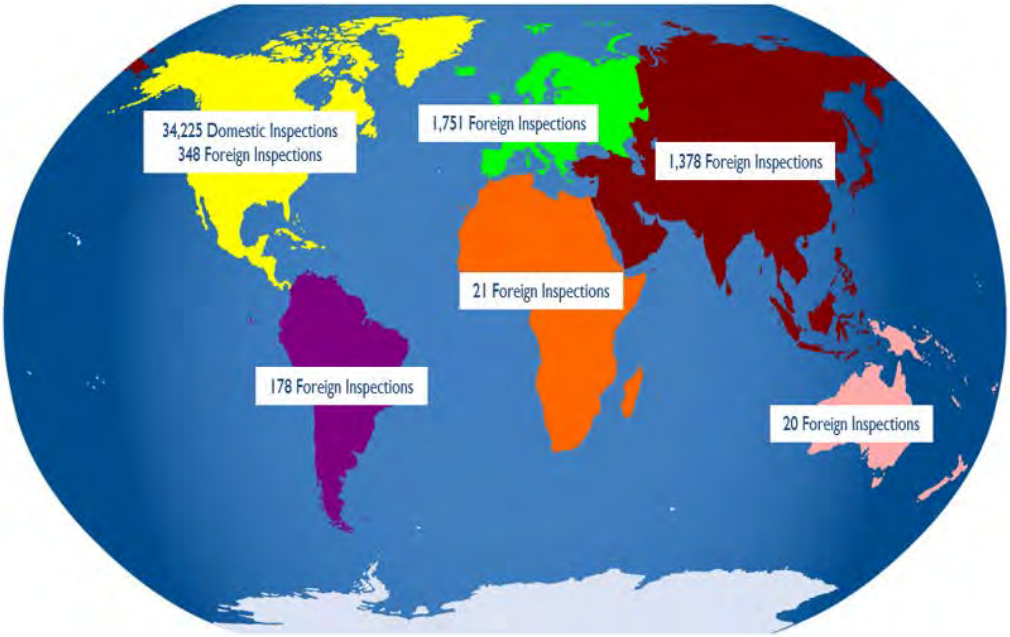

Figure 17 FY 2017 FDA Inspections by Continent *as of December 2017

ORA works with each FDA 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 outbreak investigations 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.

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.

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.

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 2017 alone, ORA conducted 141 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.

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.

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.

The Drug Quality and Security Act of 2013 created "outsourcing facilities" – a new sector of drug compounder intended to provide a safer, reliable supply of compounded drugs needed by hospitals, clinics and other providers to treat patients. After three years, this industry is still relatively small, experiencing growth challenges, and is not yet fulfilling its potential. FDA will create a Center of Excellence on Compounding for Outsourcing Facilities and an expanded FDA engagement with outsourcing facilities. The Center of Excellence will seek to identify and propose solutions to market barriers and provide much-needed education and training to improve quality, safety, and purchaser confidence. FDA will seek to improve manufacturing practices, create new programs offering FDA review of studies and protocols, and work with its state partners to reduce state regulatory diversity.

Enforcement of FDA Authorities

ORA's Office of Criminal Investigations (OCI) has the primary responsibility for criminal investigations conducted by the FDA and for all law enforcement and intelligence issues pertaining to threats against FDA-regulated products. In 2017, the criminal investigative work of OCI resulted in 275 domestic arrests, 8 foreign arrests, 226 convictions, and over $455 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, a Europol - Interpol joint operation targeting counterfeit and substandard food and beverages. This operation is conducted from December 2016 to March 2017 and across 57 countries, Operation Opson VI resulted in the seizure of 9,800 tons, 26.4 million liters, and 13 million units of counterfeit or substandard food and beverages.

Through FY 2017, OCI has conducted training sessions on cybercrime, counterfeit drugs, and drug diversion for foreign criminal law enforcement agencies in Mexico, Canada, China, Central and South America, Africa, Asia, Australia, the Middle East, and Europe. In May 2017, FDA-OCI hosted law enforcement, customs and regulatory personnel from 13 countries, Europol and Interpol at the Federal Law Enforcement Training Center for the annual case coordination and strategy meeting of the Permanent Forum on International Pharmaceutical Crime (PFIPC). PFIPC is an international enforcement forum aimed at protecting public health through the exchange of information and ideas to foster cooperation.

During June 2017, FDA-OCI participated in a joint enforcement operation in the United Kingdom focused upon non-FDA approved drugs and medical devices originating from unauthorized foreign sources. FDA-OCI partnered in this operation with personnel from Her Majesty's Revenue and Customs, Border Force, and the Medicines & Healthcare products Regulatory Agency. This operation included targeted activities against violative airfreight and informal mail shipments destined for the United States, which included counterfeit and illicit pharmaceuticals intended to breach the FDA regulated supply chain.

Improve and Safeguard Access

Premarket Activities

ORA supports the review and approval process for medical product applications by conducting inspections of the manufacturing facilities to help ensure products are produced in accordance with the specifications outlined in the application. 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 and CDER are working to decrease the amount of time required to issue inspection assignments and complete domestic and foreign inspections of establishments conducting bioavailability/bioequivalence studies. Tighter timeframes have been implemented to decrease the amount of time elapsed from application receipt to review decision for bioavailability/bioequivalence. ORA and CDER also conduct joint inspections where appropriate, and have reached agreement for ORA to conduct clinical site inspections and CDER to conduct analytical site inspections separately. This arrangement has allowed FDA to conduct more inspections in a shorter period, speeding the review of generic drug applications.

CDER and ORA have developed a streamlined process for Pre-Approval Facility Evaluation and inspections which directly support the assessment of marketing applications by assuring that any manufacturing facility named in the application can manufacture the drug in conformance to Current Good Manufacturing Practice (cGMP) requirements and that the data submitted in the application are accurate and complete. For each application submitted, an Integrated Quality Assessment (IQA) Team is assembled to perform the quality assessment of a marketing application. The IQA Team provides aligned, patient-focused, and risk-based drug product quality recommendations inclusive of drug substance, drug product, manufacturing, and facilities. The unifying hallmark of IQA is the integration of the facility evaluation and inspection and review roles in the application assessment process. The IQA Team is ultimately responsible for providing the quality recommendation for marketing applications, which includes the Pre-Approval Facility Evaluation and may also include a Pre-Approval Inspection, in advance of the Biosimilar, Generic Drug, or Prescription Drug User Fee Acts goal dates, as applicable.

Strengthen Organizational Excellence

Implementation of Program-Based Organizational Model

Over the years, the products regulated by FDA have become more complicated, the markets more global, and the rules governing our actions more complex. Changing our operational model allows ORA to continue to adapt to meet those challenges and improve our efforts to protect public health. Program Alignment (PA) was launched on September 6, 2013, when FDA's Commissioner charged the Directorates, Centers, and ORA to identify a path forward for the agency to modernize and strengthen the FDA workforce to improve FDA's public health response in a way that keeps pace with the acceleration of scientific innovation, global expansion of markets, and modern legal authorities.

Implemented in May 2017, PA realigned ORA's five geographic regions into six specialized programs for operations:

- Biological Products
- Bioresearch Monitoring
- Human and Animal Foods
- Medical Devices and Radiological Health
- Pharmaceutical Quality
- Tobacco.

In addition, ORA aligned Import Operations as its own program of specialization, although it still oversees all products regulated by ORA. ORA laboratories will also specialize and align into Human and Animal Foods Labs or Medical Product, Tobacco and Specialty Labs.

The FDA PA initiative moves the agency toward a more collaborative program-based model. PA allows employees to become more specialized in their work where appropriate and over time will modify certain processes with the goal of improved cross-agency communication, collaboration, and clarity in roles and responsibilities. For those regulated by FDA, the new organizational model will result in more uniformity in both process and policy across the organization, and more seamless and coordinated interactions within FDA between the field and the centers.

Workforce Development

Training and development of ORA staff is critical. Increasingly complex inspections, along with new regulations and legislation, require employees conducting and reviewing inspections to have specialized knowledge in the program areas. It is critical that FDA Domestic and Import Investigators, Compliance Officers, and Laboratory Analysts are trained to complete tasks specific to their regulatory program area. Under PA, staff training and development has been elevated in the reporting structure to raise its visibility and cross-organizational importance.

ORA has been actively conducting Job Task Analyses in each program area to deconstruct job functions to determine the unique knowledge, skills, and abilities needed to accomplish the work. Utilizing the analyses outcomes, existing training will be updated, and new training will be designed and developed to meet the training needs in these regulatory program areas. All specialized staff in each program will be trained similarly so that industries across the globe experience uniform application of our regulatory standards. The analyses will also provide ORA with the ability to offer new and more focused training curriculums for the various job functions/programs and provide either information to update the existing certification programs (i.e. Seafood Investigator, LACF/AF Investigator, Medical Device Investigator, Drug Investigator, Import Investigator, Clinical BIMO investigator, and Blood Bank/Plasma Center Investigator) or the ability to develop new certification programs that meet national and international standards.

It is critical that ORA provide task and program specific training to our supervisors and managers. They must be provided the tools needed to lead, guide, and maintain quality in an ever-changing regulatory environment. Training curricula is being developed in concert with ORA and the centers, resulting in a commodity-based set of competency requirements and performance assessments. Our staff will become even more familiar and more focused on a specific program area, as well as have new opportunities for professional development. It is imperative that we continue to support ongoing work to include updated course materials that incorporate the FSMA regulations in all related courses and advance a national curriculum standard in support of an integrated food safety system.

To develop the ORA leaders of the future with the skills needed to lead our complex and diverse workforce, the Management and Leadership Development Program (MLDP) continues to offer training and development opportunities for all ORA staff, with an emphasis on those seeking a future management position or career advancement. MLDP is a progressive tiered program that also provides career development guidelines for supervisors and managers at all levels of ORA. The program curriculum provides participants with successively complementary

leadership and management skills that lead to the Executive Core Qualifications necessary for senior agency leaders.

FUNDING HISTORY

Funding History	Program Level	Budget Authority	User Fees
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 Actual	$1,108,570,000	$1,040,199,000	$68,371,000
FY 2018 Annualized CR	$1,139,274,000	$1,032,904,000	$106,370,000
FY 2019 President's Budget	$1,148,674,000	$1,040,908,000	$107,766,000

BUDGET REQUEST

The FY 2019 Budget Request at the Initiative level is $1,148,674,000, of which $1,040,908,000 is budget authority and $107,766,000 is user fees. The budget authority increases by $8,004,000 compared to the FY 2018 Annualized CR and user fees increase by $1,396,000.

The FY 2019 budget allows FDA to continue to ensure that the food, feed, and medical products available to the American public are safe and effective.

BUDGET AUTHORITY

Food Safety (+$5.3 million / 0 FTE)

The FY 2019 request includes $776.125 million for ORA budget authority in support of food safety activities including $714.369 million for the Field Human Foods program and $61.756 million for the Field Animal Foods program. The FY 2019 request is a $5.272 million increase over the FY 2018 Annualized Continuing Resolution including increases of $4.852 million to the Field Foods program and $420 thousand to the Field Animal Feeds program. These increases restore both programs to the FY 2017 Enacted Level of funding for food safety and enable ORA to continue current levels of operational activities to inspect regulated products and manufacturers, conduct sample analyses of regulated products, and review imported products offered for entry into the United States.

ORA will continue to hone utilization of risk-based approaches of regulatory activities to make best use of available resources. Additionally, ORA will continue to work with its state, local, tribal, territorial, and foreign counterparts as applicable to further leverage, collaborate, and standardize the oversight of FDA-regulated products throughout the global marketplace in support of protecting public health.

Medical Product Safety (+$2.7 million / 10 FTE)

The FY 2019 request includes $264.8 million for ORA budget authority in support of medical product safety activities including $138.0 million for Field Human Drugs program, $41.1 million for the Field Biologics program, $2.9 million for the Field Animal Drugs program, and $82.9 million for the Field Devices & Radiological Health program. The FY 2019 request maintains the FY 2018 Annualized CR funding level for the Field Medical Product Safety Programs and also includes an increase of $2.7 million for Field Human Drugs program in support of the New Domestic Drug Industry initiative.

Maintaining the current funding for these Medical Product Safety programs will provide continued support of ORA's mission of protecting public health by conducting field operational activities to ensure the safety, effectiveness, and quality of FDA regulated commodities. With this sustained funding, ORA will continue to target available resources for activities focused on the highest risk inventory to protect public health through performance of field exams, import entry review, investigations, sample analysis, and inspections for surveillance, compliance, and follow up purposes both domestically and abroad.

New Domestic Drug Industry Initiative, Field Human Drugs +$2.7 million / 10 FTE
ORA will establish a specialized group of investigators who would spend a majority of their time on outsourcing facility inspectional activities, which will help ensure more substantive interactions with the young sector. ORA staff will also support the Center of Excellence on Compounding for Outsourcing Facilities and provide hands-on assistance to these facilities to improve compliance.

USER FEES

Current Law User Fees: +$1.4 Million

The ORA request includes an increase of $1,396,000 for user fees authorized under FDARA, which will allow FDA to fulfill its mission of promoting and protecting the public health by ensuring safety and efficacy of medical products and accelerating innovation in the industry.

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 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
214212: Percentage of planned import food field exams.*(Output)*	FY 2017: 94% Target: 99% (Target Not Met)	95%	95%	Maintain
214206: Maintain accreditation for ORA labs. *(Outcome)*	FY 2017: 13 labs Target: 13 labs (Target Met)	13 labs	13 labs	Maintain
214209: As required by the FSMA Legislation, cover all of the High Risk domestic inventory every three years. *(Output)*	FY 2017: 34.8% Target: 33% (Target Exceeded)	66%	99%	+33%
214305: Increase laboratory surge capacity in the event of terrorist attack on the food supply. (Radiological and chemical samples/week). *(Outcome)*	FY 2017: 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
224211: Percentage of planned foreign and domestic high-risk human drug inspections. *(Output)*	FY 2017: 68% Target: 64% (Target Exceeded)	70%	70%	Maintain
234212: Percentage of planned registered domestic blood bank and biologics manufacturing inventory inspections. *(Output)*	FY 2017: 106% Target: 99% (Target Exceeded)	95%	95%	Maintain
234213: Percentage of planned human foreign and domestic tissue establishment inspections. *(Output)*	FY 2017: 100% Target: 82% (Target Exceeded)	85%	85%	Maintain
244212: Percentage of planned domestic and foreign high-risk animal drug and feed inspections. *(Output)*	FY 2017: 107% Target: 99% (Target Exceeded)	95%	95%	Maintain
244203: Percentage of planned targeted prohibited material BSE inspections. *(Output)*	FY 2017: 97% Target: 99% (Target Not Met)	95%	95%	Maintain

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
253211: Percentage of planned Medical Device Bioresearch Monitoring (BIMO) inspections. *(Output)*	FY 2017: 91% Target: 91% (Target Met)	91%	91%	Maintain
254211: Percentage of planned domestic and foreign device inspections. *(Output)*	FY 2017: 91% Target: 57% (Target Exceeded)	80%	80%	Maintain

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

New ORA Field Performance Measures

ORA has been working to improve the field performance measures to better aligned with ORA's Program Alignment initiative. In this submission, ORA has completed the process of adjusting the performance goals, so that the FY 2018 and FY 2019 targets now complete a certain percentage of the planned inspections in ORA's annual Workplan. The ORA Workplan is the necessary mechanism that takes into account all the complex variables (geography, commodity, risk, availability, efficiency, etc.) that allows ORA to plan which inspections to do. With these newly formulated performance goals, ORA is committing to complete a certain percentage of the initially planned inspections. This revision strengthens the importance of the Workplan, but allows the flexibility to respond dynamically to changing circumstances during the year, to better handle emerging risks and evolving public health priorities (i.e. the heavy hurricane damage this past year). This is a significant departure from the previous performance goals, so FY 2018 will be an important year in resetting the new baselines. Also, since the targets are now based on a planned number of inspections, it is possible to inspect more than what was planned and thus have an actual inspection rate over 100%.

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. The new three-year cycle began again in FY 2017 during which 34.8 percent of the identified inventory was inspected. The FY 2018 and FY 2019 targets are 66% and 99% respectively.

Import Food Field Exams

During FY 2017, ORA accomplished 150,955 out of 160,189 planned import food field label exams. Although this is a high level performance, it falls short of the 99 percent target. Import

resource constraints had a significant impact on the ability to meet this target. Additional resources for entry review and shifting the focus in FY 2018 to work plan targets for food exams will help streamline this work, and improve the field's ability to meet this work plan target in FY 2018.

Prohibited Material BSE Inventory

During FY 2017, ORA accomplished 97 percent of targeted prohibited material BSE inventory coverage. Although this is a high-level performance, it falls short of the 99 percent target. While resource constraints and organization structure changes also played a part in the inability to meet this particular goal, ORA experienced IT infrastructure changes that may have prevented field tracking and notification of inspection necessity for specific BSE firms. ORA is working to correct for these infrastructure changes to ensure that this does not happen in FY 2018.

PROGRAM ACTIVITY DATA

Field Foods Program Activity Data (PAD)

Field Foods Program Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC FOOD ESTABLISHMENT INSPECTIONS	***8,484***	***8,000***	***8,000***
Domestic Food Safety Program Inspections	6,145	**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	195		
Domestic Low Acid Canned Foods/ Acidified Foods Inspections	321		
Domestic Fish & Fishery Products (HACCP) Inspections	763		
Import (Seafood Program Including HACCP) Inspections	253		
Juice HACCP Inspection Program (HACCP)	167		
Interstate Travel Sanitation (ITS) Inspections	909		
Domestic Field Exams/Tests	3,541	2,500	2,500
Domestic Laboratory Samples Analyzed	13,548	13,000	13,000
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN FOOD ESTABLISHMENT INSPECTIONS [1]	***1,548***	***1,400***	***1,400***
All Foreign Inspections	1,548	1,400	1,400
TOTAL UNIQUE COUNT OF FDA FOODS ESTABLISHMENT INSPECTIONS	***10,032***	***9,400***	***9,400***
IMPORTS			
Import Field Exams/Tests	229,129	168,200	168,200
Import Laboratory Samples Analyzed	23,774	35,300	35,300
Import Physical Exam Subtotal	**252,903**	**203,500**	**203,500**
Import Line Decisions	15,251,687	16,014,271	16,814,985
Percent of Import Lines Physically Examined	1.66%	1.27%	1.21%
Prior Notice Security Import Reviews (Bioterrorism Act Mandate)	81,035	80,000	80,000
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT FOOD ESTABLISHMENT INSPECTIONS	***8,460***	***9,062***	***9,062***
UNIQUE COUNT OF STATE PARTNERSHIPS FOOD ESTABLISHMENT INSPECTIONS	***110***	***100***	***100***
State Contract Food Safety (Non HACCP) Inspections	7,497	8,000	8,000
State Contract Domestic Seafood HACCP Inspections	902	1,000	1,000
State Contract Juice HACCP	61	100	100
State Contract LACF	129	100	100
State Partnership Inspections	110	100	100
State Contract Foods Funding	$12,465,850	$12,839,826	$13,225,020
Number of FERN State Laboratories	19	19	19
Number of Food Safety State Laboratories	15	15	15
Annual FERN State Cooperative Agreements/Operations Funding	$16,436,868	$16,929,974	$17,437,873
Total State & Annual FERN Funding	**$28,902,718**	**$29,769,800**	**$30,662,894**
GRAND TOTAL FOOD ESTABLISHMENT INSPECTIONS	***18,602***	***18,562***	***18,562***

[1] The FY 2017 actual unique count of foreign inspections includes 161 OIP inspections (118 for China, 39 for India, & 4 for Latin America).

Field Cosmetics Program Activity Data (PAD)

Field Cosmetics Program Workload and Outputs	FY 2017 Actuals	FY 2018 Estimate	FY 2019 Estimate
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***95***	***100***	***100***
Domestic Inspections	95	100	100
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA COSMETICS ESTABLISHMENT INSPECTIONS	***5***	***0***	***0***
Foreign Inspections	5	0	0
IMPORTS			
Import Field Exams/Tests	10,118	1,600	1,600
Import Laboratory Samples Analyzed	423	400	400
Import Physical Exam Subtotal	**10,541**	**2,000**	**2,000**
Import Line Decisions	2,625,555	2,756,833	2,894,674
Percent of Import Lines Physically Examined	0.40%	0.07%	0.07%
GRAND TOTAL COSMETICS ESTABLISHMENT INSPECTIONS	***100***	***100***	***100***

Field Human Drugs Program Activity Data (PAD)

Field Human Drugs Program Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC HUMAN DRUG ESTABLISHMENT INSPECTIONS	***1,758***	***1,803***	***1,814***
Pre-Approval Inspections (NDA)	85	135	135
Pre-Approval Inspections (ANDA)	91	215	215
Bioresearch Monitoring Program Inspections	681	550	550
Drug Processing (GMP) Program Inspections	668	650	650
Compressed Medical Gas Manufacturers Inspections	63	50	50
Adverse Drug Events Project Inspections	83	88	88
OTC Monograph Project and Health Fraud Project Inspections	29	70	70
Compounding Inspections[1]	141	142	142
Domestic Laboratory Samples Analyzed	1,571	1,300	1,300
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN HUMAN DRUG ESTABLISHMENT INSPECTIONS [2]	***1279***	***1360***	***1360***
Foreign Pre-Approval Inspections (NDA) incl PEPFAR	87	98	98
Foreign Pre-Approval Inspections (ANDA) incl PEPFAR	165	190	190
Foreign Bioresearch Monitoring Program Inspections incl PEPFAR	307	255	255
Foreign Drug Processing (GMP) Program Inspections	799	900	900
Foreign Adverse Drug Events Project Inspections	8	10	10
TOTAL UNIQUE COUNT OF FDA HUMAN DRUG ESTABLISHMENT INSPECTIONS	***3,037***	***3,163***	***3,174***
IMPORTS			
Import Field Exams/Tests	14,300	10,000	10,000
Import Laboratory Samples Analyzed	741	620	620
Import Physical Exam Subtotal	**15,041**	**10,620**	**10,620**
Import Line Decisions	789,853	829,346	870,813
Percent of Import Lines Physically Examined	1.90%	1.28%	1.22%
GRAND TOTAL HUMAN DRUG ESTABLISHMENT INSPECTIONS	***3,037***	***3,163***	***3,174***

[1] The number of compounding inspections includes inspections of compounders that are not registeredwith FDA as outsourcing facilities.

[2] The FY 2017 actual unique count of foreign inspections includes 105 OIP inspections (57 for China, 44 for India, & 4 for Latin America).

Field Biologics Program Activity Data (PAD)

Field Biologics Program Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,835***	***1,892***	***1,892***
Bioresearch Monitoring Program Inspections	75	100	100
Blood Bank Inspections	872	900	900
Source Plasma Inspections	192	190	190
Pre-License, Pre-Market Inspections	77	55	55
GMP Inspections	33	28	28
GMP (Device) Inspections	2	7	7
Human Tissue Inspections	621	650	650
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN BIOLOGICS ESTABLISHMENT INSPECTIONS	***67***	***47***	***47***
Bioresearch Monitoring Program Inspections	22	11	11
Foreign Human Tissue Inspections	0	0	0
Blood Bank Inspections	7	7	7
Pre-License, Pre-market Inspections	5	7	7
GMP Inspections (Biologics & Device)	33	20	20
TOTAL UNIQUE COUNT OF FDA BIOLOGIC ESTABLISHMENT INSPECTIONS	***1,902***	***1,939***	***1,939***
IMPORTS			
Import Field Exams/Tests	197	45	45
Import Line Decisions	157,080	168,076	179,841
Percent of Import Lines Physically Examined	0.13%	0.03%	0.03%
GRAND TOTAL BIOLOGICS ESTABLISHMENT INSPECTIONS	***1,902***	***1,939***	***1,939***

Field Animal Drugs & Feeds Program Activity Data (PAD)

Field Animal Drugs & Feeds Program Activity Data (PAD)									
Field Animal Drugs and Feeds Program Workload and Outputs	**FY 2017 Actual**			**FY 2018 Annualized CR**			**FY 2019 President's Budget**		
	Total	**Animal Drugs**	**Feeds**	**Total**	**Animal Drugs**	**Feeds**	**Total**	**Animal Drugs**	**Feeds**
FDA WORK									
DOMESTIC INSPECTIONS									
UNIQUE COUNT OF FDA DOMESTIC ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***1,710***	***206***	***1,517***	***1,664***	***298***	***1,398***	***1,664***	***298***	***1,398***
Pre-Approval /BIMO Inspections	28	28	0	79	79	0	79	79	0
Drug Process and New ADF Program Inspections	178	178	0	175	175	0	175	175	0
BSE Inspections	1,050	0	1,050	1,205	0	1,205	1,205	0	1,205
Feed Contaminant Inspections	26	0	26	25	0	25	25	0	25
Illegal Residue Program Inspections	312	0	312	450	0	450	450	0	450
Feed Manufacturing Program Inspections	242	0	242	200	0	200	200	0	200
Domestic Laboratory Samples Analyzed	1,599	22	1,577	1,560	20	1,540	1,560	20	1,540
FOREIGN INSPECTIONS									
UNIQUE COUNT OF FDA FOREIGN ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS [1]	***95***	***89***	***6***	***74***	***69***	***5***	***74***	***69***	***5***
Foreign Pre-Approval/Bioresearch Monitoring Program Inspections	18	18	0	40	40	0	40	40	0
Foreign Drug Processing and New ADF Program Inspections	76	76	0	33	33	0	33	33	0
Foreign Feed Inspections	6	0	6	5	0	5	5	0	5
BSE Inspections	4	0	4	0	0	0	0	0	0
TOTAL UNIQUE COUNT OF FDA ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***1,805***	***295***	***1,523***	***1,738***	***367***	***1,403***	***1,738***	***367***	***1,403***
IMPORTS									
Import Field Exams/Tests	3,847	614	3,233	3,795	495	3,300	3,795	495	3,300
Import Laboratory Samples Analyzed	704	3	701	867	2	865	867	2	865
Import Physical Exam Subtotal	**4,551**	**617**	**3,934**	**4,662**	**497**	**4,165**	**4,662**	**497**	**4,165**
Import Line Decisions	426,484	52,702	373,782	447,808			470,199		
Percent of Import Lines Physically Examined	1.07%	1.17%	1.05%	1.04%			0.99%		
STATE WORK									
UNIQUE COUNT OF STATE CONTRACT ANIMAL FEEDS ESTABLISHMENT INSPECTIONS	***3,085***	***0***	***3,085***	***3,503***	***0***	***3,503***	***3,503***	***0***	***3,503***
State Contract Inspections: BSE	3,005	0	3,005	3,500	0	3,500	3,500	0	3,500
State Contract Inspections: Feed Manufacturers	614	0	614	620	0	620	620	0	620
State Contract Inspections: Illegal Tissue Residue	124	0	124	130	0	130	130	0	130
State Contract Animal Drugs/Feeds Funding	$3,389,745	0	$3,389,745	$3,491,437	0	$3,491,437	$3,596,180	0	$3,596,180
State Contract Tissue Residue Funding	$271,600	0	$271,600	$263,452	0	$263,452	$255,548	0	$255,548
Total State Funding	**$3,661,345**	**$0**	**$3,661,345**	**$3,754,889**	**$0**	**$3,754,889**	**$3,851,728**	**$0**	**$3,851,728**
GRAND TOTAL ANIMAL DRUGS AND FEEDS ESTABLISHMENT INSPECTIONS	***4,893***	***295***	***4,611***	***5,241***	***367***	***4,906***	***5,241***	***367***	***4,906***

[1] The FY 2017 actual unique count of foreign inspections includes 11 OIP inspections (10 for China and 1 for India).

Field Devices and Radiological Health Program Activity Data (PAD)

Field Devices and Radiological Health Program Workload and Outputs	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget
FDA WORK			
DOMESTIC INSPECTIONS			
UNIQUE COUNT OF FDA DOMESTIC DEVICES ESTABLISHMENT INSPECTIONS	***2,648***	***2,498***	***2,498***
Bioresearch Monitoring Program Inspections	279	300	300
Pre-Market Inspections	61	60	60
Post-Market Audit Inspections	53	60	60
GMP Inspections	1,477	1,400	1,400
Inspections (MQSA) FDA Domestic (non-VHA)	787	700	700
Inspections (MQSA) FDA Domestic (VHA)	59	50	50
Domestic Radiological Health Inspections	61	50	50
Domestic Field Exams/Tests	5	100	100
Domestic Laboratory Samples Analyzed	191	170	170
FOREIGN INSPECTIONS			
UNIQUE COUNT OF FDA FOREIGN DEVICES ESTABLISHMENT INSPECTIONS [1]	***782***	***613***	***613***
Foreign Bioresearch Monitoring Inspections	22	14	14
Foreign Pre-Market Inspections	24	30	30
Foreign Post-Market Audit Inspections	24	20	20
Foreign GMP Inspections	712	550	550
Foreign MQSA Inspections	12	14	14
Foreign Radiological Health Inspections	71	50	50
TOTAL UNIQUE COUNT OF FDA DEVICE ESTABLISHMENT INSPECTIONS	***3,430***	***3,111***	***3,111***
IMPORTS			
Import Field Exams/Tests	23,335	19,800	19,800
Import Laboratory Samples Analyzed	636	670	670
Import Physical Exam Subtotal	**23,971**	**20,470**	**20,470**
Import Line Decisions	20,584,138	22,025,028	23,346,529
Percent of Import Lines Physically Examined	0.12%	0.09%	0.09%
STATE WORK			
UNIQUE COUNT OF STATE CONTRACT DEVICES ESTABLISHMENT INSPECTIONS	***7,505***	***7,880***	***7,880***
Inspections (MQSA) by State Contract	1,060	6,800	6,800
Inspections (MQSA) by State non-Contract	6,398	1,060	1,060
GMP Inspections by State Contract	47	20	20
State Contract Devices Funding	$5,524	$5,690	$5,860
State Contract Mammography Funding	$10,383,992	$10,695,512	$10,909,422
Total State Funding	**$10,389,516**	**$10,701,202**	**$10,915,283**
GRAND TOTAL DEVICES ESTABLISHMENT INSPECTIONS	***10,935***	***10,991***	***10,991***

[1] The FY 2017 actual unique count of foreign inspections includes 12 OIP inspections (11 for China and 1 for India).

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TOBACCO CONTROL ACT

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
Family Smoking Prevention and Tobacco Control	**596,338**	**754,076**	**592,288**	**662,043**	**69,755**
Center (UF Only)	581,438	742,641	577,489	647,493	70,004
Field (UF Only)	14,900	11,435	14,799	14,550	-249
FTE	**886**	**886**	**886**	**982**	**96**

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. The Tobacco Control Act 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 the Tobacco Control Act 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 December 31, 2017, FDA had contracts for tobacco retailer compliance check inspections in 57 states, territories, and tribal jurisdictions. During these checks, contractors commissioned as FDA inspectors determine if retailers are complying with regulations pertaining to the marketing, sales, and distribution of tobacco products, to include compliance with age and ID verification requirements. Since the program's inception in October 2010 through December 31, 2017, FDA has commissioned more than 2,500 officers and conducted more than 874,000 compliance check inspections at tobacco retail establishments.

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 a regulation. On May 10, 2016, FDA finalized a rule – Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act (FD&C Act) – which extended FDA's tobacco authorities 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 rule helps implement the 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.

On July 28, 2017, FDA Commissioner Gottlieb announced a new comprehensive plan for tobacco and nicotine regulation that will serve as a multi-year roadmap to protect kids and significantly reduce tobacco-related disease and death. The approach places nicotine, and the issue of addiction, at the center of the agency's tobacco regulation efforts. The goal is to ensure that the FDA has the proper scientific and regulatory foundation to efficiently and effectively implement the Tobacco Control Act.

For example, FDA noted that almost 90 percent of adult smokers start smoking by the age of 18,[81] and that nearly 2,500 youth smoke their first cigarette every day in the United States.[82] By

[81] U.S. Department of Health and Human Services (USDHHS). The Health Consequences of Smoking - 50 Years of Progress. A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.

[82] Substance Abuse and Mental Health Services Administration (SAMHSA). Results from the 2015 National Survey on Drug Use and Health: Detailed Tables. Rockville, MD: U.S. Department of Health and Human Services, SAMHSA, Center for Behavioral Health Statistics and Quality;

lowering nicotine levels in cigarettes to non-addictive levels, FDA explained that we could decrease the likelihood that future generations become addicted to cigarettes and allow more currently addicted smokers to quit. Therefore, FDA has begun a public dialogue about lowering nicotine levels in combustible cigarettes to non-addictive levels through achievable product standards. On March 16, 2018,FDA published an Advance Notice of Proposed Rulemaking (ANPRM) to seek input on the potential public health benefits and any possible adverse effects of limiting nicotine in cigarettes to minimally or non-addictive levels.

Further, FDA indicated that it is seeking public input on other complex issues to help ensure that the Agency has the proper science-based policies in place to meaningfully reduce the harms caused by tobacco use. On March 21, 2018, FDA published an ANPRM to seek public comment on the role that flavors in tobacco products—including menthol—play in attracting youth, as well as the role some flavors may play in helping some smokers switch to potentially less harmful forms of nicotine delivery. FDA also announced on March 23, 2018an ANPRM to solicit additional comments and scientific data related to the patterns of use and resulting public health impacts from premium cigars.

To encourage innovations that have the potential to make a notable public health difference and to put foundational rules in place to provide increased clarity and efficiency for industry, the Agency is extending the premarket application deadlines described in the deeming rule for certain products. Specifically, the FDA is deferring enforcement of deadlines to submit tobacco product review applications for newly regulated tobacco products that were on the market as of August 8, 2016. Under these revised timelines, applications for newly regulated combustible products, such as cigars, pipe tobacco and hookah tobacco, would be submitted by August 8, 2021, and applications for non-combustible products such as ENDS would be submitted by August 8, 2022.

Substantial Equivalence

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 to determine if they meet the appropriate statutory standard for marketing.

New products and product changes are reviewed following three marketing pathways:

- premarket tobacco product application (PMTA)
- report demonstrating substantial equivalence (SE) to certain commercially marketed products
- request for exemption (EX REQ) from demonstrating substantial equivalence.

Manufacturers may submit 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 product.

2016. https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015.pdf. Accessed September 9, 2016

A substantially equivalent tobacco product is a product that 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 by the applicant demonstrates that the new product does not raise different questions of public health. A predicate tobacco product[83] 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 criteria are met, FDA issues a written order permitting the product to be legally marketed in the United States.

FDA has prioritized the review of regular[84] SE Reports 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 December 31, 2017:

- 2,652 regular reports have been received
- 2,411 or 91% of regular reports have been resolved[85]
- 241 regular reports are pending. 240 have begun scientific review and 198, or 83%, have been issued a deficiency letter after a cycle of scientific review was completed.

In FY 2015, FDA implemented performance measures, including timeframes for review of regular SE Reports. 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. CTP met 4 out of 8 performance goals[86] for the FY 2016 cohort. Three of the four missed goals involved a program where FDA ceased certain activities pending an August 2016 decision on an October 2015 lawsuit. Subsequent to implementation of program changes to comply with the court's decision, FDA intends to meet all these performance measures in the future.

FDA is also continuing scientific review of provisional SE Reports.[87] As of December 31, 2017:

- 3,597 provisional reports have been received
- 1,047 or 29% of provisional reports have been resolved[88]

[83] http://www.fda.gov/TobaccoProducts/Labeling/TobaccoProductReviewEvaluation/SubstantialEquivalence/ucm304517.htm#3

[84] 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.

[85] Resolved includes refuse-to-accept, withdrawn, substantially equivalent (SE), not substantially equivalent (NSE), and closure due to administrative issues.

[86] A ninth goal had no submissions in the FY16 cohort.

[87] SE Reports received before March 23, 2011 for products introduced to market or changed between February 15, 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] SE Reports received before March 23, 2011 for products introduced to market or changed between February 15, 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.

- 2,550 provisional reports are pending. 702 have begun scientific review and 612, or 87%, have been issued a deficiency letter after a cycle of scientific review was completed.
- Approximately 1,848 of the pending provisional reports have not started scientific review

FDA expects the time required for review of SE Reports 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 is using a comprehensive public education approach 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 include 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.

The Real Cost

Launched in February 2014, FDA's award-winning youth tobacco prevention campaign, "The Real Cost," continues to educate at-risk teens aged 12 to 17 about the harmful effects of tobacco use. The goal is to prevent youth who are open to tobacco from trying it and to reduce the number of youth who move from experimenting with tobacco to regular use.

Figure 18 "The Real Cost" campaign logo

Initial advertising focused on cigarette smoking prevention, and results from a two-year outcome evaluation published in January 2017 indicate the campaign is succeeding in meeting this goal. "The Real Cost" campaign prevented an estimated 350,000 U.S. youth from smoking from February 2014 to March 2016, exceeding FDA's goals for the campaign. Considering that most tobacco dependence begins during adolescence, these results demonstrate that youth-focused tobacco prevention campaigns like "The Real Cost" can have long-term effects on future rates of tobacco-related morbidity and mortality.

FDA has refreshed the campaign with new advertising every year to keep its at-risk youth target audience engaged with the campaign. This strategy is based on target audience research that suggests that the personality trait of sensation-seeking, which is closely linked with risk taking behavior, is associated with a preference for novel messaging. FDA refreshed the campaign with a third wave of TV advertising in October 2016 and launched two new digital ads in March and April 2017. Additional advertising is planned for launch in 2018.

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 shift rural teen boys' knowledge, attitudes, and beliefs about the dangers of smokeless tobacco.

In August 2017, FDA announced it would pursue a new, strategic public health education effort designed to prevent youth from using e-cigarettes and other electronic nicotine delivery systems (ENDS). In support of this goal, the agency expanded "The Real Cost" public education campaign in October 2017 to educate teens about the dangers of nicotine to the developing brain. The new campaign materials include digital images and online video and radio ads. Additionally, FDA is planning to launch a full-scale media campaign to prevent youth ENDS use in 2018.

A nationally recognized campaign, "The Real Cost" earned a bronze Effie in the Youth Marketing category at the 2017 North American Effie Awards. The Effies are the advertising industry's most prestigious award, recognizing marketing ideas that work and have demonstrated effectiveness. The campaign previously won a 2015 gold Effie in the Disease Awareness and Education category. The campaign also received 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.

Fresh Empire

The "Fresh Empire" campaign, launched on May 12, 2015, 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.

Figure 19 "Fresh Empire" campaign logo

"Fresh Empire" is FDA's first public education campaign designed to prevent and reduce tobacco use among at-risk multicultural youth ages 12-17 who identify with hip-hop culture, specifically African American, Hispanic, and Asian American/ Pacific Islander youth. Nearly 5 million multicultural youth are open to smoking or are already experimenting with cigarettes—meaning they have already smoked up to 100 cigarettes in their lifetime[89]—highlighting a critical need for stronger, more targeted youth tobacco prevention efforts.

FDA expanded the "Fresh Empire" campaign to markets throughout the U.S. in October 2015 and launched new advertising in market in January 2017 to keep the target audience engaged with campaign messages.

The 2017 Telly Awards named the "Fresh Empire" campaign the Silver winner in the Motivational category for Video / Shows / Segments, and a Bronze winner in the Public Interest & Awareness category for Promotional Pieces. The Telly Awards honor excellence in video and television.

This Free Life

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 occasional or "social" smokers through print and digital advertising, social media, outdoor

[89] Based on 2013 data from NYTS on experimentation and openness to smoking among youth and 2014 youth population estimates from the U.S. Census Bureau.

signage, and local events 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.

Figure 20 "This Free Life" campaign logo

The 2017 Telly Awards also named the "This Free Life" campaign the Bronze winner in the Cultural category for Video / Shows / Segments. Additionally, the 2017 Ad POPs (Pride in Online and Print) Awards named the "This Free Life" campaign the Gold winner in the Non-Profit category for print ads. The Ad POPs reward the best representations of LGBT individuals in online and print advertising in regional LGBT media.

Enhance Oversight

FDA's Tobacco Program is carried out by issuing regulations and guidance that explain FDA's expectations to the regulated industry and to the public. FDA invests in tobacco regulatory research to inform regulatory activities and assess the impact of regulatory actions. Furthermore, FDA ensures industry compliance by enforcing warning label and advertising requirements, and restricting sales and marketing of tobacco products to youth through the use compliance inspections, warning letters, civil money penalties, and no-tobacco-sale-orders.

Maintaining a Strong Science Base

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 2017, FDA invested more than $239 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) and FDA's Southeast Tobacco Laboratory, 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 expertise 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 2017, FDA funded 140 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.

In FY 2017, FDA funded new grants to support regulatory science research on tobacco products in the fields of biomedical, behavioral, and social sciences.

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 will collaborate with NIH to fund new TCORS and a Center for Coordination of Analytics, Science, Enhancement and Logistics (CASEL) in FY 2018.

Figure 21 Population Assessment of Tobacco and Health logo

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 national 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 potential harm.

Data collection for Wave 4 launched in December 2016 and Wave 5 will launch December 2018. Starting in FY 2017, FDA began collecting 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. The first sub-

study will be on youth and will begin December 2017. Wave 1 Biomarker data was released in July 2017. Wave 2 questionnaire data was released to the public in June 2017.

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, 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.

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, and use behavior, and assess user and non-user beliefs about emerging tobacco products.

In FY 2016, CTP contracted with the Institute of Medicine – now called the Health and Medicine Division of the National Academy of Sciences – to conduct an evaluation of health effects from e-cigarettes and identify gap areas for future federally funded research in this area.

In FY 2017, CTP partnered with National Cancer Institute (NCI), NIH to co-sponsor the Tobacco Use Supplement to the Current Population Survey (TUS-CPS) via an interagency agreement with U.S. Census Bureau. TUS-CPS is a nationally representative tobacco survey of adults with links to social and economic Census Bureau and Bureau of Labor Statistics data and health data from the National Longitudinal Mortality Study.

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 December 31, 2017, FDA had contracts for tobacco retailer compliance check inspections in 57 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 deemed products in the scope of its retail inspections. As of December 31, 2017, FDA had issued more than 10,000 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.[90]

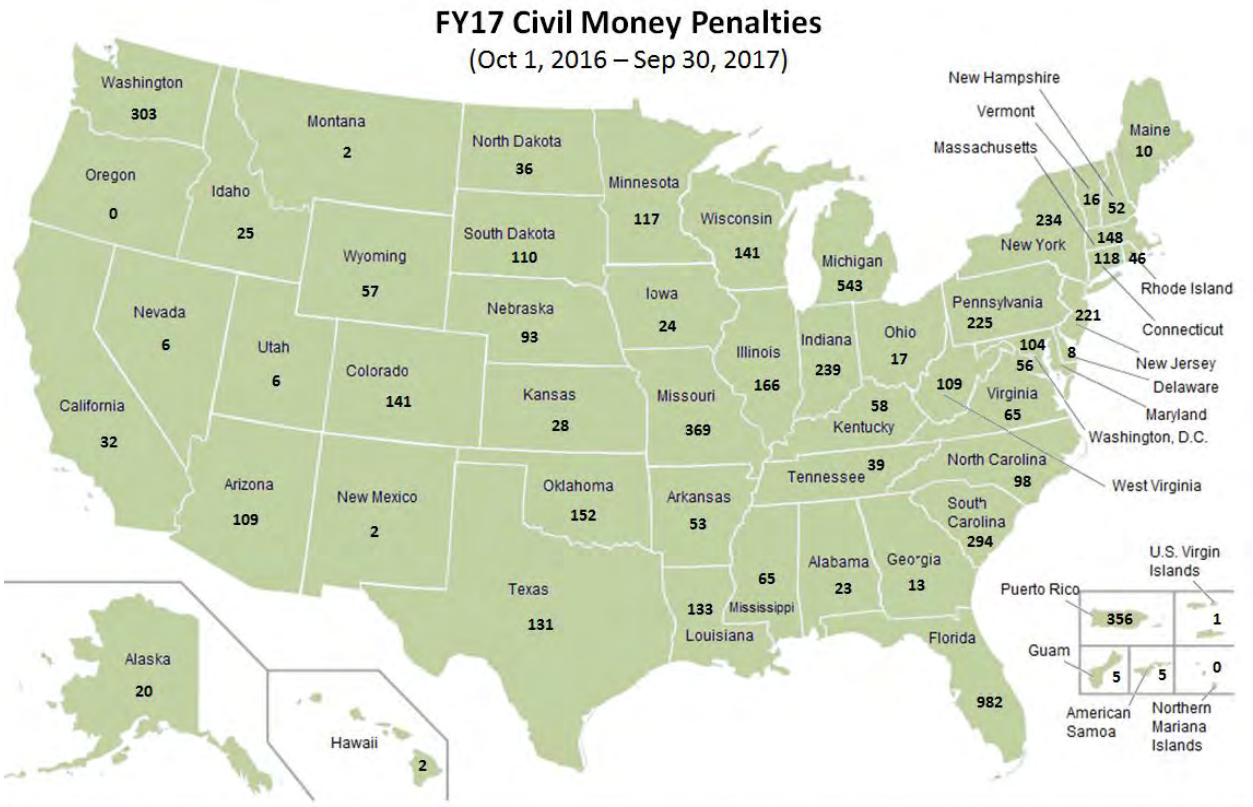
Since the Tobacco Retailer Inspection Program's inception in October 2010 through December 31, 2017, FDA has commissioned more than 2,500 officers and employees from the states, territories, and their political subdivisions, and provides a training program for those that perform inspections. FDA currently 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

Action	FY 2016 Actuals	FY 2017 Actuals	Total Since the Program's Inception on 10/1/2010 (as of 12/31/2017)
Retailer Inspections	165,089	168,696	874,578
Warning Letters	13,921	14,735	67,722
Civil Money Penalties	3,618	6,408	16,067
No-Tobacco-Sale-Orders	34	61	99

[90] These warning letters are included in the total number of warning letters reported in the "CTP Tobacco Retailer Inspection Program" table.



Although most retailers comply after receiving a warning letter, FDA has issued 6,408 civil money penalties in FY 2017 (Oct 1, 2016 – Sep 30, 2017).

Figure 22 The number of Civil Money Penalty Complaints filed by the Center for Tobacco Products in FY 2017 by state.

Tobacco Manufacturer Inspections

FDA regularly inspects registered establishments that manufacture or process tobacco products to determine compliance with existing laws and regulations. Tobacco manufacturers of deemed products were required to register by October 12, 2017. CTP's coordination with the Office of Regulatory Affairs (ORA) has increased considerably as the scope of these activities continues to expand to include manufacturers and importers of deemed tobacco products and additional provisions in the final Deeming rule. As of December 31, 2017, CTP conducted more than 350 inspections of vape shops to verify whether they were engaged in manufacturing activities, and ORA conducted more than 300 routine biennial inspections of tobacco manufacturers.

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 system (ENDS) products and took compliance actions when violations were found. Since the program's inception in October 2010, FDA has issued over 500 warning letters as a result of these surveillance activities. In FY 2017, 140 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.

Office of Small Business Assistance (OSBA)

CTP's OSBA informs small businesses of existing guidances, regulations, and submission pathways through publications and online webinars. In FY 2016 and 2017, OSBA published 18 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.

Improve and Safeguard Access to FDA-Regulated Products to Benefit Health

The Tobacco Control Act gives FDA the authority to determine whether new and modified risk products can be marketed-including reviewing and evaluating applications before the products are allowed to be marketed. Under the premarket tobacco application (PMTA) pathway, manufacturers must demonstrate to FDA that the marketing of the new tobacco product would be appropriate for the protection of the public health. This standard requires FDA to consider the risks and benefits to the population as a whole, including users and non-users of tobacco products.

As of December 31, 2017, FDA has:

- received 392 PMTAs and refused-to-accept, or refused-to-file 372
- issued marketing orders for eight products and denied zero marketing orders. Nine PMTAs are currently under review.[91]

Although a refuse-to-accept or refuse-to-file decision closes all activity for the application, 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.

In addition to the three marketing pathways, before making marketing products with claims that imply modified risk, manufacturers must submit a Modified Risk Tobacco Product Application (MRTPA), and receive an FDA order authorizing a claim that the product reduces harm or the risk of tobacco-related disease.

As of December 31, 2017, FDA has:

- received 36 MRTPAs and refused-to-accept, or refused-to-file 14
- 17 MRTPAs pending final action[92], including nine currently under review and eight with final action deferred pending response from the applicant.

[91] Does not include three PMTAs that were closed for administrative reasons such as withdrawal.

[92] MRTPAs pending final action does not include five MRPTAs closed for administrative reasons such as withdrawal.

Promote Informed Decisions

Public Education Campaigns

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 have 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. For example, the study design for "The Real Cost" campaign is longitudinal, meaning the study 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.[93]

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 11 to 18 who smoke by preventing an estimated 350,000 U.S. youth from smoking from February 2014 to March 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 tobacco-related knowledge, attitudes, beliefs, and intentions among the target audiences.

Strengthen Organizational Excellence

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 MRTP
- expand research capabilities
- support inspection efforts
- enforce the deeming regulation
- draft regulations and guidances.

[93] http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0144827

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2015 Actual	$554,469,000	---	$554,469,000
FY 2016 Actual	$476,525,000	---	$476,525,000
FY 2017 Actual	$754,076,000	---	$754,076,000
FY 2018 Annualized CR	$592,288,000	---	$592,288,000
FY 2019 President's Budget	$662,043,000	---	$662,043,000

BUDGET REQUEST

The FY 2019 Budget request is $662,043,000 all from user fees. This amount is the FY 2019 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 $69,755,000 above the FY 2018 Annualized CR.

The Center for Tobacco Products amount in this request is $647,493,000.

In FY 2019, CTP plans to continue implementing its Plan for Tobacco and Nicotine Regulation as announced by Commissioner Gottlieb on July 28, 2017, which CTP has incorporated into its six strategic priorities:

- Product Standards
- Comprehensive Nicotine and Tobacco Regulatory Policy
- Premarket and Postmarket Controls: Regulations and Product Reviews
- Compliance and Enforcement
- Public Education
- Investing in Human Capital.

Specifics on CTP's FY 2019 efforts follow the Agency-wide plan below.

FDA-wide Comprehensive Plan for Tobacco and Nicotine Regulation

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 continuum of risk among such products. FDA plans to seek public comment on the reduction of nicotine in combusted cigarettes to minimally addictive or nonaddictive levels, while encouraging innovation to reduce harm by establishing a strong regulatory framework for newer products, such as e-cigarettes. FDA also plans to seek public comment on the role that flavors in tobacco products—including menthol—play in attracting youth, as well as the role some flavors may play in helping some adult smokers switch to potentially less harmful forms of nicotine delivery. In addition, FDA plans to solicit additional comments and scientific data related to the patterns of use and resulting public health impacts from cigars.

As part of this plan, FDA has taken several steps, including:

- issuing guidance in September 2017 extending timelines for submitting tobacco product review applications for newly regulated products that were on the market as of August 8, 2016

- forming a Nicotine Steering Committee, in conjunction with CDER and FDA's Office of the Commissioner, to examine the science behind the Agency's evaluation of nicotine replacement therapies (NRTs), including the types of safety and efficacy studies FDA requires and how these products are used and labeled (with public hearing to obtain feedback on public health, regulatory, and legal considerations relating to NRT products and their use for cessation to be held on January 26, 2018)
- considering regulatory guidance on premarket review policy based on the principle of relative toxicity and risk
- preparing for publication of Advance Notices of Proposed Rulemaking (ANPRMs) on nicotine in cigarettes, flavors in tobacco products, and premium cigars
- preparing for publication a proposed rule on Substantial Equivalence, as well as pursuing proposed rules on Premarket Tobacco Product Applications (PMTAs) and Modified Risk Tobacco Products (MRTPs)
- pursuing product standards for Electronic Nicotine Delivery Systems (ENDS) and other products, as appropriate, to establish basic standards and inform and drive innovation in the direction of harm reduction.

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.

On January 23, 2017, FDA published a proposed rule - Tobacco Product Standard for N-nitrosonornicotine Level in Finished Smokeless Tobacco Products[94]- that would establish for finished smokeless tobacco products sold in the United States a limit of N-nitrosonornicotine, a potent carcinogen and major contributor to elevated oral cancer risks in smokeless tobacco users.

As with any rulemaking, it is important for the Agency to hear from the public regarding their thoughts on the proposed rule, and participation in the rulemaking process by all interested parties was robust. FDA is currently reviewing and evaluating the comments to determine appropriate next steps.

Comprehensive Nicotine and Tobacco Regulatory Policy

FDA is pursuing the nicotine work mentioned above, as well as:

- initiating a national dialogue on nicotine to increase knowledge and understanding of the addictive nature of nicotine to better protect the public's health, and
- developing opportunities for global collaboration to learn from other governments' research, experiences, and challenges to inform our domestic efforts.

[94] https://www.fda.gov/TobaccoProducts/Labeling/RulesRegulationsGuidance/ucm537091.htm

Premarket and Postmarket Control: Regulations and Product Reviews

FDA serves as a critical public health gatekeeper between tobacco product manufacturers and consumers by performing a scientific review before new tobacco products are commercially sold. Manufacturers are required to seek FDA authorization before marketing new[95] tobacco products:

- by demonstrating they are appropriate for protection of public health, or
- by demonstrating substantial equivalence[96] to certain commercially marketed products.

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 monitor 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 tobacco or are open to it; African American, Hispanic, Asian/Pacific Islander, and American Indian/Alaska Native youth; rural youth at risk of using smokeless tobacco, lesbian, gay, bisexual, and transgender (LGBT) young adults who smoke, and adult smokers who want to quit.

Several of these campaigns are also expanding to message on additional regulated tobacco products, such as ENDS, hookah, and little cigars. Campaign messaging and outreach tactics for each product type will continue to target discrete audiences and be informed by findings from formative research, results of outcome evaluations and real-time tracking efforts, as well as changes in youth tobacco use trends.

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.

[95] New tobacco product includes products with any modification after February 15, 2007.

[96] 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.

Additional FY 2019 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 research projects via NIH to address FDA time-sensitive research
- collect and analyze PATH Study participant responses and biomarker data to assess tobacco use transitions over time
- conduct priority research with research contract organizations.

In FY 2019, 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 2019. Continued planned activities include:

- conducting compliance check inspections via the Tobacco Retailer Inspection Program[97]
- 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 2019, FDA will:

- continue to implement campaigns designed to reach at-risk and vulnerable populations – especially young people – with messages about the dangers of using tobacco products.
- continue to conduct and share findings from its campaign outcome evaluation studies.
- continue to develop interactive digital communication technologies and products such as CTP's content sharing platform, the Exchange Lab.

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.

[97] The results of the Tobacco Retailer Inspection Program can be found on FDA's website at http://www.accessdata.fda.gov/scripts/oce/inspections/oce_insp_searching.cfm

Measure	Year and Most Recent Result / Target for Recent Result (Summary of Result)	FY 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
280005: Total number of compliance check inspections of retail establishments in States under contract. *(Outcome)*	FY 2017: 168,696 Target: 125,000(Target Exceeded)	130,000	140,000	+10,000
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) *(Output).*	FY 2017: 93%Target: 70%(Target Exceeded)	80%	80%	Maintain
280007: Educate at-risk general market 12-17 year olds about the harmful effects of tobacco use. *(Output)*	FY 2017: 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 168,000 compliance check inspections of retail establishments in FY 2017. Although this number was much higher than the expected FY 2017 full year target of 125,000, 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. Also, some contracts are expiring and being renewed in FY 2018, and while 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 2018 and 2019 targets consider these challenges, but have still been increased.

PROGRAM ACTIVITY DATA

CTP Workload and Outputs	FY 2017 Actuals	FY 2018 Annualized CR	FY 2019 President's Budget
Tobacco Retailer Inspections			
Number of Inspections	168,696	130,000	140,000
Tobacco Manufacture Inspections			
Number of Inspections [1]	52	75	200
Substantial Equivalence Reviews			
Number of Regular Full SE Reports	132	100	100

[1] Outyear estimates are based on the number of firms registered with FDA. FDA works to inspect each registered firm biennially.

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FDA HEADQUARTERS

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
FDA Headquarters Program	**282,678**	**302,146**	**315,546**	**347,240**	**31,694**
Budget Authority	***182,237***	***187,063***	***180,980***	***198,565***	***17,585***
User Fees	***100,441***	***115,083***	***134,566***	***148,675***	***14,109***
Prescription Drug (PDUFA)	*46,202*	*53,970*	*56,236*	*59,272*	*3,036*
Medical Device (MDUFA)	*5,732*	*8,118*	*10,373*	*10,554*	*181*
Generic Drug (GDUFA)	*25,050*	*30,587*	*44,859*	*45,568*	*709*
Biosimilars (BsUFA)	*1,388*	*1,976*	*1,659*	*1,688*	*29*
Animal Drug (ADUFA)	*947*	*874*	*654*	*1,208*	*554*
Animal Generic Drug (AGDUFA)	*453*	*212*	*267*	*971*	*704*
Tobacco Control Act	*19,132*	*19,072*	*19,002*	*27,870*	*8,868*
Mammography Quality Standards Act (MQSA)	*253*	*274*	*253*	*253*	*---*
Food And Feed Recall	*75*	*---*	*75*	*75*	*---*
Food Reinspection	*480*	*---*	*480*	*480*	*---*
Voluntary Qualified Importer Program	*277*	*---*	*277*	*277*	*---*
Third Party Auditor Program	*73*	*---*	*39*	*39*	*---*
Outsourcing Facility	*379*	*---*	*392*	*420*	*28*
FTE	**1,168**	**1,195**	**1,268**	**1,298**	**30**

*FY 2017 and FY 2018 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 2019, 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), the 21st Century Cures Act (P.L. 114-255), Food and Drug Administration Reauthorization Act of 2017 (FDARA) (P.L. 115-52).

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.

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 activities include:

- inspecting manufacturing and production facilities
- providing surveillance of adverse events
- preventing unsafe products from harming consumers.

The following, selected accomplishments demonstrate FDA HQ's delivery of its regulatory and public health responsibilities within the context of current priorities[98].

The FDA Food Safety Modernization Act (FSMA)

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. FSMA enables FDA to better protect the public health by:

- shifting the food safety paradigm from reactive to preventive

[98] Please visit http://www.fda.gov/ for additional program information and detailed news items.

- 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.[99] In 2017, FDA launched a new web page on fda.gov which compiles compliance dates for all of the foundational FSMA rules into a single graphic.

FSMA recognizes that FDA had previously-established regulations that are specific to seafood, juice, and Low-Acid Canned Foods and, therefore, some exemptions were made in the FSMA rules for these products. However, there are still some requirements in the FSMA regulations that apply to processors of these products. In FY 2017, in order to help producers of low-acid canned foods, juice, and seafood products understand which parts of the FSMA rules apply to them and how the FSMA rules may affect their operations, FDA published three guidance documents: Low-Acid Canned Foods and FSMA, Juice HACCP and FSMA, and Seafood HACCP and FSMA.

FSMA heralded a new era of enhanced collaboration between FDA and its counterparts in state governments across the country. State officials were instrumental in providing comments to help FDA create regulations that take into account the complexities of food production and are designed to be flexible and practical while meeting the agency's public health goals.

In September 2017, FDA awarded 43 states a total of $30.85 million in cooperative agreements to develop produce safety programs that will enable them to deliver education and technical assistance to farmers and create infrastructure to provide inspection, compliance and oversight.

2017 FSMA Rule Updates

In July 2017, FDA released a proposed rule to extend, for covered produce other than sprouts, the dates for compliance with the agricultural water provisions in the Standards for the Growing, Harvesting, Packing, and Holding of Produce for Human Consumption rule (FSMA Produce rule). Moreover, FDA is proposing to extend the compliance dates to address questions about the practical implementation of compliance with certain provisions and to consider how we might further reduce the regulatory burden or increase flexibility while continuing to achieve our regulatory objectives, in keeping with the Administration's policies. The FSMA Produce rule establishes, for the first time, science-based minimum standards for the safe growing, harvesting, packing, and holding of fruits and vegetables grown for human consumption.

In 2017, FDA released an online food safety training module for carriers engaged in the transportation of food by rail or motor vehicle in the United States. FDA is offering this training

[99] http://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm253380.htm

free of charge to help carriers meet the requirements of the FDA's Sanitary Transportation of Human and Animal Food Rule (Sanitary Transportation Rule). The Sanitary Transportation Rule requires rail and motor vehicle carriers covered by the rule to provide food safety training to their personnel engaged in transportation operations. The training must provide personnel with an awareness of 1) potential food safety problems, 2) basic sanitary practices, and 3) carrier responsibilities. The carrier training requirement applies when the shipper and carrier have agreed, in a written contract, that the carrier is responsible, in whole or part, for sanitary conditions during transportation operations. A carrier may wish to offer this FDA module to their operations personnel as a means of satisfying the training requirements of the Sanitary Transportation Rule or to complement other training offered by the carrier.

In August 2017, FDA announced the availability of a Small Entity Compliance Guide (SECG) to help small businesses comply with the Final Rule on Mitigation Strategies to Protect Food Against Intentional Adulteration (or Intentional Adulteration Rule), one of the seven foundational rules mandated by FSMA. It provides nonbinding recommendations on such topics as developing a food defense plan and records management. The compliance date for small businesses under the Intentional Adulteration Rule is July 27, 2020. Very small businesses are exempt from the rule, except for a documentation requirement described in the SECG, which has a compliance date of July 26, 2020.

21st Century Cures Act and Human Subject Protection Harmonization

The 21st Century Cures Act (Cures Act) Section 3023 requires harmonization of HHS' and FDA' human subject protection regulations. FDA is continuing its efforts to harmonize differences between its regulations and the Common Rule, to the extent applicable and permissible, given FDA's and HHS's different statutory mandates.

FDA HQ continues to coordinate with the Centers, ORA, and the National Institutes of Health (NIH) to finalize FDA's compliance program for the HHS regulations requiring clinical trial registration and results reporting on ClinicalTrials.gov (42 CFR part 11). FDA HQ has also provided consultation to NIH in support of reports required under the Cures Act related to ClinicalTrials.gov

Regulatory Policy and Guidance

FDA HQ led the development of FDA's regulations on acceptance of clinical data for medical devices. FDA HQ has developed a guidance to accompany the final rule.

Below are selected guidance documents on human subject protection issued by FDA HQ in 2016 and 2017. This list does not represent any degree of importance or priority ranking among those items.

Publication Date	Formal Title	Description
September 2017	Minutes of Institutional Review Board (IRB) Meetings - Guidance for Institutions and IRBs	This joint final guidance with HHS describes requirements for IRB meeting minutes and provides recommendations on the type and amount of information needed to comply with the FDA and HHS regulations.

Publication Date	Formal Title	Description
July 2017	IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More than Minimal Risk to Human Subjects	This final guidance informs sponsors, investigators, and IRBs that FDA does not intend to object to an IRB waiving or altering informed consent requirements for certain minimal risk clinical investigations.

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. FDA HQ 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). FDA HQ also provide surveillance and signal monitoring, including FDA's Emergency Operations Network Incident Management System, and Consumer Complaint reporting and monitoring functions.

In FY 2017 , FDA HQ coordinated the emergency response to 74 significant incidents including:

- 244 serious adverse or injury event incidents
- 34 natural disasters
- 13 man-made disasters
- 3 National special security events

FDA HQ evaluated 3,859 consumer complaints including 44 reports of suspected product tampering in FY 2017 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 2017 FDA HQ coordinated nine Agency responses to World Health Organization (WHO) International Food Safety Authorities Network (INFOSAN) inquiries involving food products (flour, eggs, infant formula, tuna, etc.). FDA HQ also addressed five draft notices of Public Health Emergency of International Concern (PHEIC) in FY 2017, including novel influenza variants, a regulated commodity with potential health concerns, etc. Additionally, FDA HQ responded to/coordinated 120 Rapid Alert System for Food and Feed (RASFF) requests from the European Union.

In FY 2017, FDA HQ conducted, evaluated and reported Table Top and Full Scale Exercises, for two separate Center Select Agent Laboratory facilities. These included a medically downed patient in a High Containment Laboratory, with associated minor contamination, and federal, state and local resource participation. A second Table Top exercised actions involved with a fire in the high containment area. The resulting after action reports emphasized the need for

additional training in basic patient assessment and patient transport to a "clean area" for further triage, as well as the need for additional Incident Command training. FDA HQ created and presented three training opportunities for laboratory researchers centering on patient assessment, monitoring, movement and turn over to medical authority.

FDA HQ 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.

FDA HQ completed a Table Top and Full Scale Exercise Series for cyber events. The cyber exercise is part of a series of exercises specifically designed to establish a learning environment for players to exercise emergency response notifications and procedures. The purpose of the exercise was to practice establishing an incident common operating picture and specifically focus on headquarters response efforts to a significant cyber incident.

In addition, FDA HQ supported HHS and FEMA plans with the following incident annex updates:

- Food Agriculture Incident Annex, including plant, animal and food agriculture inputs
- the Federal Evacuation Annex
- the Chemical Incident Annex
- the Biological Incident Annex

Geographic Information System Mapping

In FY 2017, FDA HQ expanded the use of the Geographic Information System (GIS) to support advanced work planning analysis related to changes in regulatory operations resulting from the Office of Regulatory Affairs realignment. FDA also used GIS to provide real-time support for the 2017 Hurricane Season. FDA HQ completed maps for 117 project requests involving FDA regulated firms.

Global Health Security and Counterterrorism

DA HQ provides leadership, coordination, and oversight for FDA's work to support national and global health security, counterterrorism efforts, and address emerging threats. The portfolios include serving as point of entry on policy and planning matters; serving as a focal point for the FDA's involvement in the HHS-led Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) and the Department of Defense (DoD) medical countermeasure (MCM) programs; and coordinating the Medical Countermeasures Initiative (MCMi) to facilitate the development and availability 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 gastrointestinal, bone marrow, and lung models based on 'organs-on-a-chip' technology to use to develop drugs to treat acute radiation syndrome
- mapping immune responses to biothreats and MCMs in humans and developing animal models to support MCM development

- analyzing disease progression and effects of Zika Virus in non-human primate animal models as part of an FDA-established interagency collaboration to inform guidance regarding organ transplant safety and related tissue products
- developing methods for obtaining safety and limited efficacy data from patients who receive MCMs during public health emergencies.

FDA scientists continued activities to support the development of MCMs for the Ebola virus, including:

- developing improved small animal models
- identifying potential markers of Ebola virus disease progression in animal models
- developing and validating analytical procedures for evaluating Ebola to use outside of specialized, high-containment laboratories
- establishing correlates of protection to support the development of Ebola vaccines
- analyzing Ebola survivors with and without chronic health problems to identify factors responsible for driving prolonged disease

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
- establishing correlates of protection to support the development of Zika vaccines.

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 an Emergency Use Authorization (EUA).

Accomplishments in FY 2016 and FY 2017 that support MCMs include:

- issuance of final guidance that explains FDA's general recommendations and procedures applicable to the authorization of the emergency use of certain medical products
- issuance of emergency dispensing orders for doxycycline and ciprofloxacin for anthrax preparedness
- issuing draft guidance for local, state, and federal government stakeholders on testing to extend the labeled expiry dating of doxycycline to support efforts to sustain adequate supplies for anthrax preparedness
- using the expiry dating extension authority to authorize use of MCMs beyond their labeled expiry date to prevent shortages of critical products
- 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 20 Zika virus diagnostic tests under the 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 accomplished the following:

- 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)[100].
- 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).

FDA HQ also continued to advance the FDA's efforts to improve domestic and military preparedness for potential public health emergencies with chemical threats. For example, FDA HQ helped lead the FDA's efforts to prevent shortages of critical auto-injector products stockpiled by DoD, the SNS, and first responders for the treatment of nerve agent and insecticide poisoning due to ongoing manufacturing quality issues of the USG's sole-source supplier by:

- determining that, if properly stored, certain lots of the manufacturer's auto-injector products held for emergency use could be used beyond the original labeled expiration date for a period specified by FDA
- providing updates about continued use of stockpiled product beyond its labeled expiry date to impacted stakeholders; and
- working closely with HHS, CDC, and DoD partners to enable the import, availability and use of a new auto-injector product for the treatment of nerve agent and insecticide poisoning under FDA's EUA authority.

International Inspections

FDA HQ 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. FDA HQ oversees four FDA country and regional offices (China, Europe, India, and Latin America) in seven locations abroad. Engagements involving other countries and regions are also covered by FDA HQ. 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
- leveraging the authority of foreign regulatory counterparts
- sharing information and expertise to strengthen foreign regulatory systems for the benefit of the U.S. consumer.

During FY 2017, according to data as of October 31, 2017, investigators based in country or on short-term assignments to China, India and Latin America from ORA conducted 196, 80 and 5 inspections, respectively. In addition, Latin America Office's CSO conducted an onsite investigation/inspection at papaya fields and a packing house involved in a Salmonella outbreak

[100] Please visit http://www.fda.gov/ for additional program information and detailed news items.

as part of FDA's outbreak investigation, alongside with the Mexican Regulatory Authority SENASICA.

In late 2016, the China Office conducted an inspection at a dietary supplement manufacturer and discovered that Ephedra was used as an ingredient in one of their products although not declared on the finished product label. The inspection also found significant deviations from dietary supplement cGMPs, as well as multiple product labels with disease claims and undeclared ingredients. The firm voluntarily recalled the product, and the firm and its products were placed on four different Import Alerts. The China Office then worked with the New York District Office to follow-up with the recall at the distributor in the U.S.

In another case, FDA cancelled an inspection of an Indian manufacturer after the firm informed ORA, and provided documentation, that an inspection was impossible because its employees were striking and had blocked the company's entrance. Working through in-country contacts, OIP's India Office confirmed that the company had neither experienced a workers' strike nor suspended operations. FDA then gained access to the facility for an inspection. In early 2017, because the company used false and misleading statements to delay and deny the FDA's inspection of its facility, FDA deemed all drugs manufactured at that facility to be adulterated. FDA placed the establishment on two Import Alerts and in April 2017, issued a Warning Letter under which FDA may withhold approval of any new applications or supplements listing the company as a drug manufacturer.

During an inspection of a food manufacturer in India, the inspector recognized that two of the ingredients observed contained soy, although there was no declaration of soy on the finished retail product. People with food allergies to soy can experience severe, life-threatening allergic reactions. As a result, a Recommendation for Recall Classification was submitted for 7 shipments of the product to remove the product from the market.

The Foreign Offices also share risk information with FDA HQ that informs FDA regulatory actions. For example, the Latin America Office provided information to ORA regarding a recall of tilapia in Costa Rica. This intelligence was used by FDA to place the firm and product on an import bulletin, which increased the surveillance of products from that firm coming into the United States to ensure that products entering the United States did not experience the same safety issues observed in Costa Rica. The Latin America Office also worked with their regulatory counterparts in Mexico to provide strategic information and support the Agency during multiple outbreaks over the last year. The Agency gained valuable intelligence on outbreak investigations from multiple-States associated to diverse Salmonella serotypes from the Latin America Office facilitating risk assessment.

Additionally, the Latin America Office routinely shares locally-acquired risk information with FDA's Coordinated Outbreak Response and Evaluation (CORE) Network to assist in investigations of U.S. food-borne illness outbreaks. For example, during an investigation of a U.S. Salmonella outbreak suspected of stemming from Mexican papaya, the Latin America Office's post in Mexico City provided feedback to CORE based on information they obtained from their regulatory counterparts in Mexico which was used by CORE to modify their list of possibly-suspect firms. The Mexico City post then shared CORE's modified list with Mexican regulatory counterparts, who agreed to deploy their own investigators to the identified sites. The Mexican regulatory authorities subsequently shared the results of their investigations with FDA. This was important in assisting FDA in its outbreak traceback activities and regulatory

decision-making with respect to whether FDA should conduct its own investigations of identified firms and this helped FDA to identify the appropriate type of such investigation for a specified firm.

Another example of communicated risk information includes India's work on tracking down information related to firms with potentially contaminated products exported to the United States. When India's Consumer Education and Research Centre published a report identifying findings of pesticides and toxic elements in specific brands of rice, the India Office was able to determine that three firms identified in the report were actively exporting rice to the United States. At the request of the India Office, ORA implemented screening criteria so that ORA would collect border samples for pesticides and toxic elements in products from the three firms.

At HQ, the Office of International Program's Office of Regional Country Affairs Office worked with ORA in 2017 and provided guidance on the protocol for obtaining contact information for competent authorities needed to be informed of upcoming inspections. The Office of Regional Country Affairs reached out to FDA counterparts in Canada, Japan, Vietnam, Egypt, Ghana and Nigeria to obtain their updated contact information. This allowed ORA to effectively notify FDA counterpart authorities of planned inspections.

International Partnerships

In FY 2017, FDA implemented 16 new Confidentiality Commitments with:

- Public Health England, to facilitate information sharing about tobacco products
- the European Commission's Directorate General for Internal Market, Industry, Entrepreneurship and SMEs, to facilitate information sharing related to cosmetics and medical devices
- the Netherlands' National Institute for Public Health and the Environment, to facilitate information sharing about tobacco and biologics, among other FDA-regulated products
- the National Agro-Alimentary Health, Safety and Quality Service of the United Mexican States to facilitate information sharing about food related issues, among other FDA-regulated products, assuring that FDA will protect the information provided
- the World Health Organization through its Department of Essential Medicines and Health Products to disclose information regarding the identification of pharmaceutical substances and active pharmaceutical ingredients
- the European Medicines Agency to facilitate the exchange of non-public information related to FDA regulated drugs, including pre- and post-market activities, as appropriate, as part of cooperative law enforcement or cooperative regulatory activities
- several European Union member states to facilitate the exchange of non-public information related to FDA regulated drugs, including pre- and post-market activities, as appropriate, as part of cooperative law enforcement or cooperative regulatory activities. Specifically, FDA signed confidentiality commitments with:
    - the Bulgaria Drug Agency
    - the Croatia Agency for Medicines Products and Medical Devices
    - the Denmark Medicines Agency
    - the Estonia State Agency of Medicines
    - the Finland Medicines Agency
    - the France National Agency for Medicine and Health Products Safety
    - the Latvia State Agency of Medicines

- the Romania National Agency for Medicines and Medical Devices
- the Slovakia State Institute for Drug Control
- the Spain Agency for Medicines and Health Products.

FDA signed two Cooperative Arrangements during 2017 to facilitate regulatory activities:

- a food safety systems recognition arrangement with Australia's Department of Agriculture and Water Resources
- a Memorandum of Understanding with China's Certification and Accreditation Administration related to the export of U.S. dairy, seafood, and infant formula products to China.

In other partnership activities, FDA Europe and China Offices, working with CFSAN and OFVM, have continued the trilateral scientific and technical engagement initiated 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 about food safety. In FY 2017, the parties met to discuss import and export controls, e-Commerce, and risk communication, all important topics to implementing existing legislative authorities. Planning has begun for the next meeting to focus on risk assessment, expected to take place in Q3 of FY 2018.

In 2017, the Europe Office has taken a more prominent role in advancing the Mutual Recognition Agreement (MRA) for pharmaceutical good manufacturing practice inspections, that was finalized on March 1, 2017. The Europe Office directly contributed to multiple member State capability determinations through inspectorate audit observation and reporting, conflict of interest analysis, and capability assessment. All 28 Member States will be assessed by July 2019, and the Europe Office is expected to continue to play a central role in contributing to these assessments. Furthermore, the Europe Office and the Office of Regions and Country Affairs have been working together to finalize expanded confidentiality commitments with the European Union and all 28 individual Member States (expected to be completed through FY 2017 and FY 2018) that will allow all parties to more fully benefit from the MRA. Europe Office is also a key participant in implementation and coordination planning for operationalizing the MRA with FDA Centers and the European Medicines Agency (EMA). The Europe Office also participates on the Joint Sectoral Committee (i.e., governance committee). Once fully implemented, FDA anticipates significant efficiencies regarding GMP inspections to be realized by FDA and our European counterparts in one another's territory, enabling those resources to be shifted to higher priority/higher risk areas.

The India Office engaged in a series of in-person Seafood HACCP and U.S. Food Labeling workshops in Mumbai and Nellore in 2017. Almost 100 individuals were trained, providing India government and industry participants with information about FDA seafood HACCP regulatory requirements provided at 21 CFR Sec. 123 – specifically information concerning the key areas of sanitation, developing a HACCP plan, and preventing seafood safety hazards. In addition, participants were provided information on procedures for importing seafood products into the United States, including Customs and Border Protection and FDA regulatory oversight and information about responding to FDA product detentions. Moreover, FDA provided information about FDA labeling requirements for food products sold in the United States, including labeling requirements for the nutrition fact label and food allergens and updates to U.S. food labeling regulations. The workshops also strengthened relationships between FDA officials and the Export

Inspection Council of India. In addition, the India Office worked with the Pharmacovigilance Programme of India to determine ways to strengthen the pharmacovigilance program in India through U.S.-Indian collaboration.

Leveraging the Regulatory Capabilities of Foreign Counterparts

On-site relationships with foreign regulatory counterparts enable FDA to leverage their respective regulatory capabilities. The following items are examples of these relationships.

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 on this information and prevent the distribution of such products in Mexico. Additionally, in response to several Cyclospora outbreaks in 2013-2015, the Latin America Office worked closely with Mexican Authorities to develop a process by which selected Mexican packing houses and supplier farms can be added to the Import Alert #24-23 Green List that allows cilantro imports to the United States when such firms comply with the Mexican voluntary verification and certification programs. Since the implementation of Import Alert #24-23 and its Green Listing process, 30 supplier farms and 12 packaging houses/firms, 22 supplier farms and 9 packaging houses/firms have been added to the Green List without concomitant outbreaks linked to Cyclospora.

The Latin America Office shared information on six specific drug products with the Brazilian regulatory authority under the terms of our Confidentiality Commitment, resulting in Brazilian regulatory actions. For example, in one case, the Brazilian regulatory authority initiated closer monitoring of GMP compliance. In other cases, the information was taken under consideration for Brazilian regulatory decisions related to marketing and clinical trial authorizations as well as in the evaluation and authorization of post-approval changes to marketing authorizations.

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 2017, the Europe Office facilitated work between European Food Safety Authority and CFSAN experts on issues such as open data, specific requests for FDA scientific reports/findings, and risk communication. This collaboration is extremely important as the health policy landscape in Europe is often politicized around issues such as endocrine disruptors and biotechnology derived products intended for human and animal consumption and EFSA often represents the most completely science-based voice in the region on relative risk and safety.

Responding to an ORA and CDER request, the Europe Office facilitated dialogue with their United Kingdom regulatory partner and ORA's Office of Enforcement and Import Operations, resulting in development of a strategy and work between joint enforcement and compliance teams. The collaboration resulted in the halt of a longstanding path of shipment of violative drugs from several United Kingdom-based companies intended for the U.S. market. The India Office shared information of FDA refusals of Indian seafood through the Confidentiality Commitment with the Export Inspection Council of India. The Export Inspection Council of India used this refusal data to follow-up at processing facilities determined to be the root cause of the deviation and were able to elicit corrective actions from the facilities.

International Exchange of Information and Sharing of Expertise

In addition to information sharing that leverages the authority of foreign regulators, FDA Foreign Offices work closely with FDA product centers and the ORA to exchange regulatory knowledge and expertise with foreign stakeholders to improve understanding of FDA regulatory requirements. For example, during FY 2017, the China Office conducted outreach to Chinese regulatory authorities on topics such as Good Clinical and Manufacturing Practices, Generic Drug Review, Medical Device Review, Good Inspection Practices, Regulation of Dietary Supplements, Combination Products, User Fee Program Updates, Postmarket Medical Device Reporting and Surveillance, the Medical Device Sing Audit Program and FSMA. The Europe Office trained foreign regulatory authorities on FSMA rules, the amended MRA, key provisions of the 21st Century Cures Act, newly issued guidance on biosimilars/interchangeability, and the potential use of big data in regulatory decision making. The India Office provided Indian regulators with training on Good Clinical Practices, FSMA, Good Aquaculture Practices and Food Safety Preventive Controls for Aquaculture Farms, and the Federal Food, Drug, and Cosmetic Act.

An objective of the foreign offices is to improve regulatory decision making and prevent divergence of regulatory standards and approaches, when appropriate, through facilitation of technical exchange with trusted international regulatory counterparts. This is done through workshops, meetings, fellowships (technical exchanges) that are intensive and topic specific. For example, the Europe Office and EMA International Affairs held a formal meeting in November 2017 to discuss collaboration in the multilateral space, MRA implementation progress, collaboration with expedited review programs and scientific advice, and technical exchange platforms. In addition, the Europe Office oversees the management and maintenance of over a dozen technical working groups - "Clusters" - with EMA and in some cases the national competent authorities of Canada, Australia, Switzerland, and Japan. In depth exchanges and efforts to align thinking on regulatory science and strategies to promote public health are themes of these exchanges. In the second half of FY 2016 and FY 2017, the Europe Office facilitated in-depth technical exchanges on topics including food fraud, Unique Medical Device Identifier database, data transparency, drug quality inspections, pediatric drugs, orphan products, real-world evidence/big data, antimicrobial resistance, combination products, MRA Implementation, statistical extrapolation, master data management, and application review management.

The Europe Office held a one-day technical experts meeting of some key European Member State regulators. The meeting focused primarily on genome editing applications in the area of plant-derived foods for humans or animals. Sharing information on regulatory challenges associated with new technologies will encourage a science-based rather than political debate. Joining FDA experts were representatives from Belgium, Germany, Ireland, Sweden, and the Netherlands.

In 2017, the European Union adopted the most sweeping medical device regulation reform in a generation. This regulation includes a number of provisions designed to move the European Union toward FDA-standards, while maintaining Europe as the regulator of first resort for new medical devices. Through regular reporting on progress, as well as challenges from stakeholders including U.S. firms operating in Europe, the Europe Office has collaborated with CDRH to provide real time reporting on progress toward the implementation.

The India Office coordinated with the Government of India's Central Drugs Standard Control Organization to develop a strategic action plan to advance drug safety in the U.S. and India. The two conducted a joint workshop to share feedback from FDA inspections observed by Government of India inspectors. The India Office will utilize this knowledge and work with the Office of Regulatory Affairs to establish best practices.

During the 2017 bilateral meeting coordinated by the China Office, the China Food and Drug Administration shared their inspection report from 2015 and 2016 with the FDA. Among other topics, these reports addressed observed inspections with multiple regulatory agencies conducting inspections in China and shared the differences observed in approaches to drug inspections. During multiple interactions with China Office staff in September and October, central and provincial investigators from the China Food and Drug Administration also shared their experiences with observed inspections of foreign regulatory agencies. The information gathered from these meetings is being utilized to develop an Inspectional Cooperation Work plan utilizing best practices to establish with the China Food and Drug Administration, expected in 2018. Additionally, after repeated diplomatic engagements on the importance of international harmonization, in FY 2017 CFDA announced joining the International Council for Harmonization.

The Latin America Office participated in meetings with Mexico's regulatory authority regarding the NIH Zika vaccine trial. FDA and COFEPRIS worked closely together to clarify questions for COFEPRIS in their regulatory protocol review, allowing COFEPRIS' review to be completed within 30 days – a time period which is significantly shorter than their typical review time. As a result, the trial is already recruiting patients, which is essential to coincide with the rainy mosquito season in Mexico. Additionally, the regulatory authorities in Mexico expressed interest in learning about FDA's expedited review process for vaccines and in developing a process aligned with FDA's that allows for an improved response to cases of public health relevance. The Latin America Office coordinated input from CBER to collaborate on the development of an alternative pathway for vaccine product approval.

In addition, the Latin America Office held two virtual meetings with Brazil's regulatory authority, along with CDER subject matter experts, during which the parties exchanged information about best practices and regulations, and discussed specific procedures and the scientific and technical basis for regulation development. These meetings resulted in Brazil's actions on program streamlining and regulatory alignment with FDA on pharmacovigilance IT systems and over-the-counter drugs.

When the FDA Drug Shortage Team identified a shortage of domestically-produced antimicrobial drugs, the Europe Office rapidly engaged with the European Medicines Agency to obtain information on the production capacities of firms in Europe that produce such drugs. Since production by those firms could help mitigate the impact of the shortage in the United States, FDA's Drug Shortage Team included that information in FDA's strategy to address the drug shortage. Additionally, to address potential drug shortages, the China Office had regular communication with FDA's Drug Shortage staff during a government controlled industry shutdown of drug substance manufacturing during over the winter, as well as when an explosion occurred at a Chinese facility that supplied certain antibiotics to the US that had to cease production until remediation efforts were completed.

The China Office interacted with the World Health Organization's local Beijing Office in 2017 on the China Food and Drug Administration's Market Authorization Pilot. The World Health Organization is providing an assessment from all the provinces involved in the pilot, and the China Office contributed to the discussion topics for further consideration. The pilot is intended to spur innovation and is expected to be an integral part of the reform taking place relating to regulatory oversight under revisions to China's Drug Administration Law.

At HQ, the Office of International Program's Office of Regional and County Affairs sent information and requested input from international counterparts in Canada, Israel, Japan, Philippines, South Africa, South Korea and Thailand on the FY 2017 microbiological surveillance sampling model for selected food products. The Office provided this information to CFSAN, and consequently, CFSAN could work more efficiently and decrease the impact on trade.

In addition, the FDA HQ Office of Women's Health has established a network of international institutes academicians and scientists within the field of sex and gender-specific women's health. In FY 2016 and FY 2017, this network has resulted in multiple international speaking opportunities enabling FDA to communicate updates in policies, guidances, and research discoveries related to women's health. These international activities included educating The Matera Group, which consists of scientific experts from across the world, about FDA policies and regulations regarding analysis and reporting of sex differences in safety and efficacy. While FDA HQ is not a formal member of the Matera Group we are often contacted to provide clarifying information on FDA regulations related to women's health. Engagement such as this assists in ensuring accurate understanding of applicable women's health policies and regulations in the United States.

China Safety Initiative

FDA expanded its efforts to regulate the quality, safety and efficacy of FDA-regulated products exported to the United States from China through the China Safety Initiative (CSI), with the primary focus being the expansion of the number of in-country FDA investigators, which was accomplished through a negotiated agreement with the Chinese government.

The increase in in-country full-time investigators and those on temporary detail (TDY) to the China Office, allowed for the completion of 69 inspections in FY2017 focused on medical products. Furthermore, the China office also completed 128 inspections focused on foods, animal feed, and animal drugs. The China Office conducted all assigned FDA food facility inspections in China. The China Office, in collaboration with the Europe office and CFSAN, led a trilateral meeting between FDA, EU and Chinese regulators on food safety issues of mutual interest with the EU, and China agreed to a set an agenda as well as participate at a two-day event in March 2017.

In September 2017, the China Office spearheaded a workshop with international regulators and industry on GMP issues that focused on Out of Specification (OOS) Investigations and Corrective and Preventive Actions (CAPAs). The FDA China Office utilized internal expertise and assembled an international panel of experts from FDA's Center for Drug Evaluation and Research (CDER) Office of Compliance and Office of Regulatory Affairs (ORA), Medicines and Healthcare Products Regulatory Agency, European Medicines Agency (EMA), Health Canada, World Health Organization (WHO), and China Food and Drug Administration (CFDA) to take part in the event. The content built upon previous efforts that focused on data integrity and

expanded to the laboratory and manufacturing operations by covering global regulatory best practices in identifying, investigating and properly resolving issues.

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.[101]

Rare Disease Designations, Rare Pediatric Disease Determinations, and Grants

In FY 2017, FDA HQ:

- received 541 first-time requests for orphan drug designation and designated 449 promising drugs and biological products for rare diseases
- received 20 first-time requests for Humanitarian Use Device designations and designated 8 promising devices for rare diseases and conditions
- received 61 Rare Pediatric Disease Designation and Consultation Requests and designated or granted 39 drugs and biologics for rare pediatric diseases[102]
- funded 15 new clinical trial grant awards and 70 ongoing grants funding clinical studies of promising therapies for rare diseases
- reviewed 89 natural history grant applications and funded 6 new natural history grant awards to inform medical product development by better understanding how specific rare diseases progress over time
- funded 7 pediatric device consortia to provide multidisciplinary advice and funding to assist pediatric device innovators.

Premarket and Postmarket Support

In FY 2017, FDA HQ responded to approximately 700 requests for combination product premarket review assistance from FDA staff and regulated industry (including products that are on the shortage list). FDA HQ issued four formal combination product requests for designation decisions with 100 percent of these decisions meeting the 60-day statutory decision time

[101] Please visit http://www.fda.gov/ for additional program information and detailed news items.

[102] Please visit http://www.fda.gov/ for additional program information and detailed news items.

requirement. FDA HQ provided timely informal jurisdictional assistance for approximately 157 separate Pre-RFD (informal inquiries). FDA HQ provided clarification and support for approximately 350 premarket applications, 1,130 intercenter consults and 50 combination product post market activities.

Pediatric Coordination

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 more than 50 adult ethics issues. These ethical consultations include complex issues related to the development of FDA policies for emergencies and crises such as the Zika outbreak and the opioid crises, study design considerations in pediatric rare disease populations and research involving the exceptions from informed consent requirements for emergency research. Each of these efforts have continued at similar levels in 2017.

FDA HQ promoted the support of therapeutic product development for neonates through internal and external collaborative efforts. These collaborative efforts included enhancing communication between FDA scientists and external neonatal groups on specific scientific issues, primarily through the International Neonatal Consortium (a consortium facilitated by the Critical Path Institute). Additional research studies have been initiated with colleagues across the FDA Centers as well as with external scientific researchers. Consultations were provided across the FDA Centers with 33 consults completed in 2017.

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 390 products have been reviewed by the PAC. In FY 2017, 34 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.

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 156 issues in FY 2017. Of the 156 issues discussed with the EMA, harmonization was achieved for 74 percent. Examples of the most frequent issues discussed included study population, primary endpoint, study design, extrapolation and safety concerns.

Women's Health Research

FDA HQ provides leadership and policy direction for the Agency on issues of women's health and coordinates efforts to establish and advance a women's health agenda through research funding that:

- identifies potential differences between males and females regarding the safety and efficacy of FDA regulated medical products
- promotes a better understanding of medical conditions that disproportionately or solely affect women.

Women's Health research provides evidence for the biological and physiological differences between males and females, and advocates for the adequate representation of women in clinical studies. In the areas of human drug, biologic and medical device development, the design and analysis of clinical trials can answer fundamental questions related to sex-based differences in the safety and efficacy of these products.

FDA HQ developed a "Women's Health Research Roadmap," an agency-wide strategic research plan that identifies regulatory and scientific knowledge gaps in women's health and defined seven priority research areas where knowledge gaps exist in order to maximally leverage research funding impact. Implementation of the Women's Health Research Steering Committee has created a direct connection regarding cross agency priorities and issues of importance to women's health.

To measure the impact of the Women's Health research program, the Research Impact and Outcomes Framework was developed. This first of its kind framework is currently in use by FDA HQ, two FDA product Centers, and upon request shared with three offices within the National Institutes of Health. It is an available resource to academic, federal, and non-government organizations and allows tangible measurement and reporting of the impact of research, education, and outreach programs.

In addition, since the establishment of the Office of Women's Health, FDA HQ has distributed $40 million to 371 projects. Scientific evidence from several of these research projects have contributed to FDA guidance development, labeling changes, and over 375 scientific publications. The scientific publications resulting from this research funding program have been referenced approximately 10,000 times throughout the scientific literature.

Women's Health Medical Initiatives and Scientific Engagement

FDA HQ established a Women's Health Medical Initiatives and Scientific Engagement program to promote women's health through medical and scientific education and collaborations with health professional organizations. FY 2017 program accomplishments include:

- Collaborations with two national clinical trials professional organizations. Activities included providing training to hundreds of national scientists and clinical trials staff on methods to increase enrollment and retention of women in clinical trials.
- A quarterly Scientific Speaker Series provides education for staff across HHS to help ensure sex and gender are incorporated into research, professional education and consumer information. Pre- and post- polls of attendees exhibited a 30 to 60% knowledge gain by attendees.

In FY 2017, FDA HQ also co-led development of a half day Workshop for the Women's Health Congress, which highlighted initiatives including women in clinical trials, precision medicine, and expanding FDA transparency and communications to an audience of clinicians, scientists, women's health advocacy and patient representatives. The workshop increased stakeholder engagement and understanding related to FDA's policies and procedures to ensure the health of women.

In collaboration with NIH's Office of Research on Women's Health, FDA HQ provided the expert educational development model in the creation of a national six hour continuing education series focused on sex as a biological variable in disease and medical research. This series of six courses is designed to educate scientists, clinicians, and health professional students. The series

will result in an increase in the incorporation of sex differences into research programs and therefore application of research to both men and women.

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.

The following, selected accomplishments demonstrate FDA HQ's delivery of its regulatory and public health responsibilities within the context of current priorities[103].

Leading FDA's Engagements with the Government Accountability Office (GAO) and the Office of the Inspector General (OIG)

In this role, FDA HQ staff coordinates the Agency response to all these requests from GAO and OIG. 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 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, FDA HQ 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, which included developing and drafting rules and regulatory impact analyses, to ensure the publication of several key proposed and final rules in 2017. A key final rule that issued in 2017 included Refuse to Accept Procedures for Premarket Tobacco Submissions. This rule clarified FDA's process for tobacco premarket submissions. In addition to these key final rules, FDA issued 7 other final rules that are related to product approvals or technical amendments to existing FDA regulations.

One of the key proposed rules FDA issued in 2017 included Nutrition Food Labeling and Serving Sizes which proposes to extend the compliance date for requirements that update the food labeling to reflect amounts of food customarily consumed at one eating occasion and provides manufacturers with additional time to reconfigure their labels. FDA also proposed to extend the compliance date for parts of the FSMA produce rule. The extension applies to provisions related to agriculture water and produce other than sprouts. This will reduce the burden on farms that require additional resources to comply with the original rule. In addition to these two proposed rules, FDA issued four additional proposed rules that related to product approvals and responded to litigation.

[103] Please visit http://www.fda.gov/ for additional program information and detailed news items.

Economic Analysis and Support for Medical Product Regulations Published

In 2016, along with the publication of the final rules themselves, FDA published the economic analyses for rules related to medical device products (Use of Symbols in Labeling) and human drug products (Abbreviated New Drug Applications and 505(b)(2) Applications). The support provided via economic analysis spanned more than five years and informed policy decisions throughout the rulemaking process. The results of data analysis and economic modeling were vital inputs into, and key to the publication of, the final rules that will clarify regulatory uncertainty among the regulated industry.

Communication with Stakeholders – Improvements to FDA.gov

FDA is working to improve the usability of FDA.gov, our public-facing web site, by implementing a new, state of the art content management system (CMS), in May 2018, named Drupal. Drupal will help visitors more easily find our content and share it through web sites, mobile applications, and social media channels. In addition, Drupal will allow FDA to more easily highlight priority content and most requested content on our home page and topic landing pages. This greater flexibility displaying top task information is what visitors to FDA.gov are looking for. To prepare for this implementation, FDA has implemented a new archiving capability and 60,000 old and outdated content items have been removed from FDA.gov and are now available through archive. In addition, FDA is working on a project to identify a new and improved information architecture for the web site to better organize our content in more intuitive ways for our visitors. This new organization of content will be based on our most requested information to ensure this content is easy for our visitors to find.

Communication Products for 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.

From January 1, 2017 through November 2017 FDA HQ issued:

- 132 MedWatch Safety Alerts (FDA's second most popular e-list) to more than 450,000 subscribers.
- 203 News Releases and other press announcements in English and/or Spanish with a total reach of more than 89,000 subscribers
- 78 FDA Voice Blogs with more than 44,000 subscribers
- 260 Consumer Updates (some new material, some revisions) in English and Spanish with more than 117,000 subscribers
- more than 100 newsletters that reach approximately 700,000 patients and health care professionals.

FDA HQ responds to key agency priorities regarding women's health by delivering credible, accurate, and easy-to-understand health messages on topics related to FDA regulated products. These materials help women and their families make informed health decisions. These materials include fact sheets, brochures, purse cards, and medication discussion guides. All materials are free and written at a fourth through sixth grade reading comprehension level. To date, in partnership with other national organizations, more than 100 million publications have been distributed nationwide. Notable FY 2017 accomplishments include:

- Reaching more than 14 million people via special campaigns and stakeholder engagement initiatives using print and digital outreach
- Distributing 2.1 million patient education materials in 19 languages
- Disseminating FDA safety alerts and health information via the Office of Women's Health (OWH) twitter account to approximately 70,000 followers, of which 58% were health professionals and researchers
- Providing grants to FDA field staff to conduct women's health outreach in 15 cities in the U.S. and Puerto Rico
- Conducting webinars, conference presentations, and consumer outreach with over 25 public and private partners through the Diverse Women in Clinical Trials Initiative.

Meetings with Stakeholders

Since January 2017, FDA HQ has conducted nearly 630 meetings or interactions with a wide range of stakeholders. Noteworthy among these has been meetings or interactions with:

- The American Congress of Obstetricians and Gynecologists (ACOG)
- American Medical Association (AMA)
- Health Professional Student Engagement
- Consumers Union (CU)
- Atrial Fibrillation (AFib) Patient Organization
- American Academy of Dermatology
- Leukemia and Lymphoma Society.

FDA HQ has also used social media to engage with our stakeholders including two Twitter chats, with one including a bilingual audience. In additional, FDA recruited and trained 30 new patient representatives, selected for their experience and advocacy with medical conditions and diseases. The added representatives, who serve as a special government employee to FDA's Advisory Committees, brought the total number of patient representatives in the program to approximately 200. In July 2017, FDA conducted a workshop for patient representatives, providing them with an opportunity to learn about the FDA regulatory process and understanding their responsibilities.

FDA HQ fully participated in the patient engagement cluster 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.

Stakeholder Outreach Activities

MedWatch Product Safety Communications: FDA HQ issued over 135 MedWatch Safety Alerts since January 2017 to inform health care professionals, consumers and patients about current and urgent product safety information. Two videos were developed, produced and disseminated to consumers and healthcare providers on reporting medical product problems to FDA. These videos were accepted by the American Public Health Association and showcased at their annual meeting (November 2017) attended by over 12,000 international public health professionals. A MedWatch video was developed and distributed to consumers and health care professionals in Spanish that provides instructions for completing a MedWatch form as a way the U.S. public can

inform FDA about possible adverse effects attributable to an FDA-regulated product or a product of poor quality. Multiple articles on the topic of boxed warning highlights on the drug label were published in four health care professional journals/publications: the American Journal of Health-System Pharmacy, the Hospital Pharmacy Journal, Federal Practitioner, and Medscape since January 2017.

Healthcare Practitioners: As part of an MOU with the American Nurses Association, FDA HQ planned/conducted a joint webinar on November 16, 2017, "An Opioid Primer: Legislative, Policy, & Practice Implications." The joint webinar described early and later opioid effects on the brain and illustrated how the brain changes over time with opioid use, IOM's four level barriers to effective pain management, the Prescription Drug Management Program and its role in state and national drug monitoring efforts, and current drug treatment options and list three barriers to medication assisted treatment programs were also discussed. ANA is the only full-service professional organization representing the interests of the nation's 3.1 million registered nurses through its constituent and state nurses associations and its organizational affiliates.

Rural Health Symposium: FDA HQ held its inaugural Rural Health Symposium on October 26, 2017, providing a forum for key stakeholders in rural and tribal communities to discuss opportunities to address the critical and unique health challenges relative to the opioids crisis; tobacco use among youth; and telemedicine. The symposium was a cross-center effort and involved other federal agencies (VAMC, HIS, FCC, HRSA).

Providing Historical Content about FDA's Activities

FDA HQ collects, processes and preserves materials that capture the history of FDA's work and the breadth of the agency's responsibilities, conducts oral histories/interviews of selected staff, educates the public, and provides counsel on precedents to regulations, statutes, policies and legal cases. In FY 2017, FDA acquired 300 artifacts, saw to the preservation through digital conversion of several thousand documents from the 1940s to the 1980s, and arranged for the preservation through digital conversion of over 200 historical videotapes in an antiquated format. FDA also promoted on social media 5 history video blogs and 19 written stories about FDA artifacts of historical significance.

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.

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. The following, selected accomplishments demonstrate FDA HQ's

delivery of its regulatory and public health responsibilities within the context of current priorities[104].

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 implemented 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 $140 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, relocate the Kansas City and SE Regional labs to new, modern and flexible leased lab space, and improve an additional lab at JLC. In addition, FDA continued efforts to relocate the leased San Francisco lab in FY 2017. FDA initiated the development or review of a Program of Requirements for three lab expansion projects (ORA's Forensic Chemistry Center and Detroit Lab, and CDER's Division of Pharmaceutical Analysis Lab in St. Louis) and for two lab relocation projects (ORA's Philadelphia Pharmaceutical Lab and CFSAN's Moffett Center Lab). A project was also initiated to make improvements for certification of a specialized lab at ORA's Northeast Human and Animal Food 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.

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.

[104] Please visit http://www.fda.gov/ for additional program information and detailed news items.

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:

- Drug Adverse events – over 7.1 million records
- Device classifications – over 6,000 records
- Structured Product Labeling for FDA-regulated human drugs – prescription or over the counter– and biologics with over 105,000 records
- Medical device adverse event reports – 6.1 million records
- Food adverse event reports over 55,000
- Food enforcement reports12,811 records
- Unique Device Identifiers – over 1.3 million records
- 510Ks – over 145,000 records
- Device pre-market approvals – over 34,000 records
- Drug enforcement reports – over 7,000 records
- Device registration and listing – over 230,000 records
- Device recalls – over 99,000 records
- Device enforcements – over 13,916 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

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2015 Actual	$261,099,000	$173,292,000	$87,807,000
FY 2016 Actual	$301,574,000	$191,374,000	$110,200,000
FY 2017 Actual	$302,146,000	$187,063,000	$115,083,000
FY 2018 Annualized CR	$315,546,000	$180,980,000	$134,566,000
FY 2019 President's Budget	$347,240,000	$198,565,000	$148,675,000

BUDGET REQUEST

The FY 2019 Budget Request is $347,240,000 of which $198,565,000 is budget authority and $148,675,000 is user fees. This level provides a net increase of $31,694,000 compared to the FY 2018 Annualized CR. Budget authority increases by $17,585,000 and user fees increase by $14,109,000.

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.

BUDGET AUTHORITY

Medical Product Safety (+$26.0 million / 17 FTE)

New Platform for Drug Development - Oncology Center of Excellence (+$20 million / 13 FTE)

As part of this initiative to support new drug development, the FY 2019 Budget includes $20 million for the Oncology Center of Excellence (OCE) to stand up a new model for team-based product review that fosters collaboration across FDA's medical product centers, improves review efficiency, and expedites the development of novel science that can improve the lives of patients with cancer. Section 3073 of the 21st Century Cures Act required FDA to establish one or more intercenter institute(s) to help develop and implement processes for coordination of activities in major disease areas between the drug, biologics, and device centers. FDA has established the OCE to create a unified policy approach and clinical review for all drugs, biologics, and devices used in medical oncology.

With these resources, the OCE will leverage the combined talents and skills of all FDA regulatory scientists and reviewers who work in medical oncology product review. OCE will also serve as a single point of contact for external stakeholders for FDA's work in cancer, including professional societies and patient advocacy groups. FDA medical and professional staff will coordinate review of oncology product applications across the medical product centers, policy development, and collaboration with external stakeholders. This Center of Excellence will help expedite the development of oncology and hematology medical products and support an integrated approach in the clinical evaluation of drugs, biologics, and devices for the treatment of cancer.

Promote Domestic Manufacturing (+$6.0 million / 4 FTE)

As part of FDA's FY 2019 initiative to promote domestic manufacturing, FDA will help reduce the cost and uncertainty of adopting new manufacturing technologies by developing a science-based framework that includes the regulatory tools and guidance for how products will be evaluated, and by funding research, development and testing of these technologies. In support of these research efforts, the FY 2019 Budget includes $6.0 million for the Office of Laboratory Science and Safety (OLSS), which will serve as the Agency's coordinator and lead for implementation of policies and procedures, centralized training, and oversight for all laboratory operations related to laboratory science, safety, and security related activities. OLSS will work closely with the Office of the Chief Scientist, the Office of Operations, the Office of Regulatory Affairs, and the other product centers and directorates across the Agency.

Food Safety (+$0.5 million)

The FY 2019 funding level restores the FY 2018 Annualized CR rescissions to the food safety program. In FY 2019, FDA will continue its statutory mission of promoting and protecting public health by ensuring that the food supply is safe, sanitary, wholesome, and properly labeled. The FY 2019 level will also allow FDA to continue its critical FSMA implementation activities.

Other Reductions (-$8.9 million)

As part of the FY 2019 budget, FDA HQ will reduce investments in lower priority areas in order to support higher priorities for food and medical product safety. In FY 2016 and 2017, FDA HQ received funding 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 ($7.4 million at the FY 2018 Annualized CR level) are no longer required in FY 2019. In addition, FDA is proposing to discontinue the transfer of $1.5 million from FDA HQ to the HHS Office of Inspector General.

USER FEES

Medical Product Safety (+$14.1 million / 13 FTE)

The FDA HQ Program request includes an increase of $14.1 million for user fees authorized under FDARA, which will allow FDA to fulfill its mission of promoting and protecting the public health by ensuring the safety and efficacy of medical products and accelerating innovation in the industry.

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 2018 Target	FY 2019 Target	FY 2019 +/- FY 2018
292201: Improve FDA's ability to respond quickly and efficiently to crises and emergencies that involve FDA regulated products.*(Output)*	FY 2017: Maintained 99.62% efficiency on response to calls to the FDA After Hours Call Center. Successfully coordinated 49 incidents involving FDA regulated products during the year. Participated in nine exercises during the year. (All Targets Met or Exceeded)	Develop 50 mapping products in support of FDA's emergency preparedness, response, and recovery activities. Successfully coordinate 20 incidents involving FDA regulated products during the year. Participate in four exercises during the year	Develop 60 mapping products in support of FDA's emergency preparedness, response, and recovery activities. Participate in five exercises during the year.	+ 10 mapping products +1 exercise

293206: 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)*	FY 2017: 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)	40 CORES projects with completed annual milestones	47 CORES projects with completed annual milestones	+7
291101: Percentage of scientists retained at FDA after completing Fellowship or Traineeship programs. (Outcome)	FY 2017: 72% Target: 40% (Target Exceeded)	50%	50%	Maintain
293205: Percentage of requests for combination product designations processed within the 60 day statutory requirement. *(Output)*	FY 2017: 100% Target: 95% (Target Exceeded)	95%	95%	Maintain

293203: 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. *(Output)*	FY 2017: 156 Target: 45 (Target Exceeded)	45	45	Maintain
293204: Number of medical products studied in children with labeling changes and safety reviews completed and presented to FDA's Pediatric Advisory Committee. *(Output)*	FY 2017: 38 Target: 30 (Target Exceeded)	30	30	Maintain
292301: The number of new multi-faceted educational programs for patient advocates and health professionals on major FDA public health issues. *(Output)*	FY 2017: 4 Target: 4 (Target Met)	4	4	Maintain

291306: 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. *(Outcome)*	FY 2017: 27 Target: 25 (Target Met)	25	25	Maintain
291406: Percentage of invoices issued on time within predefined dates in the month. *(Output)*	FY 2017: 100% Target: 98% (Target Exceeded)	98%	98%	Maintain

INFRASTRUCTURE - GSA RENT, OTHER RENT, AND WHITE OAK

	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
FDA White Oak Consolidation Program	**46,856**	**46,856**	**46,349**	**57,373**	**11,024**
Budget Authority	***43,044***	***43,044***	***42,752***	***49,430***	***6,678***
Prescription Drug (PDUFA)	*3,812*	*3,812*	*3,597*	*3,792*	*195*
Tobacco Control Act	---	---	---	*4,151*	*4,151*
Other Rent and Rent Related Program	**117,147**	**116,653**	**122,740**	**138,793**	**16,053**
Budget Authority	**71,943**	**71,943**	**71,454**	**86,497**	**15,043**
User Fees	**45,204**	**44,710**	**51,286**	**52,296**	**1,010**
Prescription Drug (PDUFA)	26,340	25,047	24,672	26,005	1,333
Medical Device (MDUFA)	4,174	4,174	5,187	5,278	91
Generic Drug (GDUFA)	6,962	6,962	12,946	13,150	204
Biosimilars (BsUFA)	633	633	805	819	14
Animal Drug (ADUFA)	236	236	720	1,000	280
Animal Generic Drug (AGDUFA)	113	113	273	379	106
Tobacco Control Act	6,250	7,545	6,208	5,190	-1,018
Food And Feed Recall	43	---	43	43	---
Food Reinspection	204	---	204	204	---
Voluntary Qualified Importer Program	170	---	170	170	---
Third Party Auditor Program	45	---	24	24	---
Outsourcing Facility	34	---	34	34	---
GSA Rental Payments Program	**232,139**	**220,653**	**238,491**	**239,916**	**1,425**
Budget Authority	**170,208**	**170,208**	**169,052**	**168,421**	**-631**
User Fees	**61,931**	**50,445**	**69,439**	**71,495**	**2,056**
Prescription Drug (PDUFA)	22,607	22,607	33,373	35,175	1,802
Medical Device (MDUFA)	7,306	6,106	8,229	8,373	144
Generic Drug (GDUFA)	14,920	12,471	12,594	12,793	199
Biosimilars (BsUFA)	1,107	461	339	345	6
Animal Drug (ADUFA)	1,184	---	522	725	203
Animal Generic Drug (AGDUFA)	681	---	376	522	146
Tobacco Control Act	13,280	8,800	13,190	12,746	-444
Food And Feed Recall	73	---	73	73	---
Food Reinspection	348	---	348	348	---
Voluntary Qualified Importer Program	290	---	290	290	---
Third Party Auditor Program	77	---	47	47	---
Outsourcing Facility	58	---	58	58	---

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); 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 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. FDA promotes the maximum utilization of Federal workspace and ensures that the appropriate information regarding the space required to support its escalating responsibilities is communicated to the Department for inclusion in the "Reduce the Footprint" Plan that HHS submits to the Office of Management and Budget.

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 13693, Planning for Federal Sustainability in the Next Decade.

Even though FDA replaced some of its geographically disparate facilities with new, state-of-the-art laboratories, office buildings, and support facilities as part of the White Oak Campus consolidation onto the Federal Research Center, FDA's geographic consolidation of its headquarters facilities is still incomplete. FDA is working with GSA to develop a housing strategy and migration plan for FDA headquarters programs and will consider using Federal space on or 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 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. Approximately 70 percent of the GSA rent charges for GSA-owned or GSA-leased space are for headquarters facilities in the Maryland suburbs of Washington, D.C. FDA occupies GSA owned or leased space in approximately262 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. 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.

In FY 2017, FDA:

- received Congressional approval of the Prospectus lease for the relocation of the ORA laboratory in Atlanta, GA
- initiated coordination of the design and construction for the relocation of ORA laboratories near Kansas City, KS, and San Francisco, CA
- relocated two ORA resident posts and one OCI field location
- vacated one office building in Rockville, MD, as part of a headquarters lease consolidation
- leased office space in two locations, both in close proximity to the White Oak Campus, for headquarters programs that cannot be accommodated on Campus until additional Federal construction is funded.

In FY 2018, FDA plans to:

- initiate coordinating the design and construction for the relocation of the ORA laboratory near Atlanta, GA
- continue coordinating the design and construction for the relocation of ORA laboratories near Kansas City, KS, and San Francisco, CA
- relocate five ORA resident posts
- lease two new ORA border stations and one new OCI field office
- vacate two office locations in Rockville, MD, as part of a headquarters lease consolidation
- expand to absorb a training center and office space in an existing leased location in Rockville, MD

- build out office space in close proximity to the White Oak Campus, in a location leased in FY 2017
- complete the build out and occupy office space in close proximity to the White Oak Campus, in a location leased in FY 2017.

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
- operation and maintenance repairs
- 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 support the FDA workforce in meeting its public health mission by providing safe, efficient, reliable, 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 $2.4 million and utility cost savings of

approximately $300 thousand annually at a simple payback of approximately eight years. Construction is underway.

FDA awarded a second UESC contract with Southern California Edison Electric Power Company at Irvine with a capital investment of $4.1 million, utility cost savings of approximately $350 thousand annually, and a simple payback of approximately 12 years. Construction was completed.

FDA has also begun an investment grade audit for our facilities at the Muirkirk Road Campus. We anticipate this study will result in identification of additional energy efficiency projects.

FDA plans to implement the design and construction of ECMs under a UESC for Dauphin Island, AL. It has a capital investment of $458 thousand, utility cost savings of approximately $36 thousand annually, and a simple payback of approximately 12.8 years. Contract awarded and construction is in progress.

GSA is performing audits in FDA-occupied leased facilities, such as the Jamaica 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 13693, Planning for Federal Sustainability in the Next Decade. 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 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 campus and buildings above-standard infrastructure, fit-out, specialized equipment, move costs, and operations and logistics at the Campus.

White Oak funding supports campus operations and requirements including:

- space alteration activities to meet the needs of changing programs
- above-standard campus and building infrastructure design and construction
- 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 10,250 as a result of completing

the occupancy of the Biodefense Laboratory Complex (two office and two lab buildings) in FY 2014 and instituting alternative office strategies, including increased telework.

In FY 2016, FDA provided funding to GSA to develop an FDA Headquarters housing strategy and migration plan to complete FDA's headquarters geographic consolidation, as well as to develop a new master plan for the Federal Research Center. This planning began in earnest in FY 2017 and will continue in FY 2018. It 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.

In FY 2018, 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 2015 Actual	$219,966,000	$168,882,000	$51,084,000
FY 2016 Actual	$220,122,000	$161,683,000	$58,439,000
FY 2017 Actual	$220,653,000	$170,208,000	$50,445,000
FY 2018 Annualized CR	$238,491,000	$169,052,000	$69,439,000
FY 2019 President's Budget	$239,916,000	$168,421,000	$71,495,000

FUNDING HISTORY - OTHER RENT AND RENT-RELATED ACTIVITIES

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2015 Actual	$115,424,000	$72,943,000	$42,481,000
FY 2016 Actual	$119,059,000	$73,484,000	$45,575,000
FY 2017 Actual	$116,653,000	$71,943,000	$44,710,000
FY 2018 Annualized CR	$122,740,000	$71,454,000	$51,286,000
FY 2019 President's Budget	$138,793,000	$86,497,000	$52,296,000

FUNDING HISTORY - WHITE OAK

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2015 Actual	$46,687,000	$43,044,000	$3,643,000
FY 2016 Actual	$48,944,000	$48,044,000	$900,000
FY 2017 Actual	$46,856,000	$43,044,000	$3,812,000
FY 2018 Annualized CR	$46,349,000	$42,752,000	$3,597,000
FY 2019 President's Budget	$57,373,000	$49,430,000	$7,943,000

BUDGET REQUEST

The FY 2019 Total Budget Request is $436,083,000, of which $304,349,000 is budget authority and $131,734,000 is user fees. This level provides a net increase of $28,502,000. Budget authority increases by $21,090,000 compared to the FY 2018 Annualized CR and user fees increase by $7,412,000.

The request will cover rent increases the agency anticipates in FY 2019 that are related to market changes, including new Occupancy Agreements replacing those expiring in FY 2018 and FY 2019 for 80 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, one in FY 2018 and one in the beginning of FY 2019 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 nonstandard 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. Accordingly, the FY 2019 budget request includes funding to address ongoing above GSA standard repairs and improvements and meet program needs, including campus utility infrastructure capacity and reliability improvements, and security infrastructure and the campus safety program.

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
- enhanced productivity and capabilities needed to achieve FDA's expanding public health mission.

GSA Rental Payments

The FY 2019 Budget request for GSA Rental Payments is $239,916,117, of which $168,421,117 is budget authority and $71,495,000 is user fees. The budget authority decreases by -$631,000 compared to the FY 2018 Annualized CR, due to updated rent estimates, and user fees increase by $2,056,000. The GSA-managed properties that provide office and laboratory space for FDA employees are essential facilities. The FY 2019 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 2019 Budget request for Other Rent and Rent Related is $138,793,435, of which $86,497,435 is budget authority and $52,296,000 is user fees. The budget authority increases by $15,043,000 compared to the FY 2018 Annualized CR and user fees increase by $1,010,000. The FY 2019 Budget will allow FDA to operate, maintain, and secure its facilities in an appropriate and sustainable manner to support over 17,000 staff members.

White Oak

The FY 2019 Budget request for White Oak is $57,372,688, of which $49,429,688 is budget authority and $7,943,000 is user fees. The budget authority increases by $6,678,000 compared to the FY 2018 Annualized CR and user fees increase by $4,346,000. The FY 2019 Budget provides the necessary resources for increased above GSA-standard repairs and improvements, and mission support services for the almost 10,250 employees assigned to the White Oak Campus on a daily basis. The FY 2019 Budget request will fund capacity and reliability improvements for the White Oak Campus utility infrastructure, support services, transportation services, labor, and loading dock services, and a centralized safety program.

BUILDINGS AND FACILITIES

(Dollars in Thousands)	FY 2017 Final	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 President's Budget	FY 2019 +/- FY 2018
Buildings and Facilities Program (Budget Authority).....	11,788	9,243	11,708	11,788	80

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. 10-140, 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 laboratory modernization efforts, 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 periodically conducting facility condition assessments 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 of the end of the third quarter of FY 2017, the BMAR for the six FDA-owned sites, including renewals, was approximately $174.6 million. Approximately 72 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, especially laboratories that require modernization.

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 2017 and Planned for FY 2018

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 2017, FDA initiated a project to conduct an investment grade audit to identify potential energy conservation measures that can be taken at the site to reduce energy and water consumption, which may also improve the condition of the buildings. In FY 2018, FDA will replace the roof of and HVAC equipment serving the main lab building.

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 2017, FDA initiated schematic designs for projects to:

- support implementing the JLC master plan
- install a new domestic water well.

In FY 2017, FDA initiated building improvement projects that included:

- replacing the processing area in Building 53B
- replacing the roof of a biological imaging lab containing an MRI machine
- funding construction administration services and change orders for the renovation of three key laboratories – Buildings 14, 53A, and 62
- installing new flooring in a critical biological safety lab
- upgrading building automation panels for Ethernet capabilities and to address vulnerabilities in support of the IT network.

In FY 2018, FDA will complete designs to:

- construct a new chiller plant
- repair site drainage, sewers, roads and sidewalks
- upgrade the sample preparation area of a lab
- replace preheat coils in a lab and animal research building
- replace two backup emergency generators servicing animal research buildings.

FDA will also initiate projects to:

- renovate the site data center
- upgrade water treatment controls in the water treatment building
- replace variable frequency drives on the HVAC system for the main administration building.

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 2017, FDA initiated a project to renovate the security entrance associated with a main laboratory building to enhance access control.

In FY 2018, FDA will initiate projects to:

- install a shelter for storage of landscaping equipment and supplies
- install epoxy flooring and emergency eyewash stations in several animal research buildings
- replace windows in the main lab building
- replace an emergency generator for a large animal quarantine building
- renovate the breakroom and kitchenette to support lab operations in a main lab 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 2017, FDA initiated projects to:

- design HVAC and controls upgrades
- conduct a geotechnical study to stabilize the driveway and slope damage to the parking area associated with an adjacent landfill
- recommission the HVAC system
- install a new compressor for increased capacity to support changing science and building demands.

In FY 2018, FDA will initiate several projects to support modernization of the lab, including:

- renovating the sample preparation and sample custodian rooms
- replacing and expanding the house nitrogen system
- renovating excess cold storage space to relocate media preparation for the microbiology operations
- renovating the vacated media preparation space into a new microbiology lab
- renovating three lab rooms to enlarge them and improve safety.

In addition, FDA will initiate a project to repair the damaged driveway and parking lot caused by ongoing settlement at the site as a temporary solution to maintain safety and operations until plans and funding are in place for a larger project that will permanently solve the problem.

San Juan District Office and the National Drug Servicing Laboratory – San Juan, PR

The National Drug Servicing Laboratory specializes in pharmaceutical analysis.

In FY 2017, FDA initiated a project to design, replace and upgrade the electrical distribution wiring system and vacuum system in the main lab building. In FY 2018, FDA will replace the air handling unit on the main lab building with a specialized unit for the harsh salt air environment, replace ductwork, and rebalance the HVAC system. Also, in FY 2018, due to damage caused by Hurricane Maria, FDA initiated a project to make necessary emergency repairs and added another generator.

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 2017 FDA initiated a project to relocate on-site hazardous materials storage units in preparation for the lab replacement project. In FY 2018, FDA will:

- utilize funding, as needed, to provide construction administration and additional support for the laboratory replacement project, including a project to demolish six (6) small out buildings that are located within the footprint of the replacement building.

FUNDING HISTORY

Fiscal Year	Program Level	Budget Authority	User Fees
FY 2015 Actual	$8,997,000	$8,997,000	---
FY 2016 Actual	---	---	---
FY 2017 Actual	$9,243,000	$9,243,000	---
FY 2018 Annualized CR	$11,708,000	$11,708,000	---
FY 2019 President's Budget	$11,788,000	$11,788,000	---

BUDGET REQUEST

The FY 2019 Budget Request is $11,788,000, consisting solely of budget authority. This amount is an increase of $80,000 compared to the FY 2018 Annualized CR. The funding level requested attempts to sustain the current condition of FDA's owned buildings at its six mission-critical sites and will support funding the projects noted below.

At the Gulf Coast Seafood Laboratory facility, FDA will:

- repair concrete floor and replace all floor tiles in lab building corridors and lab rooms
- make repairs and re-pave the main road and parking area for the site.

At the Jefferson Labs Complex, FDA will:

- replace HVAC system serving a lab
- update chemical fume hood controls for safety and energy savings
- design a renovation for the biosafety level 3 lab in the Campus bioimaging lab building
- install new electric service and standby generation for the Campus bioimaging lab building
- repair roofs on various buildings
- install meters for tracking energy consumption in various lab buildings
- install a new domestic water well.

At the Muirkirk Road Complex, FDA will:

- renovate restrooms in the animal research area of a primary lab building
- renovate aged floor, wall, and ceiling finishes in a portion of a primary lab building
- renovate offices in a primary lab building to accommodate additional lab staff
- renovate the aged atrium of a primary lab building to alleviate safety hazards and support needs for meeting space for lab program.

In the Pacific Regional Laboratory Southwest, FDA will:

- renovate lab space by converting storage rooms into a smaller freezer room, segregated storage and sample custodian room with security access, and repurposing freezer room into storage and work areas
- add automatic door opening devices to improve accessibility in the building
- repair, in phases, the HVAC and building automation systems
- design reconfiguration of sample preparation rooms that support lab operations.

In the San Juan District Office and Laboratory, FDA will:

- replace an air conditioning unit with a specialized unit designed for harsh (salt air) environments
- construct a new roadway to the generator house for improved access
- repave and restripe parking lot.

At the Winchester Engineering & Analytical Center, FDA will:

- support the ongoing operation and repair needs 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 2019 funds.

FY 2019 BUILDINGS AND FACILITIES ALLOCATION PLAN

Site	Total
CFSAN Gulf Coast Seafood Laboratory	$300,000
Jefferson Laboratories Complex (NCTR & ARL) – Jefferson, AR	$5,894,000
Muirkirk Road Complex (MOD1, MOD2, BRF) – Laurel, MD	$1,649,000
ORA Pacific Regional Laboratory SW – Irvine, CA	$2,945,000
San Juan District Office and Laboratory – San Juan, PR	$900,000
Winchester Engineering and Analytical Center – Winchester, MA	$100,000
B&F Project Total	**$ 11,788,000**

In FY 2019, 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 2019 will help reduce Scope 1, 2, and 3 greenhouse gas emissions[105] by:

- replacing or repairing aged, inefficient HVAC controls and equipment
- replacing aged, inefficient roofs
- installing water, steam and gas meters.

[105] More information can be found in the HHS Strategic Sustainability Performance Plan at: http://www.hhs.gov/sites/default/files/about/sustainability/2014-sustainability-plan.pdf.

Facility	Average FCI Score		
	FY 2017 Actual	FY 2018 Annualized CR	FY 2019 Request
CFSAN Gulf Coast Seafood Laboratory[1]	88	88	89
Jefferson Laboratories Complex[2]	67	68	69
Muirkirk Road Complex[3]	63	63	64
ORA Pacific Regional Laboratory Southwest[4]	97	97	98
San Juan District Office and Laboratory[5]	75	75	75
Winchester Engineering And Analytic Center[6]	65	65	65

[*] The Backlog of Maintenance and Repairs (BMAR) at each site is significant. 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.

[1] Based on funding levels in FY 2018 and FY 2019, the BMAR for this site will decrease by $39K. Remaining BMAR for this site is approximately $531K

[2] Based on funding levels in FY 2018 and FY 2019 the BMAR for this site will decrease by approximately $12.1M. Remaining BMAR total will be approximately $115.5M

[3] Based on funding levels in FY 2018 and FY 2019 the BMAR for this site will decrease by approximately $1M. Remaining BMAR total will be approximately $35M.

[4] Based on funding levels in FY 2018 and FY 2019, the BMAR for this site will decrease by approximately $500K. Remaining BMAR for this site is approximately $800K.

[5] Based on funding levels in FY 2018 and FY 2019 the BMAR for this site will decrease by approximately $129K. Remaining BMAR total will be approximately $3.7M.

[6] Based on funding levels in FY 2018 and FY 2019, the BMAR for this site will not decrease. Remaining BMAR total will be approximately $5.3M.

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SUPPLEMENTARY TABLES

OBJECT CLASSIFICATION TABLES

BUDGET AUTHORITY

(Dollars in Thousands)	FY 2017 Actuals	FY 2018 Annualized CR	FY 2019 President's Budget
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	941,524	950,992	968,181
Other than full-time permanent (11.3)	89,540	90,440	92,075
Other personnel compensation (11.5)	46,341	46,807	47,653
Military personnel (11.7)	62,809	63,939	65,570
Special personnel services payments (11.8)	761	769	783
Subtotal, Personnel Compensation	**1,140,974**	**1,152,947**	**1,174,262**
Benefits:			
Civilian benefits (12.1)	350,721	354,247	360,650
Military benefits (12.2)	31,911	32,485	33,314
Benefits to former personnel (13.0)	384	384	384
Subtotal, Benefits	**383,015**	**387,116**	**394,348**
Total Personnel Compensation and Benefits	**1,523,990**	**1,540,063**	**1,568,610**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	48,708	47,925	67,834
Transportation of things (22.0)	3,069	3,020	4,275
Rental payments to GSA (23.1)	170,208	169,052	168,421
Rent payments to others (23.2)	2,593	2,551	3,611
Communication, utilities, and misc. charges (23.3)	22,486	22,125	31,316
Printing and reproduction (24.0)	1,873	1,843	2,609
Subtotal, Contractual Services	**248,938**	**246,516**	**278,066**
Other Contractual Services:			
Consulting services (25.1)	52,376	51,533	72,941
Other services (25.2)	361,325	355,514	503,201
Purchase of goods and svcs from Govt Acts. (25.3)	140,364	138,108	195,480
Operation and maintenance of facilities (25.4)	85,144	83,774	118,576
Research and Development Contracts (25.5)	19,347	19,036	26,944
Operation and maintenance of equipment (25.7)	99,791	98,186	138,974
Subsistence and support of persons (25.8)		---	---
Subtotal, Other Contractual Services	**758,346**	**746,151**	**1,056,116**
Supplies and Materials:			
Supplies and materials (26.0)	50,402	49,591	70,192
Equipment (31.0)	36,635	36,046	51,020
Land and Structures (32.0)	2,941	2,893	4,095
Grants, subsidies, and contributions (41.0)	160,431	157,851	223,426
Insurance claims and indemnities (42.0)	1,538	1,513	2,142
Interest and dividends , Refunds (43.0, 44.0)	30	29	41
Receivables-collected (61.7)	---	---	---
Subtotal, Supplies and Materials	**251,977**	**247,923**	**350,916**
Total Contractual Services and Supplies	**1,259,261**	**1,240,590**	**1,685,098**
Total Budget Authority by Object Class	**2,783,250**	**2,780,653**	**3,253,708**

*For FY 2017 and 2018, the 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 2019, FDA proposes to discontinue the transfer.

USER FEE

(Dollars in Thousands)	FY 2017 Actuals	FY 2018 Annualized CR	FY 2019 President's Budget
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	594,275	662,731	681,410
Other than full-time permanent (11.3)	88,227	98,390	101,163
Other personnel compensation (11.5)	69,135	77,099	79,272
Military personnel (11.7)	47,957	48,820	50,065
Special personnel services payments (11.8)	198	220	227
Subtotal, Personnel Compensation	**799,791**	**887,260**	**912,137**
Benefits:			
Civilian benefits (12.1)	232,790	259,606	266,923
Military benefits (12.2)	24,964	25,413	26,061
Benefits to former personnel (13.0)	16	16	16
Subtotal, Benefits	**257,770**	**285,035**	**293,000**
Total Personnel Compensation and Benefits	**1,057,561**	**1,172,295**	**1,205,137**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	20,542	18,859	21,484
Transportation of things (22.0)	929	853	972
Rental payments to GSA (23.1)	51,156	69,439	71,495
Rent payments to others (23.2)	917	842	959
Communication, utilities, and misc. charges (23.3)	9,027	8,287	9,441
Printing and reproduction (24.0)	845	776	884
Subtotal, Contractual Services	**83,417**	**99,056**	**105,235**
Other Contractual Services:			
Consulting services (25.1)	52,161	47,886	54,553
Other services (25.2)	590,489	542,091	617,566
Purchase of goods and svcs from Govt Acts. (25.3)	274,077	251,612	286,644
Operation and maintenance of facilities (25.4)	17,707	16,256	18,519
Research and Development Contracts (25.5)	39,370	36,143	41,175
Operation and maintenance of equipment (25.7)	53,254	48,889	55,696
Subsistence and support of persons (25.8)			
Subtotal, Other Contractual Services	**1,027,058**	**942,877**	**1,074,153**
Supplies and Materials:			
Supplies and materials (26.0)	23,424	21,504	24,498
Equipment (31.0)	19,434	17,841	20,325
Land and Structures (32.0)	---	---	---
Grants, subsidies, and contributions (41.0)	109,859	100,855	114,896
Insurance claims and indemnities (42.0)		---	---
Interest and dividends , Refunds (43.0, 44.0)	20	18	21
Receivables-collected (61.7)	556	511	582
Subtotal, Supplies and Materials	**153,293**	**140,729**	**160,322**
Total Contractual Services and Supplies	**1,263,769**	**1,182,662**	**1,339,710**
Total Reimbursable by Object Class	**2,321,330**	**2,354,957**	**2,544,847**

TOTAL PROGRAM

(Dollars in Thousands)	FY 2017 Actuals	FY 2018 Annualized CR	FY 2019 President's Budget
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	1,535,798	1,613,723	1,649,591
Other than full-time permanent (11.3)	177,767	188,830	193,238
Other personnel compensation (11.5)	115,476	123,906	126,925
Military personnel (11.7)	110,766	112,759	115,635
Special personnel services payments (11.8)	959	989	1,010
Subtotal, Personnel Compensation	**1,940,765**	**2,040,207**	**2,086,399**
Benefits:			
Civilian benefits (12.1)	583,511	613,853	627,573
Military benefits (12.2)	56,875	57,898	59,375
Benefits to former personnel (13.0)	400	400	400
Subtotal, Benefits	**640,786**	**672,151**	**687,348**
Total Personnel Compensation and Benefits	**2,581,551**	**2,712,358**	**2,773,747**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	69,251	66,784	89,318
Transportation of things (22.0)	3,999	3,873	5,247
Rental payments to GSA (23.1)	221,364	238,491	239,916
Rent payments to others (23.2)	3,509	3,393	4,570
Communication, utilities, and misc. charges (23.3)	31,514	30,412	40,757
Printing and reproduction (24.0)	2,719	2,619	3,493
Subtotal, Contractual Services	**332,355**	**345,572**	**383,301**
Other Contractual Services:			
Consulting services (25.1)	104,537	99,419	127,494
Other services (25.2)	951,814	897,605	1,120,767
Purchase of goods and svcs from Govt Acts. (25.3)	414,441	389,720	482,124
Operation and maintenance of facilities (25.4)	102,851	100,030	137,095
Research and Development Contracts (25.5)	58,717	55,179	68,119
Operation and maintenance of equipment (25.7)	153,045	147,075	194,670
Subsistence and support of persons (25.8)	---	---	---
Subtotal, Other Contractual Services	**1,785,404**	**1,689,028**	**2,130,269**
Supplies and Materials:			
Supplies and materials (26.0)	73,826	71,095	94,690
Equipment (31.0)	56,069	53,887	71,345
Land and Structures (32.0)	2,941	2,893	4,095
Grants, subsidies, and contributions (41.0)	270,290	258,706	338,322
Insurance claims and indemnities (42.0)	1,538	1,513	2,142
Interest and dividends , Refunds (43.0, 44.0)	50	47	62
Receivables-collected (61.7)	556	511	582
Subtotal, Supplies and Materials	**405,270**	**388,652**	**511,238**
Total Contractual Services and Supplies	**2,523,030**	**2,423,252**	**3,024,808**
Total Program Level by Object Class	**5,104,580**	**5,135,610**	**5,798,555**

*For FY 2017 and 2018, the 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 2019, FDA proposes to discontinue the transfer.

SALARY AND EXPENSES

(Dollars in Thousands)	FY 2017 Actuals	FY 2018 Annualized CR	FY 2019 President's Budget
Personnel Compensation and Benefits:			
Personnel Compensation:			
Full-time permanent (11.1)	941,524	950,992	968,181
Other than full-time permanent (11.3)	89,540	90,440	92,075
Other personnel compensation (11.5)	46,341	46,807	47,653
Military personnel (11.7)	62,809	63,939	65,570
Special personnel services payments (11.8)	761	769	783
Subtotal, Personnel Compensation	**1,140,974**	**1,152,947**	**1,174,262**
Benefits:			
Civilian benefits (12.1)	350,721	354,247	360,650
Military benefits (12.2)	31,911	32,485	33,314
Benefits to former personnel (13.0)	384	384	384
Subtotal, Benefits	**383,015**	**387,116**	**394,348**
Total Personnel Compensation and Benefits	**1,523,990**	**1,540,063**	**1,568,610**
Contractual Services and Supplies			
Contractual Services:			
Travel and transportation of persons (21.0)	48,708	47,925	67,834
Transportation of things (22.0)	3,069	3,020	4,275
Rent payments to others (23.2)	2,593	2,551	3,611
Communication, utilities, and misc. charges (23.3)	22,486	22,125	31,316
Printing and reproduction (24.0)	1,873	1,843	2,609
Subtotal, Contractual Services	**78,730**	**77,464**	**109,645**
Other Contractual Services:			
Consulting services (25.1)	52,376	51,533	72,941
Other services (25.2)	361,325	355,514	503,201
Purchase of goods and svcs from Govt Acts. (25.3)	140,364	138,108	195,480
Operation and maintenance of facilities (25.4)	85,144	83,774	118,576
Research and Development Contracts (25.5)	19,347	19,036	26,944
Operation and maintenance of equipment (25.7)	99,791	98,186	138,974
Supplies and materials (26.0)	50,402	49,591	70,192
Total Contractual Services and Supplies	**875,283**	**873,206**	**1,235,953**
Rental payments to GSA (23.1)	**170,208**	**169,052**	**168,421**
Grand Total, Salaries and Expense and Rent	**2,583,477**	**2,582,321**	**2,972,984**
Direct FTE	**10,461**	**10,417**	**10,546**

*For FY 2017 and 2018, the 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 2019, FDA proposes to discontinue the transfer.

DETAIL OF FULL-TIME EQUIVALENTS

	FY 2017 Actual			FY 2018 Estimate			FY 2019 Estimate		
	Civilian	Military	Total	Civilian	Military	Total	Civilian	Military	Total
Center for Food Safety and Applied Nutrition	1,049	39	1,088	1,042	39	1,081	1,042	39	1,081
Center for Drug Evaluation and Research	4,498	491	4,989	4,795	491	5,286	4,831	491	5,322
Center for Biologics Evaluation and Research	1,118	59	1,177	1,076	59	1,135	1,084	59	1,143
Center for Veterinary Medicine	602	13	615	613	13	626	697	13	710
Center for Devices and Radiological Health	1,600	82	1,682	1,781	82	1,863	1,803	82	1,885
National Center for Toxicological Research	314	---	314	314	---	314	314	---	314
Office of Regulatory Affairs	4,655	346	5,001	4,734	346	5,080	4,751	346	5,097
Headquarters and Office of the Commissioner	1,127	68	1,195	1,200	68	1,268	1,230	68	1,298
Export Certification	24	---	24	26	---	26	26	---	26
Color Certification	40	---	40	37	---	37	37	---	37
Family Smoking Prevention and Tobacco Control Act	814	29	843	814	29	843	903	29	932
Priority Review Vouchers (PRV) Pediatric Disease	24	---	24	---	---	---	---	---	---
MCMi - No Year	4	---	4	---	---	---	---	---	---
21st Century Cures (BA Only)	26	---	26	26	---	26	26	---	26
Total	**15,895**	**1,127**	**17,022**	**16,458**	**1,127**	**17,585**	**16,744**	**1,127**	**17,871**

Five Year History of GS/GM Average Grade

Year	Grade
FY 2015	13
FY 2016	13
FY 2017	13
FY 2018	13
FY 2019	13

* FTE figures do not include an estimated 79 reimbursable, 2 CRADA, 2 FOIA, 26 PEPFAR and 3 Zika.

DETAIL OF POSITIONS

	FY 2017 Actuals	FY 2018 Annualized CR	FY 2019 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**
Total - Exec. Level Salaries[3]	**$155,500**	**$158,532**	**$159,285**
Executive Service (ES)			
Executive Service	65	67	68
Total Executive Service	**65**	**67**	**68**
Total - ES Salary	**$11,719,060**	**$12,315,184**	**$12,558,363**
General Schedule (GS)			
GS-15	1,305	1,351	1,375
GS-14	3,440	3,562	3,624
GS-13	4,955	5,131	5,221
GS-12	2,142	2,219	2,258
GS-11	802	831	846
GS-10	11	11	11
GS-9	575	595	606
GS-8	94	97	99
GS-7	360	372	379
GS-6	64	66	67
GS-5	68	71	72
GS-4	47	49	49
GS-3	21	21	22
GS-2	6	6	6
GS-1	2	2	2
Total General Schedule	**13,892**	**14,384**	**14,637**
Total - GS Salary	**$1,489,361,320**	**$1,572,179,758**	**$1,607,432,015**
Scientific/Senior Level (ST/SL)	4	4	4
Senior Biomedical Research Service (RS)	47	49	49
Scientific Staff Fellows (RG) (Title 42)	932	965	981
Distinguished Consultants/Senior Science Managers (RF) (Title 42)	156	161	164
Former Performance Mgmt Recognition System Employees (GM)	2	2	2
Physicians and Dentists - (GP) (Title 38)	762	789	802
Commissioned Corps (CC):			
Commissioned Corps - 08/07/06	282	282	282
Commissioned Corps - Other	845	845	845
Total Commissioned Corps	**1,127**	**1,127**	**1,127**
Wage Grade	15	16	16
Consultants[2]	19	20	20
Total FTE (End of Year)[1]	**17,022**	**17,585**	**17,871**
Average ES Level	3	3	3
Average ES Salary	$180,293	$183,809	$184,682
Average GS grade	13	13	13
Average GS Salary	$107,210	$109,301	$109,820
Average GM Salary	$150,928	$153,871	$154,602
Average GP Salary	$213,804	$217,973	$219,009

[1] Does not include an estimated 79 reimbursable, 2 CRADA, 2 FOIA, 26 PEPFAR and 3 Zika FTE.
[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.
[3] On a prorated basis, the FDA Commissioner's actual executive level salary for FY 2017 was approximately $61,000 in accordance with his start date of May 11, 2017.

SIGNIFICANT ITEMS

HOUSE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

HOUSE COMMITTEE REPORT (115-232)

1. Animal Drug Compounding

The Committee has been concerned that the FDA's proposed draft Guidance for Industry (GFI) for animal drug compounding (#230) would apply certain human drug compounding requirements to animal drug compounding. There also is concern that some state regulatory agencies are implementing the guidance even though it is not finalized. The Committee appreciates that in the FY 2018 budget request FDA stated, ''In the draft guidance, FDA is not proposing to apply sections 503A or 503B of the FDCA to the compounding of animal drugs from bulk drug substances.'' FDA further explains how some of the concepts may be appropriate for animal drugs as well as human drugs. Within 30 days of enactment of this Act, the Committee directs FDA to communicate to state regulatory agencies that the guidance is still in draft form. The Committee expects that any final guidance on animal drug compounding will only reference statutory provisions that specifically relate to veterinary practices and will not exceed statutory authority.

FDA Response:

FDA withdrew Guidance for Industry #230, "Compounding Animal Drugs from Bulk Substances," on November 7, 2017, after listening to stakeholders and considering more than 150 public comments. FDA is drafting a new proposed guidance that will be focused on the veterinary medical needs of the multiple animal species within a veterinary-client-patient relationship.

2. 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 has a multi-phase communication plan for communicating with stakeholders about biosimilars. This includes conducting extensive stakeholder outreach for each biosimilar guidance released and for biosimilar approvals.

Initially, FDA conducted surveys, focus groups, and interviews with clinicians to learn about their perceptions of biosimilar and interchangeable products, and potential information gaps. The information gained from this research was used to inform education and outreach materials for health care professionals.

FDA released a continuing education (CE) course in February 2016 titled "FDA Overview of Biosimilar Products." This CE course provides an understanding of biological products and biosimilar products and a description of FDA's general approach to the development and approval of biosimilar products. The target audience for this course is healthcare professionals, including physicians, physician assistants, nurses, nurse practitioners, and pharmacists. As of

October 2017, 1,149 health care professionals have taken the course for CE credit and 1,275 have taken the course without CE credit for a total of 2,424 students.

On October 23, 2017, FDA released new educational materials for health care professionals about biosimilar and interchangeable products and updated the FDA Biosimilars website (www.fda.gov/biosimilars).

The agency developed these educational materials to help increase understanding about biosimilar and interchangeable products among health care professionals. The materials include four fact sheets and graphics for health care professionals that:

- Define relevant terms such as: biological product, reference product, biosimilar, interchangeable; and other terms to facilitate understanding the relationship between biosimilars and their reference products;
- Describe the rigorous standards any biosimilar must meet prior to approval and explain how the FDA approval pathway works for these products;
- Contain details about the data and information FDA reviews to determine biosimilarity, and how to find more information; and
- Provide information about prescribing biosimilar and interchangeable products.

FDA has also developed tools to help professional societies and stakeholder organizations share information about biosimilars with their colleagues and members. The outreach strategy includes working with professional societies and other organizations to reach health care professionals who work in key clinical areas that use biologics to treat diseases and conditions (such as Dermatologists, Gastroenterologists, Hematologists, Nephrologists, Oncologists, and Rheumatologists). FDA also placed advertisements in health care provider journals and on targeted web sites for health care providers, and released an updated Consumer Update on biosimilars.

FDA plans to release additional communication materials to educate health care professionals, including a video series that discusses key concepts about biosimilar products and their benefits, as well as other graphics and editorial products for stakeholders. FDA has also released articles on labeling and interchangeability, and held stakeholder calls about naming of biosimilar and interchangeable products.

FDA is working on conducting additional research to learn about health care professionals' experiences communicating with their patients about biological products (including biosimilars), what they think their patients will need to know about them, and what information and materials prescribers think they will need to explain these drugs to patients. FDA will also collect information from patients who have taken biologic medicines to obtain general feedback from them about various aspects of biosimilar and biological products.

FDA regularly presents at conferences and participates in meetings to provide information about biosimilar and interchangeable products to multiple audiences (industry, health care providers, patient and consumer groups, etc.). Moving forward, FDA will continue to implement other phases of its biosimilars communication plan to increase health care provider and consumer confidence in biosimilar products.

3. Dairy Labeling Requirements

The Committee is aware of the concerns with labeling certain foods and beverages as a dairy product when the product is plant-based rather than derived from animals. The Committee directs the FDA to develop a standard of identity for dairy products based upon the dairy product terms described in parts 131, 133, and 135 of subchapter B of chapter I of title 21, Code of Federal Regulations within 180 days from the date of enactment of this Act. The FDA should issue guidance to industry on how to implement the standard of identity, including how this standard will be enforced.

FDA Response:

The FDA understands the concern about food products marketed using the names of standardized dairy foods, such as "milk," when the products do not meet the relevant standard(s) of identity for those foods. FDA's approach to these issues seeks to be one that is science-based, relies on FDA's statutory authorities, and keeps the interest of consumers foremost in mind. The agency will take this request into consideration as it reviews the existing standard of identity regulations – including the standards for many individual dairy products contained in parts 131, 133, and 135 of Title 21 of the Code of Federal Regulations – as part of the agency's regulatory reform agenda. As part of this agenda, on September 8, 2017, the FDA published a request for comments on ways the agency can change its regulations to achieve meaningful burden reduction while continuing to achieve its public health mission. The comment period was originally scheduled to close on December 7, 2017; however, at the request of stakeholders, the agency has extended the comment period to February 5, 2018. Further, the FDA is currently reviewing a petition requesting a common or usual name for "soymilk," and a final decision has not been made on the petition.

4. Feminine Hygiene Cosmetics

The Committee is concerned about the use of unsafe colorants by manufacturers of feminine hygiene cosmetic products. The Committee strongly encourages the FDA to issue appropriate guidance on the use of colorants in such products, and expects a prompt final response to the citizen petition submitted by Women's Voices for the Earth on August 18, 2015.

FDA Response:

FDA is actively working on reviewing and responding to the citizen petition submitted by Women's Voices for the Earth, which requests that FDA issue guidance on the appropriate use of colorants in feminine hygiene cosmetic products.

5. Grape Varietals

The Committee is aware that the FDA has excluded certain produce that is rarely consumed raw from having to comply with the FSMA Produce Safety Final Rule entitled ''Standards for Growing, Harvesting, Packing, and Holding of Produce for Human Consumption.'' There is concern that the FDA has not been able to distinguish between grape varietals that are consumed raw and those that are grown, harvested and used for wine and further processing. The Committee directs the FDA to initiate a process within 30 days of enactment of this Act that makes a distinction between grape varietals so that wine grape varietals may be included on the list of produce that is rarely consumed raw.

FDA Response:

The characterization of fruits and vegetables as "rarely consumed raw" in the Food Safety Modernization Act (FSMA) Produce Safety Final Rule was based on consumption patterns reported in the National Health and Nutrition Examination Survey[106], which is the most comprehensive and robust, nationally-representative dataset currently available on dietary intake in the U.S. The reported consumption of uncooked wine grapes – by 18.6 percent of consumers and on 1.9 percent of eating occasions in two days of dietary intake data, and by 11.4 percent of consumers and on 1.5 percent of eating occasions in a single day of dietary intake data – was high enough to exclude them from the rarely consumed raw list (and, therefore, wine grapes are covered produce subject to the rule). Furthermore, according to the National Grape Registry, some grapes used to make wine can be used for other purposes as well. For example, the Malaysia Bianca grape cultivar can be used as wine grapes and table grapes, and the Muscat of Alexandria grape cultivar can be used to make wine or raisins or as table grapes. For these reasons, FDA concluded that ''wine grapes'' are not rarely consumed raw.

In the FSMA Produce Safety Final Rule, FDA stated that it did not have information on the specific grape cultivars or varieties that are solely and exclusively grown for use in winemaking that would allow the agency to establish a category covering only ''wine grapes'' and evaluate their eligibility for the rarely consumed raw list, using currently available dietary consumption data. FDA also indicated its intent to consider updating the list of rarely consumed raw commodities in the future, as appropriate. FDA encourages interested stakeholders to identify or submit data that are sufficiently robust and representative to allow FDA to draw scientifically-valid conclusions that the criteria are met for including the commodities on the rarely consumed raw list. The criteria for inclusion are that the commodity is consumed raw by less than 0.1 percent of population; is consumed raw on less than 0.1 percent of eating occasions; and that consumption in any form – raw, processed, or other – was reported by at least one percent of a weighted number of survey respondents. FDA has discussed this with interested stakeholders that have contacted FDA about adding wine grapes to the list of rarely consumed raw commodities.

Although grapes used in the production of wine currently are not considered "rarely consumed raw," grapes used to produce wine are eligible for an exemption provided certain documentation requirements are met. FDA determined that winemaking adequately reduces the presence of microorganisms of public health significance and, therefore, added "wine" to the list of examples of products of commercial processing. FDA has extended the compliance dates for some of the documentation needed to qualify for the commercial processing exemption while the agency considers the best approach to address feasibility concerns – see 81 FR 57784, August 24, 2016. FDA remains committed to working with the food industry throughout FSMA implementation to ensure that requirements are as practical as possible while still protecting public health.

6. Human Drug Compounding—Compound Pharmacist on Pharmacy Compounding Advisory Committee

The Committee is concerned that the Pharmacy Compounding Advisory Committee (PCAC) established under the DQSA does not adequately represent the interests and needs of providers

[106] Available at: https://www.cdc.gov/nchs/nhanes/index.htm

and patients who use and depend on compounded medications. The Committee expects that, at the earliest possible date, whether filling open positions or replacing existing members, the FDA shall appoint voting members with recent, actual, and diverse experience in the preparation, prescribing, and use of compounded medications.

FDA Response:

FDA appreciates the Committee's concern regarding the membership of the Pharmacy Compounding Advisory Committee (PCAC), and is committed to ensuring the membership continues to conform to the parameters set by statute.

In terms of current PCAC membership, seven committee members are pharmacists and five committee members are physicians. Twelve committee members have experience related to drug compounding, including experience in the preparation, prescribing, and use of compounded medications, as well as compounding-related research activities.

The committee consists of a core of up to twelve voting members including the Chairperson, which are selected by the Commissioner or designee from among authorities knowledgeable in the fields of pharmaceutical compounding, pharmaceutical manufacturing, pharmacy, medicine, and related specialties.

In accordance with sections 503A and 503B of the FDCA, one member is a representative from the United States Pharmacopeia (USP), a nonprofit organization that sets standards for the identity, strength, quality, and purity of medicines manufactured, distributed, and consumed worldwide, and one member is a representative from the National Association of Boards of Pharmacy (NABP), a professional organization that supports the state boards of pharmacy in protecting public health.

Industry participated in the selection of two additional committee members—one from the pharmaceutical manufacturing industry and one from the compounding industry. Additionally, a consortium of consumer advocacy representatives participated in the selection of a consumer representative.

More than 100 names were submitted to the agency in response to the January 13, 2014 Federal Register Notices requesting nominations. In addition, FDA identified qualified candidates from its own pool of special government employees. The selection process of candidates that were not designated representatives of certain groups included evaluation for conflicts of interest (as required by 21 CFR 14.80) and for the relevancy of their qualifications for the purpose of the committee.

In general, members are invited to serve for overlapping terms of up to four years. The agency will consider future nominations for membership and strive to select members with robust and relevant experience and expertise related to drug compounding.

7. 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 maintains its position that FDA should 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. FDA agrees that proposed changes in policy require feedback from the affected community; to that end FDA has held multiple public meetings, opened public dockets, had numerous meetings with stakeholders and visited several laboratories. FDA would welcome the opportunity to work with Members of Congress and continue to work with stakeholders on any legislative proposals on this topic.

8. Menu Labeling

The FDA extended the compliance date for menu labeling requirements until May 7, 2018, stating that, ''This extension allows for further consideration of what opportunities there may be to reduce costs and enhance the flexibility of these requirements beyond those reflected in the final rule.'' In providing flexibility, the Committee urges FDA to consider provisions of H.R. 772 as well as other proposals that reduce burden and add flexibility for businesses to implement the rule and provide consumers with certain nutrition information. FDA should ensure that businesses are protected from regulatory enforcement from federal, state, municipal or other oversight agencies until after a potential revised rule is promulgated and effective.

FDA Response:

"FDA takes seriously the authority Congress granted the agency in overseeing federal food labeling standards, including the mandate to make calorie information available on menus. FDA is committed to making sure the agency implements these provisions in a way that is practical, efficient, and sustainable. Earlier this year, FDA solicited another round of feedback on ways to increase the flexibility and decrease the regulatory burden of the regulation. On November 7, 2017, FDA released the draft guidance "Menu Labeling: Supplemental Guidance for Industry."[107] It addresses comments the agency received on the May 2017 interim final rule extending the compliance date for the menu labeling final rule from May 5, 2017 to May 7, 2018.

The question-and-answer style draft guidance features approximately 20 different graphics to illustrate the agency's new and expanded interpretations of the menu labeling provisions and practical ways for industry to comply with these provisions. It addresses concerns some stakeholders have raised including calorie disclosure for self-service foods, such as buffets and grab-and-go foods; accounting for the natural variation of foods; compliance and enforcement of the rule; criteria for covered establishments; determining standard menu items; criteria for distinguishing between menus and other information presented to the consumer, like marketing materials; and various methods for providing calorie disclosure information on foods such as pizza.

[107] https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm583487.htm

The menu labeling final rule[108] when applied to marketing materials, is intended to be flexible and not prescriptive. As an example, the draft guidance explains that marketing materials such as pizza coupons, posters in store windows, signs on gas pumps, or paper inserts, generally would not be considered a menu or menu board and would not require calorie declarations. The agency is withdrawing two questions from the April 2016 menu labeling guidance[109] that pertained to marketing materials.

The agency will accept comments on this draft guidance from November 9, 2017, to January 8, 2018, after which it will move to finalize it to ensure industry has adequate time to implement the requirements. Consumers can expect to see menu labeling in covered establishments nationwide by May 7, 2018.

9. 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 Colors and Cosmetics (OCAC). Funding provided for OCAC is for direct support of the operation, staffing, compliance, research and international activities performed by this office. The Committee welcomes FDA's support of the Cosmetic Ingredient Review and FDA's participation in that program as an ex officio member, as well as the FDA efforts in maintaining the Voluntary Cosmetic Reporting Program and the CFSAN Adverse Event Reporting System (CAERS). The Committee appreciated OCAC's willingness to engage with China in May 2016 for a cosmetics regulatory dialogue. In light of China's interaction with U.S.-based manufacturers and consumers, the Committee directs FDA to seek ways to continually enhance engagement with Chinese regulators on cosmetic technical and regulatory issues. The Committee directs FDA to promote international regulatory harmonization in cosmetic products by continued support to the International Cooperation on Cosmetics Regulation (ICCR) initiative, participation in ISO Technical Committee 217—Cosmetics and supporting trade through other bilateral and multilateral trade agreements.

FDA Response:

FDA will use funding for direct support of operations, staffing, compliance, research, and international activities. FDA continues to support and maintain the Voluntary Cosmetic Reporting Program (VCRP) and recently modified VCRP forms to make them easier to use. FDA relies on its Center for Food Safety and Applied Nutrition Adverse Event Reporting System and VCRP data to help in priority setting for activities relating to cosmetic safety and public health. Additionally, FDA continues to attend the Cosmetic Ingredient Review Expert Panel meetings as a non-voting member.

Internationally, FDA has continued to support trade negotiations and cosmetic cooperation efforts through participation in the International Cooperation on Cosmetics Regulation and its various work groups and has offered technical assistance and opinion to the U.S. Technical Advisory Group to the International Standards Organization Technical Committee 217. Further, FDA continues to support negotiation and bilateral discussions with other countries, such as China and Brazil, and has engaged in U.S.-China Joint Commission on Commerce and Trade activities involving China Food and Drug Administration and General Administration of Quality

[108] https://www.federalregister.gov/documents/2014/12/01/2014-27833/food-labeling-nutrition-labeling-of-standard-menu-items-in-restaurants-and-similar-retail-food

[109] https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm461934.htm

Supervision, Inspection, and Quarantine activities. FDA will continue to identify opportunities to further these goals by providing technical assistance in support of the U.S. government's international trade negotiations.

10. Oncology Clinical Trials

The Committee recognizes the value of clinical trials in the development of innovative procedures, diagnostics, and drugs to prevent, detect, and treat cancer. The Committee understands that the percentage of cancer patients who participate in oncology clinical trials remains low, especially among minorities and those socioeconomically disadvantaged, and barriers to participation include ancillary financial costs, such as travel and lodging expenses. Many clinical sites and sponsors of clinical trials are wary of working with independent third parties to provide even ancillary financial support given current guidance warning against anticipated financial benefits that may create ''coercion or undue influence'' to research participants under 21 CFR 50.20. The Committee believes that the reimbursement of ancillary costs by independent third parties does not constitute coercion or undue influence and instead helps improve access to cancer clinical trials. As noted in FDA's draft guidance entitled ''Informed Consent Information Sheet: Guidance for IRBs, Clinical Investigators, and Sponsors,'' the FDA considers payment to clinical trial subjects to be compensation for ''expenses and inconveniences'' and not a benefit of participation. Therefore, the Committee encourages the FDA to develop more precise guidance regarding the meaning of ''coercion or undue influence'' as it relates to the reimbursement of ancillary expenses to research participants under 21 CFR 50.20 in finalizing the draft guidance on informed consent content and the informed consent process (''Informed Consent Information Sheet: Guidance for IRBs, Clinical Investigators, and Sponsors''') so as to increase enrollment, retention, minority participation, and equitable access to oncology clinical trials.

FDA Response:

FDA shares the Committee's recognition of the value of clinical trials in the development of innovative diagnostics and drugs to prevent, detect, and treat cancer, and recognizes the importance of increasing enrollment, retention, minority participation, and equitable access to oncology clinical trials. FDA's draft guidance entitled ''Informed Consent Information Sheet: Guidance for IRBs, Clinical Investigators, and Sponsors,'' provides recommendations on the issue of additional cost and payment to research subjects, including that FDA considers payment to clinical trial subjects to be compensation for ''expenses and inconveniences'' and not a benefit of participation. FDA generally would not consider reimbursement for travel costs such as parking and lodging to be undue influence or coercion intended to induce participation in a clinical trial. FDA intends to address this issue as we finalize this guidance. In addition, FDA plans to seek additional outreach opportunities and communication strategies to clarify this issue for cancer patients and the research community.

11. 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 and Opioid Policy Steering Committee, 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 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, should be promoting the full suite of available treatment options, including abstinence-based models and nonopioid medications, rather than picking winners and losers. The Committee supports efforts at the FDA and elsewhere to develop MATs that improve the efficacy of daily administration, are resistant to diversion and misuse, and/or help patients on a path to recovery. Finally, the Committee has been supportive of naloxone distribution among trained licensed healthcare professionals and emergency responders. When considering the appropriateness of providing naloxone over-the-counter, the Committee directs 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 fighting the opioid crisis and will continue to advance using a multipronged strategy. FDA is focusing on three broad areas to help address the opioid crisis: lowering overall exposure to opioid drugs and, in turn, reducing the number of new cases of addiction; enabling more opportunities for those currently addicted to opioid drugs to seek MAT that can help them recover; and helping expedite the development of progressively more-effective abuse deterrent formulations of opioid drugs, and non-opioid alternatives for the treatment of pain. To advance these goals, FDA is supporting cutting-edge research to facilitate the evaluation of abuse-deterrent formulations, alternatives to opioids for pain, and the development of medications that can help patients with addiction recover as well as overdose reversal drugs, such as naloxone.

FDA continues efforts to make naloxone more broadly available. FDA has reached out to, and met with, sponsors of prescription naloxone products to offer advice and assistance on expediting development of a nonprescription (OTC) naloxone drug product. Prescription drug products, including prescription naloxone, require the supervision of a healthcare professional for safe and effective use. OTC drug products, on the other hand, must be able to be used safely and effectively without the supervision of a healthcare professional. The information necessary for safe and effective use of OTC drug products is conveyed to consumers by the Drug Facts labeling (DFL). Typically, DFLs are developed and scientifically tested by drug manufacturers prior to submission of an application for approval of an OTC drug to show that consumers can follow the DFL to understand how to use the product without the help of a healthcare professional. In the case of naloxone, FDA has taken the unprecedented step of developing a model DFL that is intended to convey all the important information a consumer would need to use naloxone effectively and safely in an emergency overdose situation. After developing the model DFL, FDA awarded a contract to an experienced consumer research firm, for rigorous scientific testing of consumer comprehension of the DFL. Once complete, the results of the study will be made

publicly available for use by manufacturers of naloxone products who wish to submit an application to FDA for an OTC naloxone product.

12. Performance Measures

The Committee directs FDA to comply with title 31 of the United States Code, including the development of their organizational priority goals and outcomes such as performance outcome measures, output measures, efficiency measures, and customer service measures.

FDA Response:

FDA will comply with title 31 of the United States Code.

13. 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:

FDA finalized the Tobacco Deeming final rule in August of 2016. In the preamble to the proposed deeming rule, FDA sought comment on two options regarding the categories of cigars that would be covered by this rule—specifically, whether all cigars should be subject to deeming or if only those cigars not considered "premium" should be subject to deeming. FDA sought comments on these two options because it has been suggested that different kinds of cigars may have the potential for varying effects on public health.

FDA carefully reviewed all comments, data, and information submitted to the docket, including many comments from cigar users and the cigar industry, and concluded in the deeming final rule that regulating all cigars, rather than a subset, more completely protects the public health. Ultimately, FDA concluded that all cigars pose serious negative health risks and "premium" cigars are used by youth and young adults.

FDA is aware that there is still interest in the regulation of premium cigars and intends to provide an opportunity for the public to provide new information for the agency to consider. On July 28, 2017, FDA announced that it intends to issue an Advance Notice of Proposed Rulemaking to provide interested parties an opportunity to develop and submit new information or data related to the patterns of use and resulting public health impacts from so-called premium cigars. We will explore any new and different questions raised, and carefully consider any additional data submitted relevant to the appropriate regulatory status of premium cigars.

14. Prescription Drug Labeling Inserts

The Committee is aware of FDA's previous proposal 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 expressly 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. If finalized, the rule would have modernized the system for disseminating drug information to healthcare professionals and utilized available technological advancements to deliver content in a more user-friendly format. 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. 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.

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. Finalizing this rule would reduce outdated regulations, with projected annual cost savings.

15. Product Standards

The Committee is concerned about the feasibility of achieving a 1 parts per million level for Nnitrosonornicotine levels as established in the proposed product standard rule dated January 23, 2017 (82 Fed. Reg. 8004). The Committee encourages FDA to work with stakeholders involved in the production and growth of these products to determine a reasonable level while fulfilling its statutory mission to protect public health.

FDA Response:

The FDA proposed a tobacco product standard that would establish a limit of N-nitrosonornicotine (NNN) in finished smokeless tobacco products sold in the United States. The proposed rule would require that the mean level of NNN in any batch of finished smokeless tobacco products not exceed 1.0 microgram per gram (μg/g) of tobacco (on a dry weight basis) at any time through the product's labeled expiration date as determined by product testing. As discussed in the proposed rule, an NNN level of 1.0 μg/g of tobacco has been achieved in some smokeless tobacco products sold in the United States and is thus achievable using current technology.

In setting the NNN limit, FDA considered epidemiological evidence demonstrating differences in observed cancer risks between users of smokeless tobacco products manufactured in the United States and in Sweden (whose smokeless tobacco products tend to have comparatively lower levels of NNN) as well as the technical achievability of the proposed limit.

As with any rulemaking, it is important for the agency to hear from the public regarding their thoughts on the proposed rule. The FDA extended the original 75day comment period for the proposed rule by 90 days (from April 10, 2017 to July 10, 2017) to allow stakeholders and other interested parties additional time to submit comments on all aspects of the proposed rule, including whether the proposed approach is appropriate.

FDA received almost 8,000 comments on the proposed rule from smokeless tobacco manufacturers, tobacco farmers, public health organizations, trade associations, academia, elected officials (Federal, state, local), Tribes, and individuals. The participation in the rulemaking process by all interested parties was robust. The issues most frequently raised by commenters related to technical achievability, impact on tobacco growers, the effective date, and FDA's public health benefit analysis ("appropriate for the protection of public health"). FDA is currently reviewing and evaluating the comments to determine appropriate next steps.

16. Radiation Safety

The Committee urges the Agency to review and update its current regulations on fluoroscopy radiation safety. The current regulations do not adequately address all available options to protect surgical and interventional health care personnel and patients from radiation exposure. The FDA should issue new regulations that include the use of sterile, disposable, lead-free shields to protect against radiation exposure.

FDA Response:

The agency appreciates the Committee's concerns. The agency regularly considers what additional measures may be needed to address radiation exposure risks during fluoroscopy. Agency staff participate actively in the development of national and international voluntary consensus standards for fluoroscopes with the National Electrical Manufacturers Association (NEMA) and the International Electrotechnical Commission. These standards address the basic safety and essential performance of fluoroscopy, and interventional fluoroscopy devices, among others.

In addition, agency staff participate in drafting national and international guidelines on device capability and appropriate use of fluoroscopes through the National Council on Radiation Protection and Measurements (NCRP), International Commission on Radiological Protection

(ICRP), International Atomic Energy Agency (IAEA), World Health Organization (WHO), Society of interventional Radiology (SIR), and the Conference of Radiation Control Program Directors (CRCPD).

Agency authority regarding fluoroscopy is limited to manufacturers and devices. With respect to sterile, disposable, lead-free shields, these are Class 1, low-risk devices under 21 CFR 892.6500. A number of these devices are legally marketed in the U.S. However, use of these devices is part of the practice of medicine, and is subject to regulation by the individual states, not the agency. Model state regulations for medical radiation use have been developed by CRCPD, and are available at http://c.ymcdn.com/sites/www.crcpd.org/resource/resmgr/docs/SSRCRs/F_Part_2015.pdf.

17. 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:

There are generally two types of spent grain by-products from the alcoholic beverage production process that are used as animal food: unprocessed spent grains – "wet spent grains" – and processed spent grains – "dried spent grains." The by-product that undergoes more processing – such as dried spent grains – may be more likely to be contaminated because the processing allows more opportunities for the introduction of contamination.

Current Good Manufacturing Practices (CGMPs) are baseline manufacturing standards to protect food against contamination. Alcoholic beverage manufacturing facilities are subject to human food CGMP requirements for production of their alcoholic beverages and animal food CGMPs for spent grains used as animal food. The animal food CGMPs are similar to the human food CGMPs but include more flexibility for implementation. FDA understands the Committee's concern with respect to the hazard analysis and preventive control requirements of the Preventive Controls for Animal Food (PCAF) rule, and the agency, as directed, will not apply these requirements to alcoholic beverage manufacturers processing spent grains for use as animal food.

FDA has continued dialogue and outreach with representatives from both the brewing and distilled spirits components of the alcoholic beverage industry. In January 2017, FDA and the Distilled Spirits Council partnered to develop an educational outreach opportunity for FDA, state regulators, and representatives of the distilled spirits and craft brewing industries. During this outreach, regulators and industry reaffirmed the shared goal of achieving compliance with the CGMPs to maintain standards for food safety and public health. The opportunity allowed industry to better understand the various FDA regulations applicable to it and FDA's current outlook on enforcing new regulations, including the agency's approach of applying CGMP requirements to their by-products but not enforcing preventive controls requirements.

FDA has been using the information gained at this event to develop both training materials and guidance for field staff to ensure a uniform understanding of how to apply the PCAF rule to the production of both wet and dry spent grains in a manner that aligns with the agency's understanding of the Committee's intent in the appropriations bill language with respect to dried spent grain by-products. FDA is committed to working with the alcoholic beverage industry to develop education and outreach for the industry and regulatory staff on the FDA regulations that impact this industry.

18. 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 agricultural 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 [sic] models to ensure we have the appropriate workforce available in the future to inspect and certify this growth in agricultural 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 U.S. Customs and Border Protection's (CBP) Automated Commercial Environment (ACE) system. FDA's import entry screening tool (PREDICT) calculates a customized risk score based on a wide variety of factors, including, but not limited to, inherent risk of the product, data anomalies, data quality, and the compliance history of firms (such as 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. In addition, PREDICT screening rules reflect the Foreign Supplier Verification Program (FSVP) discussed below.

FDA is developing new system-based, import-centric processes under FSMA, such as the FSVP regulation and the Voluntary Qualified Importer Program (VQIP), that are risk-based and are less reliant on an increased level of import 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 is produced in a manner that meets applicable U.S. safety standards. The first compliance date for FSVP was May 30, 2017. FDA developed and implemented an inspection program designed to assess importer compliance with this rule.

The agency is in the process of developing a VQIP program. The VQIP program 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 more efficient use of FDA resources than placing staff at ports of entry without consideration of product risk.

FDA's Office of Regulatory Affairs (ORA) recently completed the realignment of the import program and consolidated import operations under the Office of Enforcement and Import Operations (OEIO). This realignment of the import program is designed to provide direction, assistance, management, and oversight of all FDA field import operations, as well as coordinating agency import activities with CBP, including the development and institution of

joint regulations, procedures, policies, and operations. Additionally, the realignment into five import divisions allows the import divisions the flexibility to shift resources when necessary.

19. 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 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 conducted a great deal of work following the 2011 OIG study. Significant resources were allocated to evaluating the study findings, internal processes, and procedures, and enhancing FDA operations and policies. 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 field division 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.

FDA collaborated with our state regulatory partners to review, modify and enhance the Manufactured Food Regulatory Program Standards (MFRPS) revised October 1, 2016, as well as the Animal Food Regulatory Program Standards (AFRPS) revised February 1, 2017. These standards establish a uniform foundation for the design and management of state programs responsible for the regulation of human food and animal food. FDA continues to provide technical assistance and assessments to states for the implementation of the national program standards, including the MFRPS, AFRPS, and Voluntary National Retail Food Regulatory Program Standards (VNRFRPS). FDA continues to see enhanced participation from the states in

the MFRPS program, as well as the AFRPS program. In addition, FDA is collaborating with states to develop new standards for egg and shellfish regulatory programs.

Both FDA and the states continue to expand and leverage resources and abilities using Rapid Response Teams (RRTs), which are activated in response to 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 provide financial support to the states for the implementation of the national program standards (MFRPS, AFRPS, and VNRFRPS), and RRTs through flexible funding models.

FDA continues to improve its IT capabilities, working with the agency's 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. As one of the Integrated Food Safety System initiatives, ORA has implemented the initial operating capability for the National Food Safety Data Exchange (NFSDX) to automate electronic sharing of contracted inspection data with select partner states. Seven states have signed up to participate in the NFSDX pilot testing. 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.

20. 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 the support of the Cancer Moonshot Initiative in the 21st Century Cures Act to prevent and cure cancer, the FDA has still not approved a new OTC sunscreen ingredient through the process created by the SIA. While the FDA published the final guidance in November 2016 entitled ''Nonprescription Sunscreen Drug Products—Safety and Effectiveness Data'', there is still confusion in how the regulated industry can comply with FDA's current approach to the toxicological risk assessment. The Committee directs the FDA to work with stakeholders and help manufacturers understand what they need to do to achieve approval for sunscreen products in order to lower the risk of skin cancer to the 5 million Americans that will be diagnosed with the condition this year. The funding level for the FDA includes the $700,000 originally provided 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:

Given the recognized public health benefits of sunscreen use, the FDA is committed to finding ways to help facilitate the marketing of safe and effective sunscreen products that include additional over-the-counter (OTC) sunscreen active ingredients. As noted in the GAO's November 2017 report FDA Reviewed Applications for Additional Active Ingredients and Determined More Data Needed, the FDA relies on industry to submit the data needed to make the required safety and effectiveness determinations for each pending sunscreen active ingredient currently being evaluated under the SIA framework. In every case, the FDA has determined that the evidence supplied to date is insufficient to support a determination that the active ingredient is

Generally Recognized as Safe and Effective (GRASE) for use in sunscreens.[110] The agency has also identified current data gaps for each active ingredient and communicated them in proposed sunscreen orders and, when requested, granted meetings with active ingredient sponsors. Although not required to do so by the SIA, FDA continues to meet with sponsors upon request to discuss data development, including a recent meeting to discuss preliminary aspects of a Maximal Use Trial (MUsT) to assess potential human absorption of sunscreen active ingredients[111] In addition, FDA expects to publish a draft guidance in the near future to provide manufacturers with recommendations for how to conduct a MuST for topically applied OTC drugs including sunscreens. To date, the agency has not received any additional data from manufacturers for any of the pending sunscreen ingredients that were the subject of SIA-required proposed sunscreen orders issued in 2015.

The FDA will continue to work with industry and public health stakeholders as it implements the SIA to help ensure that the sunscreens consumers use every day are safe and effective for daily, life-long use.

To date FDA has met all statutorily mandated SIA deadlines and remains committed to achieving that goal in the future

[110] US Government Accountability Office (November 15, 2017). Retrieved November 15, 2017, from www.gao.gov/products/GAO-18-61.

[111] Regulations.gov (November 15, 2017). Retrieved November 15, 2017, from www.regulations.gov/document?D=FDA-2005-N-0453-0051.

SENATE APPROPRIATIONS COMMITTEES SIGNIFICANT ITEMS

SENATE COMMITTEE REPORT (S. 115-131)

1. Atypical Actives

The Committee requests that the FDA provide an update on how it regulates ''atypical actives.''

FDA Response:

FDA does not have an official definition for the term "atypical actives;" however, an atypical active is generally understood to mean an excipient, food additive, or cosmetic ingredient used as an active ingredient in pharmaceutical products.

The safety and quality of atypical actives are covered by the same policies applicable to all active pharmaceutical ingredients (API) in marketed drugs, including those with approved drug applications or those conforming to an over-the-counter (OTC) drug monograph. The definition of a "drug" under section 201(g)(1)(D) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) includes "articles intended for use as a component" of a drug. Section 501(a)(2)(B) of the FD&C Act states that a drug shall be deemed to be adulterated if a drug's "manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice [CGMP] to assure that such drug meets the requirements of this chapter as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess." Section 501 further states that the meaning of CGMP "includes the implementation of oversight and controls over the manufacture of drugs to ensure quality, including managing the risk of and establishing the safety of raw materials, materials used in the manufacturing of drugs, and finished drug products."

The agency has not promulgated CGMP regulations specifically for APIs or excipients; however, with the International Conference on Harmonisation (ICH), the agency has published a guidance document regarding good manufacturing practices (GMP) for the manufacturing of APIs entitled ICH Q7 *Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients.*[112] The guidance is "intended to help ensure that APIs meet the quality and purity characteristics that they purport, or are represented, to possess." As stated in the guidance document, firms may use alternative approaches if they satisfy the requirements of applicable statutes and regulations. Accordingly, firms may employ other approaches for atypical actives if they can demonstrate they meet the requirements of 501(a)(2)(B).

2. Autoantibody Qualification

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:

Biomarkers of islet autoimmunity that can be shown to accurately and reliably predict an individual's future risk of Type 1 diabetes would be valuable. Such biomarkers could enhance clinical care by enabling healthcare professionals to potentially identify at-risk individuals,

[112] www.fda.gov/downloads/Drugs/.../Guidances/ucm073497.pdf.

prevent or delay disease onset, and manage the disease. Such biomarkers could also inform the planning and design of clinical studies, and the evaluation of Type 1 diabetes therapeutics.

The FDA is committed to working with stakeholders to make safe and effective drugs to treat diabetes available to patients with this condition and last year sponsored a workshop in collaboration with diabetes professional organizations, healthcare providers, researchers and other advocates of patients with diabetes. The purpose of the workshop was to have a forum for dialogue with the public, patients, patient advocacy groups and industry to gain greater appreciation of the extent to which the current regulatory paradigm for antidiabetic drug therapies addresses the needs of patients with diabetes.[113]

In addition, the 21st Century Cures Act established a statutory framework for the qualification of drug development tools (DDTs), including biomarkers. This authority allows the agency to work with submitters as they develop or refine a DDT that, once qualified for a context of use, can be used by anyone to develop new drugs in a particular area. FDA hopes that this will be a useful tool in many areas in need of improved treatments, including diabetes.

3. Botanical Dietary Supplements Research

The Committee appreciates the work CFSAN has done to ensure the safety of botanical dietary supplements. Existing work to develop authentication and identification tools for evaluation of botanical supplements is promising, and the Committee directs the Center to invest further in this important research.

FDA Response:

In 2001, CFSAN established a highly successful cooperative agreement with the National Center for Natural Products Research (NCNPR) at the University of Mississippi to promote the efficient development and dissemination of natural products research and science. The programs developed under this agreement, which relate to FDA-regulated commodities such as dietary supplements and cosmetics, complement the diverse activities of both public and private sectors. The cooperative research, education, and outreach programs developed by NCNPR address scientific issues related to the identity and safety of botanical dietary ingredients. FDA values NCNPR's contributions and intends to continue to work closely with the principal investigators at NCNPR on the development of additional projects.

Additionally, CFSAN's Office of Dietary Supplement Programs, the Office of Regulatory Science, and Office of Applied Research and Safety Assessment, and the Department of Health and Human Services work together on research focused on identity and safety concerns with botanical dietary supplements.

4. Botanical Drug and Drug Interactions

The Committee commends CDER for its work to ensure that botanical drugs available to the public are safe and effective. However, little is known about potential drug interactions caused by botanical drugs, and given the recent publication of the Botanical Drug Development Guidance for Industry, the Committee is concerned that this will likely catalyze additional applications for approval of botanical drugs. Therefore, the Committee directs the FDA to invest in this research

[113] www.fda.gov/AdvisoryCommittees/Calendar/ucm499281.htm

by working with its Center of Excellence network partners with expertise in developing analytical methods and reference standards for botanical formulations.

FDA Response:

Botanical drugs have a number of unique characteristics that may pose challenges during drug development. The goal of the Botanical Drug Development Guidance for Industry is to provide a practical and feasible approach to support sponsors who are working to develop botanical drugs and ensure the safety, efficacy, and quality of these drugs. The guidance describes CDER's current thinking on appropriate development plans to be submitted in new drug applications (NDAs) and includes specific recommendations on submitting investigational new drug applications in support of future NDA submissions.

The guidance also includes analytical methods and reference standards for quality control of botanical drug products. In addition, raw material control, manufacturing process control, bioassays, as well as in vitro and in vivo drug-drug interaction studies will play important roles to ensure batch-to-batch consistency and reduce the potential risks of drug-drug interactions. The guidance specifically recommends that sponsors evaluate the potential for interactions with drugs or other botanicals.

Currently, two botanical prescription drugs are approved: Veregen (sinecatechins) for the treatment of genital warts; and Fulyzaq (now known as Mytesi, crofelemer) for the treatment of HIV/AIDS related diarrhea. Numerous other botanical products are currently being investigated in various phases of clinical trials with the eventual goal of seeking FDA approval and providing additional options for disease management.

Since 2001, the Center of Excellence for Botanical Dietary Supplement Research at the National Center for Natural Products Research (NCNPR) at the University of Mississippi has worked with FDA to develop analytical methods and reference standards for botanical formulations sold as dietary supplements in the U.S. CFSAN is the lead liaison for FDA, while CDER interacts with CFSAN and the Center of Excellence for Botanical Dietary Supplement Research at the National Center for Natural Products Research (COE) on botanical drug quality related issues. In addition, the newly established FDA-wide Botanical Natural Products Special Interest Group will work closely with the COE in order to leverage their botanical expertise and laboratory resources.

5. Caloric Content

The Committee is concerned that the FDA Nutrition Facts Label final rule does not include specific requirements for certain carbohydrates that may have insignificant or no caloric content. Consumers generally rely on the caloric information provided on food and beverage labels. The Committee is aware that the FDA is working to provide additional information for food manufacturers clarifying how certain carbohydrates, as appropriate, that may have insignificant or no caloric content should be labeled. The Committee urges the FDA to provide clarity to food manufacturers on the labeling of such carbohydrates, as appropriate.

FDA Response:

FDA has issued draft guidance documents on dietary fibers, added sugars, and Reference Amounts Customarily Consumed (RACCs) to assist industry in complying with the Nutrition Facts Label (NFL) final rule and is working to finalize these guidance documents

expeditiously.[114] FDA is also actively working on additional guidance documents on other NFL topics. The agency plans to issue additional information to clarify for industry the labeling of carbohydrates that may have insignificant or no caloric content.

On October 2, 2017, FDA proposed to extend the compliance dates for the NFL/SFL (Supplement Facts Label) and serving size final rules to provide additional time for implementation.[115] The proposed rule would extend the compliance dates from July 26, 2018, to January 1, 2020, for manufacturers with $10 million or more in annual food sales. Manufacturers with less than $10 million in annual food sales would have until January 1, 2021, to comply.

The comment period on the proposed rule closed on November 1, 2017.[116] FDA is considering all comments received concerning the compliance date and is working expeditiously to finalize the rule on the compliance date extension. The agency is committed to issuing final guidance on NFL-related topics noted above on a timeline that will ensure industry has sufficient time to comply with the new requirements. FDA may consider whether, under some circumstances, it should consider exercising enforcement discretion pending further rulemaking.

6. 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 agency's Centers of Excellence (COEs), their contributions to critical basic research, and their role in facilitating the FDA Food Safety Modernization Act (FSMA) implementation. FDA plans to continue utilizing COEs, including supporting their contribution to FSMA implementation activities.

7. 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. 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

[114] 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 (21 CFR 10.30): https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm528532.htm, 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: https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm535371.htm Draft Guidance for Industry: Reference Amounts Customarily Consumed: List of Products for Each Product Category: https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm535368.htm

[115] https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/LabelingNutrition/ucm385663.htm

[116] Food Labeling: Revision of the Nutrition and Supplement Facts Labels and Serving Sizes of Foods That Can Reasonably Be Consumed at One Eating Occasion; Dual-Column Labeling; Updating, Modifying, and Establishing Certain Reference Amounts Customarily Consumed; Serving Size for Breath Mints; and Technical Amendments; Proposed Extension of Compliance Dates: https://www.federalregister.gov/documents/2017/10/02/2017-21019/food-labeling-revision-of-the-nutrition-and-supplement-facts-labels-and-serving-sizes-of-foods-that

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 locations in the CERSI network at their original funding level for a period of at least 5 years to ensure their efficacy and to capitalize on existing studies.

FDA Response:

FDA appreciates the recognition of the importance of the Centers of Excellence in Regulatory Science and Innovation, and their contributions to regulatory science. FDA plans to support four CERSIs in the future within the parameters of their existing or new grant awards.

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 is aware of the cotton ginning industry's concerns regarding whether certain entities are classified as farms or facilities. The agency also is aware of their concern related to whether ginning results in a "processed food." FDA is examining the farm definition and will consider the concerns of the cotton ginning industry in that evaluation. To facilitate this effort, the agency extended the compliance dates for cotton ginners to January 28, 2019, or later depending on business size to provide FDA time to consider the issues raised by the industry. Please see the following webpage for more information about the compliance date extensions: www.fda.gov/Food/GuidanceRegulation/FSMA/ucm517545.htm.

FDA has had multiple meetings with the cotton ginning industry on this topic. FDA representatives met with them in August 2017. FDA staff subsequently participated in an educational tour with representatives from the cotton ginning industry, cotton farmers, the Alabama Department of Agriculture and Industries, and Rep. Robert Aderholt's office.[117] During the meetings and the educational tour, FDA reiterated its commitment to resolve the cotton ginning industry's concerns about the applicability of the PCAF rule to ginning operations prior to the extended compliance date. In the meantime, FDA has committed to a continuing dialogue with the cotton ginning industry as the agency works to address these concerns. 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.

[117] https://blogs.fda.gov/fdavoice/index.php/2017/11/talking-fsma-in-the-land-of-cotton-and-looking-for-middle-ground/

9. Dietary Fiber

The Committee is concerned that the FDA has not issued final guidance regarding the definition of dietary fiber, and encourages the FDA to issue these final guidance documents and provide sufficient time for food manufacturers to comply.

FDA Response: FDA is committed to working with manufacturers covered by the Nutrition and Supplement Facts Labels (NFL/SFL) and serving size final rules, published on May 27, 2016, to understand the time needed to complete and print updated NFLs/SFLs for their products before they are expected to be in compliance.
FDA defined dietary fiber to ensure that the amount of non-digestible carbohydrates declared as dietary fiber on the NFL/SFL will assist consumers in maintaining healthy dietary practices. A non-digestible carbohydrate must provide a beneficial physiological effect to be declared as a dietary fiber on the NFL/SFL. The definition does not prevent companies from continuing to add a non-digestible carbohydrate to a food product, even if the ingredient does not meet the new definition of dietary fiber; in that circumstance, the added non-digestible carbohydrate would be declared as Total Carbohydrate only.

FDA received 12 citizen petitions asking the agency to amend the definition of "dietary fiber" to include specified ingredients in the definition as dietary fibers. FDA is reviewing these petitions as expeditiously as possible. After FDA completes its scientific review, it will notify the petitioners concerning the agency's decision. For those non-digestible carbohydrates for which FDA's determination is that they meet the new "dietary fiber" definition, the agency intends to amend the regulatory definition by adding those non-digestible carbohydrates to the existing list of dietary fibers.

As FDA works to complete the petition review process, stakeholders who use isolated or synthetic non-digestible carbohydrates have expressed a need for clarity from FDA, and the need for clarity has also resulted in requests to extend the NFL/SFL compliance dates.

On October 2, 2017, FDA proposed to extend the compliance dates for the NFL/SFL and serving size final rules to provide additional time for implementation. The proposed rule would extend the compliance dates from July 26, 2018, to January 1, 2020, for manufacturers with $10 million or more in annual food sales. Manufacturers with less than $10 million in annual food sales would have until January 1, 2021, to comply.

The comment period on the proposed rule to extend the compliance date closed on November 1, 2017. FDA is considering all comments received concerning the compliance date. FDA's goal is to complete the rulemaking as quickly as possible. The agency is committed to issuing final guidance on NFL-related topics, including dietary fiber, on a timeline that will ensure industry has sufficient time to comply with the new requirements. FDA intends to consider whether, under some circumstances, it should consider exercising enforcement discretion pending further rulemaking.

10. Dietary Ingredients Guidance

The Committee encourages FDA to meet with representatives of the supplement industry as well as consumer groups and to review all comments received regarding the ''Dietary Supplements: New Dietary Ingredient [NDI] Notifications and Related Issues'' guidance.

FDA Response:

On August 11, 2016, FDA published a revised draft guidance entitled "Dietary Supplements: New Dietary Ingredient Notifications and Related Issues" (FDA-2011-D-0376).[118] The purpose of this revised draft guidance is to help companies decide whether to submit a premarket safety notification to FDA for a product that is, or contains, a new dietary ingredient (NDI). The revised draft guidance is also intended to provide recommendations on how to conduct a safety assessment for an NDI and to help companies improve the quality of their NDI notifications. In response to stakeholder requests, FDA extended the initial comment period to December 2016. FDA currently is reviewing more than 300 comments on the revised draft guidance. As with any draft or final guidance document, FDA will accept comments at any time; the agency suggests a comment period for draft guidance documents to encourage stakeholders to respond in a time frame that allows the agency to most efficiently and effectively review and consider the information submitted. FDA does not implement draft guidance; the final guidance may vary from the draft, depending on the comments and information submitted.

FDA is committed to addressing issues raised in comments and during stakeholder meetings and continues to devote significant resources to stakeholder engagement. FDA has met with representatives from the dietary supplement industry, including firms and trade associations, as well as representatives from consumer groups, to discuss specific issues relating to the revised draft NDI guidance. The agency also is examining whether there are specific issues for which additional stakeholder engagement might enable us to more effectively work towards finalizing the guidance. For example, on October 3, 2017, FDA held a public meeting to discuss development of a list of pre-Dietary Supplement Health and Education Act dietary ingredients, a topic that was mentioned in a number of comments on the revised draft guidance. The agency also has planned stakeholder meetings to discuss implementing a system for accepting master file submissions, another topic that was raised in the comments.

11. Fatal and Debilitating Diseases

The Committee directs the FDA to exercise its current law authorities, as provided under the FDA Safety and Innovation Act and the 21st Century Cures Act, when reviewing new drug applications for patients with 100 percent fatal and debilitating diseases. The Committee further encourages the FDA to afford patients, caregivers and treating physicians the opportunity to participate in the drug review process.

FDA Response:

FDA agrees that patient experience data can play an important role in the development of new drugs. The agency agreed to a systematic effort to learn more about patient experience under PDUFA V and has been able to commit more staff to expand its activities dedicated to providing review divisions with greater patient input. FDA has held a number of public meetings as part of its Patient Focused Drug Development Initiative (PFDDI) and found them very informative. The agency believes that, in addition to these meetings, it is important to develop validated methods and standards that will facilitate the incorporation of patient input in the drug development and review process.

[118] https://www.fda.gov/food/guidanceregulation/guidancedocumentsregulatoryinformation/dietarysupplements/ucm257563.htm

The agency is also working to implement the patient-focused drug development provisions included in the 21st Century Cures Act. In May 2017 FDA published a 5-year plan for the issuance of draft and final patient-focused drug development guidances and workshops, including one held on December 18, 2017, "Public Workshop on Patient-Focused Drug Development: Guidance 1 - Collecting Comprehensive and Representative Input."[119] At this workshop, FDA obtained feedback from stakeholders including patients, caregivers, patients' advocates, researchers, practitioners, drug developers and others, on considerations for: (1) standardized nomenclature and terminologies for patient-focused drug development; (2) methods to collect meaningful patient input throughout the drug development process; and (3) methodological considerations for data collection, reporting, management, and analysis of patient input.

FDA believes that methods and approaches to the collection of relevant and objective patient data should be developed; that the guidance process is an appropriate means of developing and disseminating such information to drug developers, patients and their advocates; and that public meetings are an effective means for gathering information from varied stakeholders.

Regarding patients with 100 percent fatal and debilitating diseases, many factors may be considered in the drug approval process, including the nature and severity of disease for which a drug would be indicated and whether other safe and effective treatments are available. The provisions in the FDA Safety and Innovation Act and the 21st Century Cures Act reinforce the agency's longstanding commitment to regulatory flexibility regarding the evidence required to support product approval for the treatment of serious or life-threatening diseases with limited therapeutic options.

The Center for Biologics Evaluation and Research (CBER) and the Center for Drug Evaluation and Research (CDER) published a guidance in 2014 on Expedited Programs for Serious Conditions – Drugs and Biologics. This guidance addresses the various expedited development and review programs available to drugs and biologics intended for serious or life-threatening conditions, including accelerated approval (and the use of surrogate and intermediate endpoints to support accelerated approval), fast track designation, priority review, and breakthrough designation, a very successful program that was established in the FDA Safety and Innovation Act in 2012.

FDASIA created section 506(a) of the FD&C Act, which enables FDA to designate certain drugs as "breakthrough therapies" if (1) the drug is intended to treat a serious or life-threatening disease or condition AND (2) preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Breakthrough therapy designation enables sponsors to receive intensive FDA guidance on an efficient drug development program, an organizational commitment to intensively involving senior managers and experienced review staff, and rolling review of its application, as well as any other expedited programs (e.g., priority review) for which the drug might qualify.

Building on the FDA's existing expedited programs, which have always been available to eligible regenerative medicine products for serious conditions, the Regenerative Medicine Advanced Therapy (RMAT) Designation was established though the 21st Century Cures Act in December 2016. In November 2017, CBER published a draft guidance (Expedited Programs for

[119] www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM563618.pdf

Regenerative Medicine Therapies for Serious Conditions), which supplements the 2014 Expedited Programs guidance and provides information about all of the expedited programs available for regenerative medicine therapies, including the new RMAT designation program.

The agency has been applying its expedited programs, including breakthrough therapy designation and RMAT designation, as well as its fast track, priority review, and accelerated approval authority, to all applications meeting the criteria, including any such applications for drugs to treat 100 percent fatal and debilitating diseases.

In addition, in 2016, FDA took a number of actions to streamline expanded access, also known as "compassionate use," which provides a pathway for patients to gain access to certain investigational drugs, biologics and medical devices for serious diseases or conditions.

12. Food Safety Mission

The Committee directs the FDA Foods Program to report to the Committee all activities and resources spent on nutrition-related activities for the Center for Food Safety and Applied Nutrition [CFSAN], associated field offices [ORA], and support components.

FDA Response:

The FDA Foods Program works to ensure that the nation's food supply is safe, sanitary, wholesome, and honestly labeled, and that nutrition labeling is informative and accurate. Nutrition information obtained through the labeling of food is a key tool for advancing public health by allowing consumers to build healthy dietary patterns and avoid obesity and diet-related chronic diseases such as heart disease and diabetes. In September 2017, FDA Foods Program leadership met with Senate Committee staff to discuss activities and resources related to nutrition. If the Committee would like additional information, the Foods Program, including Center and Field components, would be happy to offer another briefing.

13. Food Safety Modernization Act

The Committee is aware that some states that have entered into cooperative agreements under the State Produce Implementation Cooperative Agreement Program to provide education, outreach, and technical assistance are considering changing the state agency responsible for implementing these agreements. The Food and Drug Administration is directed to work with any state that designates a new implementing agency to ensure it can continue to receive funding under existing cooperative agreements without delay or loss of funding.

FDA Response:

FDA is aware of several states that are considering changing the grantee (funded) state agency under the State Produce Implementation Cooperative Agreement Program. FDA has been in discussions with both current and potential grantee state agencies. As of October 2017, FDA has not received formal requests to change the grantee state agency. If received, FDA will follow the appropriate grants policies and procedures to change the grantee state agency without delay or loss of funding.

14. Foreign High Risk Inspections

The Committee has provided robust funding for this initiative over the last several years and directs the FDA to provide an update on these efforts, including estimated efficiencies and concerns, and plans to continue or expand this effort in the future.

FDA Response:

The Committee provided robust funding for foreign site verifications of high risk facilities which provided FDA with additional data on entities of interest. This funding enabled FDA to better identify foreign food facilities, with a goal of reducing "washout" inspections. The funding is also of value in the medical device space, which has seen a boom in manufacturing of devices and device components in emerging economies. FDA does, however, face obstacles in expanding the program. To identify data that best expands FDA's coverage of pharmaceutical products, FDA needs to seek a Paperwork Reduction Act waiver. In addition, many of the sites identified for in-person verification are in China, where it is difficult to perform this work.

15. FSMA Clarification for Small Farms

The Committee directs the FDA to provide further clarification to small farms on the requirements for compliance with the Food Safety Modernization Act, including information on the qualified exemptions available to small and very small farms and the actions required to achieve compliance under these exemptions. The Committee also urges the Food and Drug Administration to communicate with (including through appropriate guidance) and offer technical assistance to assist small farms with compliance.

FDA Response:

FDA is committed to ensuring that farms, in particular small and very small farms, have the assistance they need to understand and comply with the rules issued under the FDA Food Safety Modernization Act (FSMA). In September 2017, FDA issued a small entity compliance guide on the FSMA Produce Safety Rule, intended to assist small and very small farms to better understand the rule. The guidance provides the definitions for small and very small businesses and explains the qualified exemption provision. Thus, the small entity compliance guide can help farmers determine whether they are eligible for a qualified exemption, which would modify the requirements they are subject to under the Produce Safety Rule[120]. In addition, FDA has issued small entity compliance guides for the current good manufacturing practice, hazard analysis, and risk-based preventive controls regulations for both human food and animal food that can help small and very small farms that also engage in on-farm manufacturing and processing.

FDA has engaged in other activities intended to provide technical assistance to farmers on the requirements of the Produce Safety Rule and how to comply. For example, the FSMA Technical Assistance Network is a central source of information for questions related to FSMA rules, programs, and implementation strategies, including for small and very small farmers, who have questions on complying with the Produce Safety Rule. FDA - along with USDA and Cornell University - created a Produce Safety Alliance (PSA) to develop and deliver training on the produce safety regulation requirements that would be of particular assistance to small and very small farms. PSA training courses have been available since Fall 2016. FDA also awarded a cooperative agreement, called the Local Food Producer Outreach, Education, and Training to Enhance Food Safety and FSMA Compliance Cooperative Agreement, intended to address small entities, in August 2016. The cooperative agreement is intended to develop and provide science-based, culturally specific food safety training, education, and outreach for local food producers and processors.

[120] https://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm574281.htm

16. Grape Varietals

The Committee is aware that the FDA has excluded certain produce that is rarely consumed raw from having to comply with the FSMA Produce Safety Final Rule entitled ''Standards for Growing, Harvesting, Packing, and Holding of Produce for Human Consumption.'' There is concern that the FDA did not distinguish between grape varietals that are consumed raw and those that are grown, harvested and used for wine and further processing. The Committee directs the FDA to consider any relevant distinctions between grape varietals, including grape varietals from different regions, that may provide additional flexibility to wine grape growers in demonstrating a product is eligible for exemption or exclusion from the produce safety regulation, including through listing as a produce that is rarely consumed raw.

FDA Response:

The characterization of fruits and vegetables as "rarely consumed raw" in the Food Safety Modernization Act (FSMA) Produce Safety Final Rule was based on consumption patterns reported in the National Health and Nutrition Examination Survey[121], which is the most comprehensive and robust, nationally-representative dataset currently available on dietary intake in the U.S. The reported consumption of uncooked wine grapes – by 18.6 percent of consumers and on 1.9 percent of eating occasions in two days of dietary intake data, and by 11.4 percent of consumers and on 1.5 percent of eating occasions in a single day of dietary intake data – was high enough to exclude them from the rarely consumed raw list (and, therefore, wine grapes are covered produce subject to the rule). Furthermore, according to the National Grape Registry, some grapes used to make wine can be used for other purposes as well. For example, the Malaysia Bianca grape cultivar can be used as wine grapes and table grapes, and the Muscat of Alexandria grape cultivar can be used to make wine or raisins or as table grapes. For these reasons, FDA concluded that ''wine grapes'' are not rarely consumed raw.

In the FSMA Produce Safety Final Rule, FDA stated that it did not have information on the specific grape cultivars or varieties that are solely and exclusively grown for use in winemaking that would allow the agency to establish a category covering only "wine grapes" and evaluate their eligibility for the rarely consumed raw list, using currently available dietary consumption data. FDA also indicated its intent to consider updating the list of rarely consumed raw commodities in the future, as appropriate, such as if new data become available. FDA encourages interested stakeholders to identify or submit data that are sufficiently robust and representative to allow FDA to draw scientifically valid conclusions that the criteria are met for including the commodities on the rarely consumed raw list. The criteria for inclusion are that the commodity is consumed raw by less than 0.1 percent of population; is consumed raw on less than 0.1 percent of eating occasions; and that consumption in any form – raw, processed, or other – was reported by at least one percent of a weighted number of survey respondents. FDA has discussed this with interested stakeholders that have contacted FDA about adding wine grapes to the list of rarely consumed raw commodities.

Although grapes used in the production of wine currently are not considered "rarely consumed raw," grapes used to produce wine are eligible for an exemption provided certain documentation requirements are met. FDA determined that winemaking adequately reduces the presence of microorganisms of public health significance and, therefore, added "wine" to the list of examples

[121] Available at: https://www.cdc.gov/nchs/nhanes/index.htm

of products of commercial processing. FDA has extended the compliance dates for some of the documentation needed to qualify for the commercial processing exemption while the agency considers the best approach to address feasibility concerns – see 81 FR 57784, August 24, 2016. FDA remains committed to working with the food industry throughout FSMA implementation to ensure that requirements are as practical as possible while still protecting public health.

17. Improving Diversity in Clinical Trials and Safety Studies

The Committee supports FDA's efforts, including the FDASIA 907 Action Plan, to promote inclusion of racially and ethnically diverse populations into clinical trials. The Committee encourages FDA to address the specific lack of racial and ethnic diversity in genome wide association studies, precision medicine studies, and post-market surveillance safety monitoring for drugs, biological products, and devices. The Committee further encourages FDA to also include data for Hispanics in the Clinical Trials Drug Snapshots, including stating when no data is available based on the study design of the clinical trial. The Committee also directs FDA's to help ensure that public-facing resources are available in Spanish, including MedWatch reporting forms and online portal, and consumer information materials.

FDA Response:

FDA has implemented 26 of 27 action items in the "FDA Action Plan to Enhance the Collection and Availability of Demographic Subgroup Data" and posted "Questions and Answers" about the Plan. In 2016, FDA hosted a meeting "Enhancing the Collection, Analysis, and Availability on Demographic Subgroup Data," to update the public about progress in implementing the Plan. Progress includes:

- Issuing two guidance documents: "Collection of Race and Ethnicity Data in Clinical Trials" and "Evaluation and Reporting of Age, Race, and Ethnicity Data in Medical Device Clinical Studies." Both provide clear and detailed guidance for regulated industry on matters related to clinical trial inclusion data. FDA released its "Women's Health Research Roadmap" to better coordinate women's health research across the agency.
- Updating MedWatch forms for adverse event reporting to include fields for race and ethnicity. Portions of the MedWatch portal are now available in Spanish as well as 14 other languages and language assistance is available for those wishing to access the portal.
- Conducting meetings/workshops and making the information publicly available:
    - The Institute of Medicine and FDA joint meeting (2015), "Strategies for Ensuring Diversity, Inclusion, and Meaningful Participation in Clinical Trials: A Workshop." More than 100 participants attended and a publication detailing the proceedings was released.
    - FDA and Johns Hopkins University joint workshop (2015), Clinical Trials: Assessing Safety and Efficacy for a Diverse Population.
    - FDA public meeting (2016), Progress on Enhancing the Collection, Analysis and Availability of Demographic Subgroup Data.
- Launching Drug Trials Snapshots to inform consumers about demographic data indicating who participated in clinical trials that supported FDA approval of new drugs and biologics. Drug Trials Snapshots also highlight whether there were any differences in the

benefits and side effects among sex, race and age groups, when such data are available. The agency has published more than 100 Drug Trials Snapshots, which are written in clear, consumer-friendly plain language.

- Developing tools to support clinical trial participation. FDA's Office of Minority Health collaborated with the National Library of Medicine to help consumers and patients find clinical trials, and conducted an ongoing multi-media Minorities in Clinical Trials Campaign which encompasses public service announcements, educational materials, webinars, and print/digital outreach that highlights the importance of clinical trial participation. FDA's Office of Women's Health developed and disseminated, through collaboration with Association of Clinical Research Professionals, a national training webinar series titled "Engagement, Recruitment and Retention of Diverse Women in Clinical Trials". As part of FDA's Language Access Plan, the agency released multiple consumer information materials and updates in Spanish that describe why representation of minorities in clinical trials is important and how FDA is working to increase participation.
- FDA's Office of Women's Health launched its Diverse Women in Clinical Trials initiative. Developed in collaboration with the National Institute of Health's Office of Research on Women's Health, this multipronged effort includes a national awareness campaign, scientific dialogues and webinars/ workshops designed to raise awareness and share best practices about clinical research design, recruitment, and subpopulation analyses. Since January 2016, OWH has mobilized a network of 275 partners to disseminate FDA clinical trials educational materials, host workshops for health professionals, and conduct digital and community-based outreach.

18. In Silico Clinical Trials

The Committee appreciates FDA's interest in in silico medicine and directs the Office of the Chief Scientist to enter into an affiliation agreement with an academic institution with expertise in physiological modeling for the purpose of bridging the gaps between genetics and clinical practice with in silico clinical trials, allowing the development of personalized medicine and optimizing the regulatory process, pursuant to the goals set forth in the Critical Path Initiative.

FDA Response:

FDA appreciates the Committee's interest in advancing the goals of the Critical Path Initiative and developing tools to support personalized medicine. FDA currently partners with the University of Mississippi Medical Center (UMMC), using its sophisticated computer models to predict in silico how drugs and devices may affect the human body. This partnership is currently focused on the kidney, but UMMC's model may also be used to evaluate drugs and devices across the entire body, project the long-term effects of an intervention, and study ways in which drugs might impact populations differently.

In addition, FDA has a Memorandum of Understanding with the Avicenna Alliance, an association comprised of industry and academic partners, to seek actionable ways to harness in silico clinical trials. The existing grant from the Office of the Chief Scientist to the Stanford/UCSF Center of Excellence in Regulatory Science and Innovation, provides another opportunity to pursue physiological modeling in conjunction with the Precision Medicine Initiative-focused projects.

19. Misleading Maple Marketing

The Committee is concerned about the explosion of products marketed using the word maple and related iconography, which intentionally misleads consumers who perceive the use of the word maple and related iconography to mean that a food product contains some measurable quantity of maple syrup to flavor or sweeten the product, which consumers identify as a characterizing ingredient. The Committee directs the FDA to perform a detailed analysis of consumer perception of foods marketed with the word maple or related iconography.

FDA Response:

FDA shares your concern for the truthful labeling of food products and intends to continue to monitor the marketplace for potentially false and misleading labeling. If a food does not contain the ingredient maple syrup, the label cannot include the term "maple syrup" in the ingredient statement or as a part of the statement of identity. FDA will consider taking action, as appropriate, consistent with our food safety priorities and resources, against products that are misbranded.

Further, FDA shares your concern to avoid consumer confusion. In September 2016, FDA developed an FDA Consumer Update to help educate consumers about the differences in the ways that ingredients and flavors are declared on product labels; this update included "maple" and "maple syrup." The update is available at: https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm521518.htm. FDA may develop additional educational materials if further needs are identified.

FDA has worked with representatives of the maple syrup industry and is happy to meet with them to discuss available data and other industry information on consumer perceptions regarding maple and maple syrup. This information would be valuable in assessing and analyzing the impact that the use of the term "maple" and related iconography have on consumer perceptions. FDA also would welcome the opportunity to meet with Committee staff to discuss the labeling regulations regarding the use of the terms "maple syrup" and "maple" and the Committee's directive to perform a detailed analysis of consumer perceptions of foods marketed using these terms.

20. Opioids

The Committee is deeply concerned about the opioid abuse epidemic that took the lives of more than 33,000 Americans in 2015. As the Agency that oversees the approval of these drugs, the FDA has a responsibility to consider the public health impact of opioid misuse, abuse, diversion and overdose death. The Committee supports FDA's commitment to addressing this crisis through all available authorities, and encourages them to work with other Federal Agencies in their efforts.

The Committee continues its directive for FDA 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 is not in the interest of protecting and promoting the public health.

The Committee notes that the vast majority of patients prescribed opioids are dispensed a substantially larger amount of pills than what is effective for pain management, and that 8 percent of patients who receive a week's supply of opioids continue to use them 1 year later.

Additionally, despite promotion of abuse deterrent varieties of opioid medication, FDA has itself recognized that these drugs are still misunderstood as being abuse-proof by prescribers.

Therefore, the Committee believes that it is imperative that FDA, consistent with its own Advisory Committee recommendations, take any and all steps necessary to require continuing medical education, aligned with the most recent Center for Disease Control and Prevention's Guidelines for Prescribing Opioids for Chronic Pain, for providers who write opioid prescriptions, including through the Risk Evaluations and Mitigation Strategy. The Committee directs FDA to establish authoritative opioid labeling guidelines that align prescribing and dispensing volumes with the lowest number of pills needed to be effective for pain management. Additionally, the Committee believes that FDA should develop messaging to mitigate the risk that healthcare practitioners will confuse the term ''abuse-deterrent'' for ''abuse-proof''.

The Committee is also concerned that the Drug Enforcement Administration's approved annual aggregate production quota for opioids, which are established through engagement with the FDA, have increased dramatically in the last two decades. The Committee directs the FDA to account for changes in the currently accepted medical use of opioids and the downstream public health impact when informing DEA's quota-setting process, and provide public justification for any future recommended changes to the DEA's aggregate production quote for opioids.

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").

FDA remains committed to increasing the number of prescribers who receive training on pain management and safe prescribing of opioid analgesics to decrease inappropriate opioid prescribing. FDA continues to explore potential methods to increase prescriber training, bearing in mind that clinicians may be receiving opioid analgesic prescribing education from sources other than training provided under the existing REMS.

Accordingly, the agency held a public workshop on May 9-10, 2017, "Training Health Care Providers on Pain Management and Safe Use of Opioid Analgesics – Exploring the Path Forward," to obtain input on issues and challenges associated with Federal efforts to support training on pain management and the safe prescribing, dispensing, and patient use of opioids (safe use of opioids) for health care providers. During the workshop, the agency discussed how FDA might best use Risk Evaluation and Mitigation Strategy (REMS) to ensure training of prescribers, including adequate training in the appropriate management of pain. This training would help prescribers make the best treatment decisions, including the careful use of opioids under appropriate circumstances.

In a related action, on September 28, 2017, FDA notified sponsors that it was requiring updates and modifications to the existing Risk Evaluation and Mitigation Strategy (REMS) for extended-release/long-acting (ER/LA) opioid analgesics, and for the first time, the agency's decision to require immediate-release (IR) opioid analgesic products be subject to the same REMS requirements. The modified REMS will include revisions to the existing FDA Blueprint for

prescriber education, which describes the content that must be covered in an educational program for it to be considered REMS-compliant. As one part of the education, FDA intends to broaden information on pain management, including the principles of acute and chronic pain management; non-pharmacologic treatments for pain; and pharmacologic treatments for pain (both non-opioid analgesic and opioid analgesic).

The Blueprint will also enhance the information about the safe use of opioid analgesics, basic elements of addiction medicine, and opioid use disorders, and the new REMS will require that training be made available to other health care providers involved in the management of patients with pain, including nurses and pharmacists. FDA believes that all healthcare providers involved in the management of pain should be educated about the safe use of opioids. The new training will also be aimed at making sure providers are prescribing opioids only for properly-indicated patients, and only under appropriate clinical circumstances. This is part of a broader effort to take new steps to make sure providers are properly informed about suitable prescribing and the risks and benefits associated with opioid drugs.

One approach to reducing the rate of new addiction is to reduce exposure to prescription opioid analgesics. To accomplish this, FDA is exploring ways to use our regulatory authorities to influence how opioid analgesics are prescribed to make sure that only appropriately indicated patients are prescribed opioids, and that the prescriptions are written for durations and doses that properly match the clinical reason for which the drug is being prescribed in the first place. FDA is also exploring whether the agency should take additional steps to make sure that prescribing practices, and the number of opioid doses that an individual patient can be dispensed, are more closely tailored to the patient's medical need. Among other steps, FDA is soliciting public input on these questions in the form of a public docket that was established the week of September 25, 2017.

Abuse-deterrent (AD) technology is still evolving and epidemiological studies are in progress to assess AD products' effectiveness in reducing abuse in the real world. While the FDA recognizes that the AD formulations are not failsafe and more data are needed, AD opioids are expected to reduce abuse compared to non-AD opioids, which make them an important part of a much larger strategy to combat opioid abuse. FDA held a public meeting in July 2016 to discuss ways to improve the science of evaluating the postmarketing impact of AD formulations, both by improving use of existing data and methods and developing new data streams and methods. FDA has since awarded several contracts to support cutting edge research to facilitate evaluation of AD products, despite the limitations of currently available data.

FDA provides DEA an annual estimate of medical, scientific, and reserve stock needs for Schedule I and II substances, including opioids, based in significant part on prescribing data. It is FDA's understanding that these estimates are used by DEA to determine the amount of controlled substances (Aggregate Production Quota (APQ)) that is appropriate to set as an upper limit on the amount of that substance that can be manufactured in the coming year, as outlined in the Controlled Substances Act and 21 CFR Part 1303. However, DEA relies on data and information to which FDA does not have access, such as diversion data and data on international need, to determine the final published APQ. The exact methods DEA uses to determine quotas, including opioid quotas, are not known to FDA. Over time, FDA has observed significant differences between our estimates of projected trends for medical need of certain drugs and the actual aggregate quotas DEA establishes.

21. Orphan Products Development

The Committee is encouraged by the Office of Orphan Products Development and recognizes the importance of the work being supported by Orphan Product Grants. The Committee requests for the FDA to provide a review of the indication for which the drug is intended to treat and for the number of pediatric clinical trials that have received a grant since fiscal year 2015.

FDA Response:

FDA's Orphan Products Clinical Trials Grants Program provides grants for clinical studies of products (drugs, biologics, medical devices, or medical foods) for use in rare diseases or conditions where no current therapy exists or where the proposed product has a plausible hypothesis that it will be superior to the existing therapy. Since the program's inception in 1983, OOPD has funded over 600 studies and the program has contributed to bringing nearly 60 products to marketing approval.

In FY 2015-2017, the Orphan Products Clinical Trials Grants Program supported 48 clinical trials that included pediatric (

Pediatric Only Trials:

Phase 1 Study of Ursodeoxycholic Acid Therapy for Pediatric Primary Sclerosing Cholangitis

Phase 2 Study of rhCC10 to Prevent Neonatal Bronchopulmonary Dysplasia

Phase 2 Study of Levetiracetam in the Treatment of Neonatal Seizures

Phase 2 Study of Dextromethorphan in the Treatment of Rett Syndrome

Phase 3 Study of Triiodothyronine Supplementation for the Treatment of Young Infants After Cardiopulmonary Bypass

Phase 1/2 Study of Aerosolized Survanta for the Treatment of Neonatal Respiratory Distress Syndrome

Phase 2 Study of Imatinib for the Treatment of Airway Tumors in Children with Neurofibromatosis Type 1

Phase 1 Study of Omigapil for the Treatment of Congenital Muscular Dystrophy (CMD)

Phase 3 Study of Standard vs Reduced IV Fat for the Prevention of Parenteral Nutrition-Associated Cholestasis (PNAC)

Phase 2 Study of Selective Cytopheretic Device for the Treatment of Pediatric Patients w/ Acute Kidney Injury

Phase 2 Study of EDI200 for the Treatment of X-Linked Hypohidrotic Ectodermal Dysplasia

Phase 2 Study of Furosemide for the Prevention of Bronchopulmonary Dysplasia in Premature Infants

Phase 2 Study of Oxytocin for the Treatment of Hyperphagia in Prader-Willi Syndrome

Phase 1 Study of HSV G207 & Radiation for the Treatment of Pediatric Brain Tumors

Phase 2 Study of Inhaled Activase for the Treatment of Acute Plastic Bronchitis

Phase 3 Study of Dichloroacetate (DCA) for the Treatment of Pyruvate Dehyrugenase Complex Deficiency

Phase 3 Study of Magnetic Alteration of Pectus Excavatum

Phase 2 Study of Radioactive Iodide Therapy for Pediatric Graves Disease

Phase 2A Study of Exendin for the Treatment of Congenital Hyperinsulinism

Pediatrics and Adult Trials:

Phase 2 Study of High TC Susceptometer to monitor Transfusional Iron Overload

Phase 2 Study of Vitamin D for Prevention of Respiratory Complications from Sickle Cell Disease

Phase 3 Study of Cheatham Platinum Stent for Prevention or Treatment of Aortic Wall Injury Associated with Aortic Coarctation

Phase 2 Study of T-Cell Depleted Familial Haploidentical SCT for the Treatment of High-Risk Sickle Cell Anemia

Phase 2 of Defibrotide for the Prevention of Complications in High-Risk Sickle Cell Disease Patients Following AlloSCT

Phase 2 Study of the HemiBridge System for the Treatment of Idiopathic Scoliosis

Phase 2 Study of Etanercept for Children with Kawasaki Disease

Phase 2/3 Study of Sitagliptin in the Prevention of Cystic Fibrosis Diabetes

Phase 3 Study of Anacoral (Coralmyn) Antivenom for Emergency Treatment of Coral Snake Envenomation

Phase 2 Study of Glycomacropeptide vs. Amino Acid Diet for Management of PKU

Phase 2 Study of Mexiletine in Treatment of Myotonic Dystrophy Type 1

Phase 1 Study of HSV1716 in Patients with Non-CNS Solid Tumors

Phase 2 Study of [18F] FLT for PET Imaging of Brain Tumors in Children

Phase 1/2 Study of Taurine for the Treatment of Cystathionine Beta-Synthase Deficient Homocystinuria

Phase 2 Study of Esophageal String Test in Diagnosing Eosinophilic Esophagitis

Phase 1 Study of IL-2 for the Treatment of Wiskott-Aldrich Syndrome

Phase 1 Study of ALK001 for the Treatment of Stargardt Disease

Phase 2 Study of Abatacept combined with Calcineurin Inhibition and Methotrexate for Prophylaxis of Graft Vs Host Disease

Phase 2 Study of Deferiprone in the Treatment of Neurodegeneration with Brain Iron Accumulation

Phase 2 Study of Vincristine vs. Sirolimus for the Treatment of High Risk Kaposiform Hemangioendothelioma

Phase 1 Study of Quercetin for the Treatment of Fanconi Anemia

Phase 2 Study of Carbidopa for the Treatment of Familial Dysautonomia

Phase 2 Study of L-Arginine Therapy for the Treatment of Pediatric Sickle Cell Disease Pain

Phase 2 Study of the Melanocortin 4 Receptor Agonist RM-493 for the Treatment of Prader Willi Syndrome

Phase 2 Study of Gamunex (Intravenous Gammaglobulin) for the Treatment of Sickle Cell Acute Pain

Phase 1 Study of Viralym-A for the Treatment of Adenovirus Disease

Phase 2 Study of a Networked Neuroprosthesis (NNP) for Grasp, Reach, and Trunk Function in Cervical Spinal Cord Injury

Phase 1 Study of Humanized 3F8 MoAb and NK cells for the Treatment of Neuroblastoma

Phase 1 Study of Dual PI3K/BRD4 Inhibitor SF1126 for the Treatment of Neuroblastoma

22. Pediatric Cancer Drug Approvals

The Committee is encouraged by the enactment of the RACE for Children Act as part of the reauthorization of the Prescription Drug User Fee Authorization Act. RACE for Children could improve the treatment options for children battling cancer and close the divide between adult and pediatric oncology therapies. The Committee encourages the FDA to fully implement the provisions specific to the lists of molecular targets and FDA guidance on pediatric study plans under the Pediatric Research Equity Act and the Best Pharmaceutical Practices for Children Act.

FDA Response:

FDA appreciates the Committee's support for the development of oncology drugs for cancers affecting pediatric patients, and is committed to fully implementing the provisions specific to the lists of molecular targets included in the FDA Reauthorization Act (FDARA), and issuing FDA guidance on pediatric study plans under section 505B of the Federal Food, Drug, and Cosmetic Act (FD&C Act). FDA is working internally and with external stakeholders to solicit input regarding the molecular targets that are substantially relevant to the growth or progression of a pediatric cancer and the process for updating the list of molecular targets that may impact the application of the requirements of the FDA Reauthorization Act of 2017 (FDARA).

Consistent with the requirements of FDARA, FDA intends to publish a list of molecular targets considered to be substantially relevant to the growth and progression of a pediatric cancer and that may be subject to the requirements of section 505B of the FD&C Act, as well as a list of molecular targets of new cancer drugs and biological products that will be granted automatic waivers by August 2018. FDA also intends to issue a final guidance regarding the implementation of the new section 505B requirements regarding molecularly targeted cancer drugs for pediatric patients by August 2019.

23. Seafood Advisory

The Committee is concerned that the FDA published final seafood advice for pregnant and nursing women on January 18, 2017, without going through necessary interagency review, consumer focus group testing, or the opportunity for the public to comment on the scientific peer review. Therefore, the Committee directs the FDA to review its final seafood advice and to make

such technical corrections as are necessary to ensure the advice is consistent with the FDA's scientific review of the net effects of seafood consumption. In addition, the Committee directs the FDA to follow the Administration's review process prior to publishing the updated seafood advice.

FDA Response:

The 2017 final fish advice, entitled "Fish: What Pregnant Women and Parents Should Know,[122]" is based on extensive scientific research and expertise across a range of disciplines as well as multiple opportunities for public comment and stakeholder input. The 2017 advice reflects the work of experts in a range of disciplines within both FDA and the Environmental Protection Agency (EPA), with assistance and input from the National Institutes of Health and other operating divisions within the Department of Health and Human Services. The 2017 advice went through an extensive interagency review process as well as an external peer review process. The agency posted a peer review plan for "Technical Information on Development of Fish Consumption Advice" as part of the agency's peer review agenda. Documentation of the technical information and external scientific peer review process is available on FDA's website.[123]

Furthermore, FDA and EPA received and considered more than 220 public comments on the 2014 draft version of the advice; these comments came from academia, industry, nongovernmental organizations, and consumers. In light of these comments and updated research and technical information, FDA and EPA developed a revised method for categorizing fish and conducted an external peer review of the information and method used.

In November 2014, the FDA's Risk Communications Advisory Committee held a meeting that addressed the draft updated fish advice in great detail and included presentations by FDA and EPA on the substance and presentation of the draft advice as well as presentations by invited experts in risk communications. Members of the public were given an opportunity to express their views to the Risk Communications Advisory Committee and to the agency officials in attendance. Documentation of the public and expert input is available at FDA's website. FDA believes this additional information demonstrates the rigor of our process for reviewing and updating the fish advice.

On October 13, 2017, FDA issued a denial letter in response to a citizen petition requesting that FDA withdraw and reissue the 2017 seafood advice. FDA's response letter, which includes information about FDA's consideration of the FDA Net Effects Assessment, is available in Docket No. FDA-2017-P-3296 at https://www.regulations.gov/document?D=FDA-2017-P-3196-0071.

24. Sunscreen Labeling Regulations

The Committee remains significantly concerned that the FDA has not approved a new over-the-counter [OTC] sunscreen ingredient since the 1990s, despite having a number of ingredients pending approval for more than a decade. After the U.S. Surgeon General issued ''A Call to Action to Prevent Skin Cancer,'' which concluded that nearly 5 million people are treated

[122] https://www.federalregister.gov/documents/2017/01/19/2017-01073/advice-about-eating-fish-from-the-environmental-protection-agency-and-food-and-drug-administration

[123] https://www.fda.gov/Food/ResourcesForYou/Consumers/ucm393070.htm

annually for all skin cancers at a cost of approximately $8.1 billion per year, Congress passed the Sunscreen Innovation Act of 2014 to improve the process by which the FDA reviews sunscreen ingredients and to require the FDA to finalize an effective sunscreen monograph within 5 years. The Committee directs the FDA to work with stakeholders to develop a testing regimen, consistent with current scientific standards, that appropriately balances the benefit of additional skin cancer prevention tools versus the risk of skin cancer within 90 days of enactment. The Committee also directs FDA to maintain funding for agency efforts to clear this backlog of sunscreen applications.

In addition, the Committee is disappointed that FDA has not yet finalized a rule limiting the maximum Sun Protection Factor [SPF] to ''50'' or ''50+'' as directed by the fiscal year 2017 Consolidated Appropriations Act, and as such the Committee directs FDA to finalize the rule immediately. The Committee is also disappointed that FDA failed to issue a proposed rule to establish testing and labeling standards for sunscreen sprays and directs FDA to do so immediately.

FDA Response:

Given the recognized public health benefits of sunscreen use, the FDA is committed to finding ways to help facilitate the marketing of safe and effective sunscreen products that include additional over-the-counter (OTC) sunscreen active ingredients. As noted in the GAO's November 2017 report *FDA Reviewed Applications for Additional Active Ingredients and Determined More Data Needed*, the FDA relies on industry to submit the data needed to make the required safety and effectiveness determinations for each pending sunscreen active ingredient currently being evaluated under the SIA framework. In every case, the FDA has determined that the evidence supplied to date is insufficient to support a determination that the active ingredient is Generally Recognized as Safe and Effective (GRASE) for use in sunscreens.[124]

There is no backlog of pending sunscreen applications. The agency has identified current data gaps for each active ingredient being evaluated under the SIA framework and communicated them in proposed sunscreen orders and, when requested, granted meetings with active ingredient sponsors. To date, the agency has not received any additional data from manufacturers for any of the pending sunscreen ingredients that were the subject of SIA-required proposed sunscreen orders issued in 2015.

The FDA will continue to work with industry and public health stakeholders as it implements the SIA to help ensure that the sunscreens consumers use every day on themselves and their families are safe and effective for daily, life-long use.

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 in order to provide the opportunity for public comment.

[124] US Government Accountability Office (November 15, 2017). Retrieved November 15, 2017, from www.gao.gov/products/GAO-18-61.

25. 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:

In FY 2016, FDA's Center for Food Safety and Applied Nutrition (CFSAN) awarded an annual cooperative agreement to the Interstate Shellfish Sanitation Conference (ISSC) for $440,000. This cooperative agreement supported funding of state, academic, and shellfish industry studies to advance the science of Vibrio parahaemolyticus (Vp) through, among other things, improving risk assessment and identifying opportunities to develop and validate methods to detect virulent Vp strains. CFSAN funded this partnership in FY 2017 and will continue this funding in future fiscal years, subject to funding availability. The cooperative agreement helps fund research to assess the efficacy of various control strategies for reducing the risk of Vp illness associated with raw shellfish consumption, which FDA uses to inform its guidance to industry. Most recently the ISSC held a workshop to disseminate the latest practices that industry could use to minimize and mitigate risks associated with raw bivalve shellfish consumption.

FDA will continue to offer program assistance to states and industry for research and technical assistance aimed at improving the science and expanding and enhancing measures for the control of Vp in molluscan shellfish. FDA's Vibrio Assistance Review Board (VARB) reviews, prioritizes, and tracks submissions to FDA from State Shellfish Control Authorities (SSCA) and industry requesting Vibrio species-related research and technical assistance. To date, the VARB has supported joint FDA-SSCA projects, with industry participation in many cases, that generated data used to inform control practices for Vp. For example, a project established baseline levels of Vp to aid states in the determination of whether to allow the summer harvest of shellfish, such as in South Carolina, and in the understanding of Vp levels in a location associated with illnesses, such as in Massachusetts. The most recent joint FDA-SSCA project evaluates risk mitigation strategies that could be applied to typical aquaculture practices that could otherwise promote Vibrio species growth.

In addition, FDA will continue to work directly with the ISSC Vibrio Management Committee and the Centers for Disease Control and Prevention to examine the incidence of Vp illness as part of FDA and ISSC efforts to understand illness trends to aid in the adoption of improved controls into the National Shellfish Sanitation Program.

26. 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:

The Consolidated Appropriations Act, 2016, authorized $5,000,000 for FDA to complete a feasibility study to update and issue a revised Master Plan for land inside and contiguous to the White Oak campus to address its expanded workforce and the facilities needed to accommodate them.

FDA provided GSA with a $5,000,000 Reimbursable Work Authorization in 2016. Since then, GSA and FDA have collaborated and awarded contracts for development of an FDA Headquarters Housing Strategy/Migration Plan and a new Federal Research Center (FRC) Master Plan at White Oak. These documents, which are still under development, will address the feasibility of and options for accommodating FDA 's existing headquarters staff that have not yet been consolidated at White Oak, as well as FDA's growing headquarters staff on or near the FRC. Alternatives being considered as part of the effort include both additional federal construction and leasing office space in close proximity to the FRC to support Congress' intent to geographically consolidate FDA Headquarters.

FDA must depend on GSA to satisfy its office housing needs. GSA considered a partnership opportunity proposed by a non-Federal Government entity that provided a leasing option to enable the FDA to maintain very close proximity to its campus headquarters in White Oak, including space contiguous to the White Oak campus. In response to the proposal, GSA determined that FDA’s housing need first had to be documented through the process of developing the Housing Strategy/Migration Plan before the acquisition of space could occur. GSA also determined that FDA’s housing need required Congressional prospectus authority and, after Congressional approval, it would have to be satisfied through a competitive leasing process. Sufficient progress has been made on the development of the Housing Strategy/Migration Plan to provide the data needed for GSA and FDA to collaborate on a lease prospectus to be submitted for FY 2019 approval.

FDA SPECIFIC ITEMS

GEOGRAPHICAL DISTRIBUTION OF FDA FACILITIES

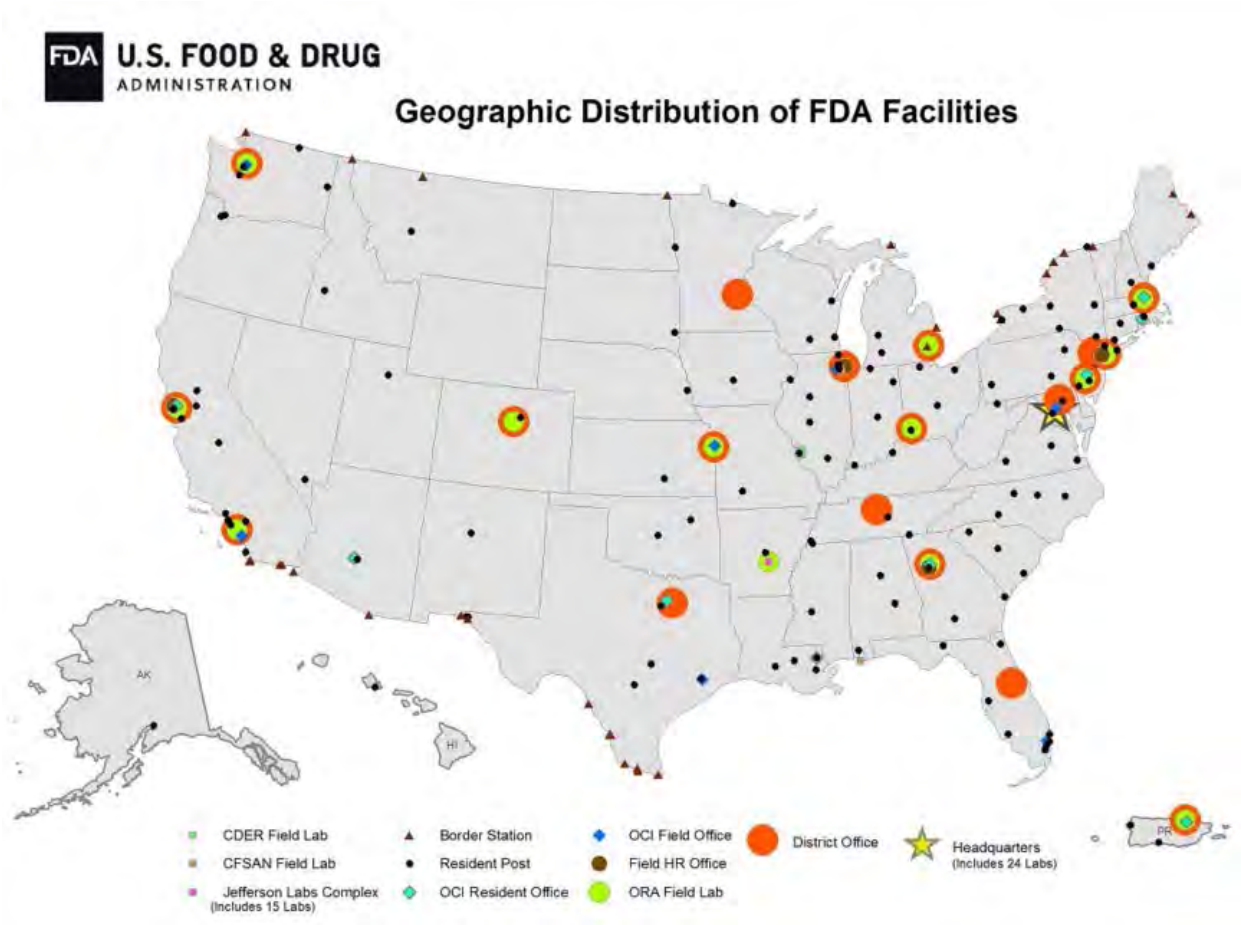

Figure 23 Geographical Distribution of FDA Facilities

HIV/AIDS FUNCTIONAL TABLE

	FY 2017 Actual	FY 2018 Estimate	FY 2019 Estimate
Human Drugs	25,749	25,749	25,749
Biologics	29,006	28,809	32,839
Medical Devices	309	309	309
Field Activity	34,320	34,980	35,640
Toxological	108	51	44
Other Activities	3,307	3,307	3,307
Total HIV/AIDS	**$92,799**	**$93,205**	**$97,888**

CROSSCUTS

(Dollars in Thousands)	FY 2017 Actual	FY 2018 Estimate	FY 2019 Estimate
Aging	**3,933**	**3,453**	**3,273**
Budget Authority (non-add)	*1,572*	*974*	*785*
AIDS/HIV	**92,799**	**93,205**	**97,888**
Budget Authority (non-add)	*92,799*	*93,205*	*97,888*
Alzheimer's	**6,206**	**5,450**	**5,344**
Budget Authority (non-add)	*3,939*	*3,093*	*2,979*
Antimicrobial Resistance	**44,776**	**42,819**	**47,809**
Budget Authority (non-add)	*42,054*	*40,135*	*45,125*
Asthma	**5,242**	**5,418**	**5,418**
Budget Authority (non-add)	*2,659*	*2,733*	*2,733*
Behavioral Health	**34,764**	**36,877**	**36,995**
Budget Authority (non-add)	*11,890*	*13,007*	*13,125*
Breast Cancer	**25,702**	**29,028**	**29,123**
Budget Authority (non-add)	*6,763*	*6,840*	*6,935*
Drug Abuse (Prescription)	**13,205**	**13,703**	**13,636**
Budget Authority (non-add)	*3,992*	*4,114*	*4,047*
Global Health	**157,051**	**164,867**	**176,880**
Budget Authority (non-add)	*90,557*	*89,066*	*99,150*
Immunization	**26,908**	**28,240**	**31,175**
Budget Authority (non-add)	*16,603*	*16,424*	*18,784*
Laboratory Safety	**12,262**	**12,192**	**12,576**
Budget Authority (non-add)	*12,095*	*12,109*	*12,451*
Mental Health	**18,791**	**19,942**	**19,942**
Budget Authority (non-add)	*6,751*	*7,358*	*7,358*
Methamphetamines	**467**	**489**	**489**
Budget Authority (non-add)	*293*	*307*	*307*
Minority Health	**2,683**	**3,033**	**2,983**
Budget Authority (non-add)	*2,620*	*2,979*	*2,929*
Opioids	**39,707**	**40,723**	**40,183**
Budget Authority (non-add)	*4,615*	*5,157*	*4,617*
Pandemic Influenza	**36,291**	**36,681**	**43,252**
Budget Authority (non-add)	*32,853*	*32,655*	*38,865*
Patient Safety	**435,847**	**441,186**	**571,491**
Budget Authority (non-add)	*183,790*	*179,918*	*300,371*
Pediatric Drugs	**11,502**	**13,665**	**13,594**
Budget Authority (non-add)	*3,714*	*5,403*	*5,268*
Prevention	**4,675,920**	**4,665,508**	**5,231,960**
Budget Authority (non-add)	*2,472,582*	*2,457,380*	*2,867,571*
Precision Medicine	**4,892**	**4,892**	**4,892**
Budget Authority (non-add)	*4,892*	*4,892*	*4,892*
Quality Improvement	**22,666**	**23,496**	**23,496**
Budget Authority (non-add)	*14,751*	*15,287*	*15,287*
Tobacco	**754,076**	**592,288**	**662,043**
Budget Authority (non-add)	---	---	---
Women's Health	**95,316**	**101,181**	**101,786**
Budget Authority (non-add)	*40,350*	*40,758*	*41,281*
Office of Women's Health (non-add)	*6,133*	*6,133*	*6,133*
Breast Cancer (MQSA) (non-add)	*24,884*	*28,422*	*28,623*

CENTRAL ACCOUNTS

Program (dollars in thousands)	FY 2017 Actuals		FY 2018 Estimates		FY 2019 Estimates	
	BA	UF	BA	UF	BA	UF
Foods	**16,892**	**00**	**16,024**	**00**	**16,572**	**00**
Center	5,425	-	5,246	-	5,351	-
Field	11,466	-	10,778	-	11,222	-
Human Drugs	**18,070**	**58,635**	**15,058**	**58,637**	**15,176**	**57,887**
Center	14,821	55,819	11,973	55,819	12,212	56,044
Field	3,249	2,817	3,085	2,818	2,964	1,844
Biologics	**5,411**	**7,580**	**4,907**	**7,580**	**4,992**	**8,037**
Center	4,455	6,709	4,005	6,709	4,085	6,739
Field	956	871	903	871	908	1,298
Animal Drugs and Feeds	**3,386**	**1,825**	**3,077**	**1,870**	**3,125**	**1,902**
Center	2,048	1,792	1,804	1,837	1,840	1,869
Field	1,338	33	1,273	33	1,285	34
Devices and Radiological Health	**7,800**	**8,348**	**7,125**	**8,348**	**7,248**	**8,912**
Center	5,698	8,223	5,139	8,223	5,242	8,257
Field	2,102	125	1,986	125	2,006	655
National Center for Toxicological Research	**852**	**-**	**807**	**-**	**824**	**-**
FDA Headquarters	**12,714**	**6,801**	**10,007**	**5,618**	**10,208**	**5,644**
Totals	**65,124**	**83,189**	**57,005**	**82,053**	**58,145**	**82,383**

HHS CHARGES AND ASSESSMENTS

Food and Drug Administration Department of Health and Human Services Charges and Assessments Fiscal Year 2017 Actuals	
Assessments:	**189,676**
NIH eRA Grants Management System Pilot phase to support migration of FDA Grants Data into the Department's consolidated eRA Grants Management System	186,602
Federal Audit Clearinghouse	3,074
Fee For Service:	**50,347,571**
Program Support Center/ Office of the Secretary Provides various services to the FDA, including some Information and Systems Management Services	**11,922,372**
Financial Management Portfolio (FMP)	681,653
Procurement Management Portfolio (PMP)	
Administrative Operations Portfolio (AOP)	8,501,139
Includes costs for security, building operations, shredding, storage, graphics, property disposal, trans-share, mail	
Real Estate and Logistics Portfolio Includes building operations, shredding, storage, property disposal,	2,739,579
Federal Occupational Health (FOH): FDA agency health units and services	**2,541,189**
Information & System Management Services	**28,335,746**
Freedom of Information (FOIA)	170,000
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 HCAS O&M services provide support for daily operations of the HCAS application.	2,228,402
Information Technology Infrastruction & Operations (ITIO) Telecommunications team offers expertise on Network / Telecomunnications / Security.	981,061
Department IT Management	3,457,585
Office of Enterprise Application Development (OEAD) 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	5,833,275
Office of Information Security (OIS) Includes computer security incident reponse center. Trusted Internet Connections and IT Security.	4,480,482

Food and Drug Administration Department of Health and Human Services Charges and Assessments Fiscal Year 2017 Actuals	
Office of Security and Strategic Information (OSSI) HSPD-12 System: FICAM Services, identity & logical access, etc. Badging Operations	4,688,943
Office of Human Resource Services Includes HR Center services teir I, payroll liaison, systems planning and implemenation	**7,548,264.17**
Jointly Funded Projects:	**$3,586,825**
International Health Bilateral Agreement 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	1,231,159
Other Jointly Funded Projects	**2,355,666**
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.	454,254
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	147,000
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 Agreement with NIH/OD to support costs associated with the negotiation of indirect cost rates with commercial organizations	38,000
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.	97,274
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
Biosafety and Biosecurity Coordinating Council This will support the administrative management of the Council in efforts to coordinate and collaborate on biosafety and biosecurity issues within HHS.	78,556
Implementation of the DATA Act (PMO) Responsible for leading implementation of the DATA Act within HHS.	416,663
Tick-Borne Disease Working Group Provide Congress a summary of ongoing tick-borne disease research related to causes, prevention, treatment, surveillance, diagnosis, diagnostics, duration of illness, and intervention for individual with tick-borne diseases and identify advances made and gaps that remain in such research.	-
Pain Management Interagency Task Force Supports the Secretary's priority to combat opioid abuse, and supports the HHS Mission and aligns with relevant objectives and strategies within the HHS Strategic Goals.	-

HHS CHARGES AND ASSESSMENTS: FY 2017 - FY 2019

Activity	FY 2017 Actual	FY 2018 Estimate	FY 2019 Estimate
Assessments	**$ 189,676**	**$ 195,000**	**$ 214,517**
Fee for Service	**$ 50,347,571**	**$ 62,660,699**	**$ 65,237,000**
Program Support Center/OS	$ 11,922,372	$ 15,406,922	$ 16,754,000
Federal Occupational Health	$ 2,541,189	$ 3,324,855	$ 3,405,000
Information System Management Service	$ 28,335,746	$ 36,288,950	$ 37,438,000
Human Resource Center – Rockville, Maryland	$ 7,548,264	$ 7,639,972	$ 7,640,000
Jointly Funded Services	**$ 3,586,825**	**$ 3,794,775**	**$ 3,673,336**
International Health - Bilateral Agreement	$ 1,231,159	$ 1,231,159	$ 1,231,159
Other Jointly Funded Projects	$ 2,355,666	$ 2,563,616	$ 2,442,177
Total	**$ 54,124,072**	**$ 66,650,474**	**$ 69,124,853**

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GLOSSARY

ACRONYMS

ACOG	American College of Obstetricians and Gynecologists
ADF	Animal Drugs and Feeds
ADHD	Attention Deficit Hyperactivity Disorder
ADUFA	Animal Drug User Fee Act
AFRPS	Animal Feed Regulatory Program Standards
AGDUFA	Animal Generic Drugs User Fee Act
AMP	Asset Management Plan
AMR	Antimicrobial Resistance
ANA	Association of National Advertisers
ANDA	Abbreviated New Drug Application
ANPRM	Advance Notice of Proposed Rulemaking
APAP	Center for Drug Evaluation and Research
APQ	Aggregate Production Quota
BIMO	Bioresearch Monitoring Program
BMAR	Backlog of Maintenance and Repair
BPD	Biosimilar Product Development
CAERS	CFSAN Adverse Event Reporting System
CAP	Cooperative Agreement Program
CARA	Comprehensive Addiction and Recovery Act
CASEL	Collaborative for Academic, Social, and Emotional Learning
CBER	Center for Biologics Evaluation and Research
CBP	Customs and Border Protection
CBRN	Chemical, Biological, Radiological and Nuclear
CCFICS	Codex Committee on Food Import an Export Inspection and Certification Systems
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
CDRH	Center for Devices and Radiological Health
CECTR	Coordination of Training and Research
CFSAN	Center for Food Safety and Applied Nutrition

CGM	Continuous Glucose Monitoring
CMD	Congenital Muscular Dystrophy
COE	Center of Excellence
CORE	Coordinated Outbreak Response and Evaluation
CSI	China Safety Initiative
CTP	Center for Tobacco Products
CUP	Central Utility Plant
CVM	Center for Veterinary Medicine
DAC	Data Analytics Commons
DFL	Drug Facts labeling
DHHS	Department of Health and Human Services
DOX	Center for Drug Evaluation and Research
DQSA	Drug Quality and Security Act
DSCSA	Drug Supply Chain Security Act
EAP	Expedited Access Pathway
EMA	European Medicines Agency
EPA	Environmental Protection Agency
EQUIP	Enhancing Quality Using the Inspection Program
EUA	Emergency Use Authorization
FACA	Federal Advisory Committee Act
FAERS	FDA Adverse Event Reporting Systems
FARA	Friedreich's Ataxia Research Alliance
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act
FDAMA	Food and Drug Administration Modernization Act of 1997
FDARA	Food and Drug Administration Reauthorization Act of 2017
FDASIA	Food and Drug Administration Safety and Innovation Act of 2012
FERN	Food Emergency Response Network
FRC	Federal Research Center
FSMA	Food Safety Modernization Act
FSPB	Food Safety Plan Builder
FSVP	Foreign Supplier Verification Programs

FVM	Foods and Veterinary Medicine
GAO	Government Accountability Office
GDUFA	Generic Drug User Fee Act
GFI	Guidance for Industry
GIS	Geographic Information Systems
GMP	Good Manufacturing Practices
GRAS	Generally Recognized as Safe
GRASE	Generally Recognized as Safe and Effective
GSA	General Services Administration
GUDID	Global Unique Device Identification Database
HAE	Hereditary Angioedema
HDE	Humanitarian Device Exemption
HUD	Humanitarian Use Device
IAEA	International Atomic Energy Agency
ICCR	International Cooperation on Cosmetics Regulation
ICH	International Conference on Harmonisation
ICRP	International Commission on Radiological Protection
IFSAC	Interagency Food Safety Analytics Collaboration
IFSS	Integrated Food Safety System
IMEDS	Innovation in Medical Evidence and Development Surveillance
IQA	Integrated Quality Assessment
ISO	International Organization for Standardization
ITACS	Industry Trade Auxiliary System
JLC	Jefferson Labs Complex
KASA	Knowledge-aided Assessment & Structured Application
KCCQ	Kansas City Cardiomyopathy Questionnaire
LACF	Low-Acid Canned Foods
LSBC	Laboratory Complex
MDDT	Medical Device Development Tools
MDIC	Medical Device Innovation Consortium
MDSAP	Medical Device Single Audit Program
MFRPS	Manufactured Food Regulatory Program Standards

MQSA	Mammography Quality Standards Act
MRA	Mutual Recognition Agreement
MRTPA	Modified Risk Tobacco Product Application
MUMS	Minor Use Minor Species
NABP	National Association of Boards of Pharmacy
NARMS	National Antimicrobial Resistance Monitoring
NCBI	National Center for Biotechnology Information
NCI	National Cancer Institute
NCNPR	Natural Products Research
NCRP	National Council on Radiation Protection and Measurements
NCTR	National Center for Toxicological Research
NEF	Non-recurring Expense Fund
NEMA	National Electrical Manufacturers Association
NEST	National Evaluation System for health Technology
NEXT	Nationwide Evaluation of X-ray Trends
NFL	Nutrition Facts Label
NFSDX	National Food Safety Data Exchange
NIAID	National Institute of Allergy and Infectious Disease
NIH	National Institutes of Health
NIPP	New Inspection Protocol Project
NLEA	Nutrition Labeling and Education Act
NNN	N-nitrosonornicotine
NNP	Neuroprosthesis
NYTS	National Youth Tobacco Survey
OCAC	Office of Colors and Cosmetics
OCE	Oncology Center of Excellence
OCI	Office of Criminal Investigations
ODA	Orphan Drug Act
OFVM	Office of Foods and Veterinary Medicine
OLSS	Office of Laboratory Science and Safety
OOS	Out of Specification
ORA	Office of Regulatory Affairs

OTC	Over-the-Counter
OWH	Office of Women's Health
PAC	Pediatric Advisory Committee
PAD	Program Activity Data
PASE	Professional Affairs and Stakeholder Engagement
PATH	Population Assessment of Tobacco and Health
PCAC	Pharmacy Compounding Advisory Committee
PCAF	Preventive Controls for Animal Food
PDMA	Prescription Drug Marketing Act
PDUFA	Prescription Drug User Fee Act
PEAC	Patient Engagement Advisory Committee
PFDDI	Patient Focused Drug Development Initiative
PHEIC	Public Health Emergency of International Concern
PHEMCE	Public Health Emergency Medical Countermeasures Enterprise
PMA	Premarket Approval
PREA	Pediatric Research Equity Act
PREDICT	Predictive Risk-based Evaluation for Dynamic Import Compliance Targeting
PRV	Priority Review Voucher
PSA	Produce Safety Alliance
PSP	Produce Safety
RASFF	Rapid Alert System for Food and Feed
RCC	Regulatory Cooperation Council
REMS	Risk Evaluation and Mitigation Strategy
RFI	Request for Information
RMAT	Regenerative Advanced Medicine Therapy
SCORE	Strategic Coordinated Oversight of Recall Execution
SECG	Small Entity Compliance Guide
SIA	Sunscreen Innovation Act
SIR	Society of Interventional Radiology
SRD	Swine Respiratory Disorder
STEC	Shiga toxin-producing Escherichia coli
TAN	Technical Assistance Network

TCA	Tobacco Control Act
TCORS	Tobacco Centers of Regulatory Science
TTIMS	Transmissible Infections Monitoring System
UDI	Unique Device Identification
UESC	Utility Energy Service Contract
UMMC	University of Mississippi Medical Center
USDHHS	Advance Notice of Proposed Rulemaking
USP	United States Pharmacopeia
USPS	United States Postal Service
VARB	Vibrio Assistance Review Board
VNRFRPS	Voluntary National Retail Food Regulatory Program Standards
VQIP	Voluntary Qualified Importer Program
VRBPAC	Vaccines and Related Biological Products Advisory Committee
WCF	Working Capital Fund
WEAC	Winchester Engineering and Analytical Center
WHO	World Health Organization

TABLES

All-Purpose Table	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.

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.